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THE ULTRASTRUCTURE OF GAP JUNCTIONS BETWEEN LEYDIG CELLS UNDER THE EFFECT OF D ETILSTILBESTEROL

Belgin Can* **Cengiz Güven**** **Yüksel Saran*****

SUMMARY

Estrogen treatment inhibits testosterone synthesis. In this study the ultrastructural effects of dietilstilbesterol (DES) application on Leydig cells were studied on 30 male Wistar type rats. After the administration of estrogen, instead of typical Leydig cells immature dedifferentiated Leydig cells were seen in the majority. Intercellular spaces were expanded and the gap junctions were rarely seen. These findings were in conformity with the previous data and observations.

Key words: *Estrogen, Gap junction, Leydig cell.*

Leydig cells have an exceptional situation among the cell categories of the testis. They have an endocrine function regulated by gonadotropins of the pituitary gland (8). They are responsible for testosterone release. The administration of estrogens causes a decrease in serum testosterone levels and this decrease has been attributed to a direct effect on the Leydig cells and an indirect effect by suppression of gonadotropins (3,4,7,8,9).

In this study the ultrastructure of gap junctions between Leydig cells under the effect of dietilstibesterol is investigated. Gap junctions coordinate metabolic, hormonal, and physiological processes in a wide variety of tissues in vertebrates (1). Many of the treatments are known to influence gap functional communications in various tissues (2). Although immunohistochemical methods are more sensitive than electronmicroscopy in detecting gap junctions (5), the aim of this study is to show the ultrastructural changes that correlate well with the endocrine status.

MATERIALS AND METHODS

A total of 30 (10 for control and 20 for the study group) Wistar type male rats were used. The study group was given 0.25 mg/per rat dose dietilstilbesterol every other day subcutaneously for 2 months and the control group was injected serum physiologic simultaneously.

After ether anesthesia testes were taken from the rats and fixed at 0 °C for 1 hour in a phosphate buffered 2% glutaraldehyde and then postfixed in 1% OsO4 for approximately 2 hours. After alcohol dehydration the samples were embedded in Araldite CY-212. Sections were cut on a LKB Ultratome III with a glass knife, stained with uranly acetate and lead citrate and viewed on a Jeol 100 Electronmicroscope.

RESULTS

In the control group large gap junctional areas were frequently observed on the cell membranes (Figure 1). After estrogen therapy Leydig cells displayed no uniform morpholical appearance, the typical leydig cells were rarely seen. Instead, there were clusters of immature small cells in which decreased smooth endoplasmic reticulum, lipid droplets, osmiophilic inclusions enclosed by filamentous material and lobulated irregularly shaped

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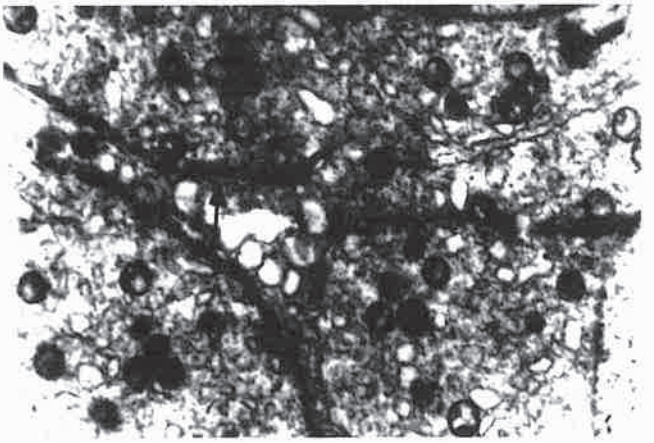

Figure 1: Control group. Gap jucntions (arrow), X 7200.

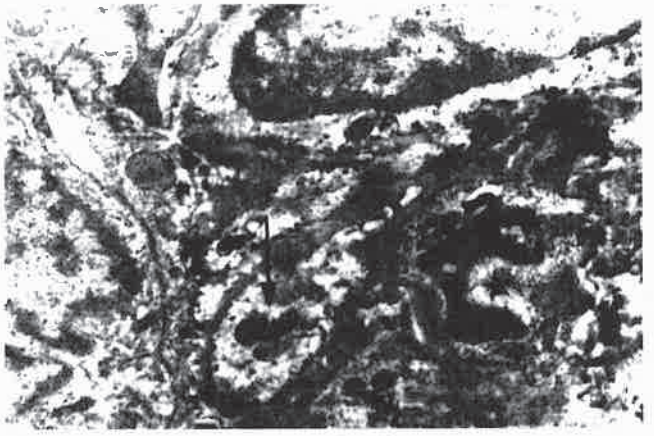

Figure 2: Experimental group. Leydig cell population from testis displays no uniform morphology. Leydig cell with altered cell morpology that have lobulated nucleus.* containing electron dense inclusions (arrow); X 7200.

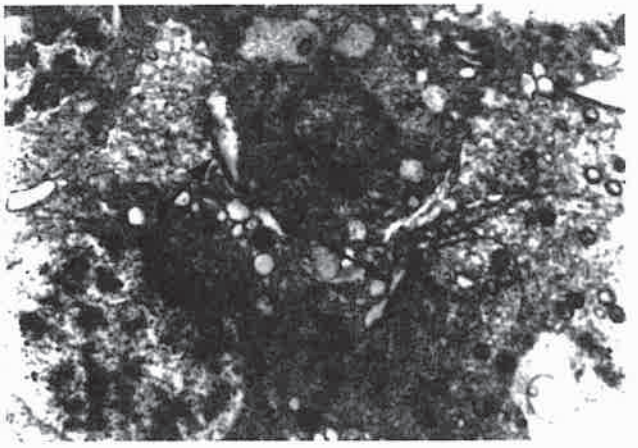

Figure 3: Experimental group. Leydig cells are joined by gap junction like connections (arrow); X 3600.

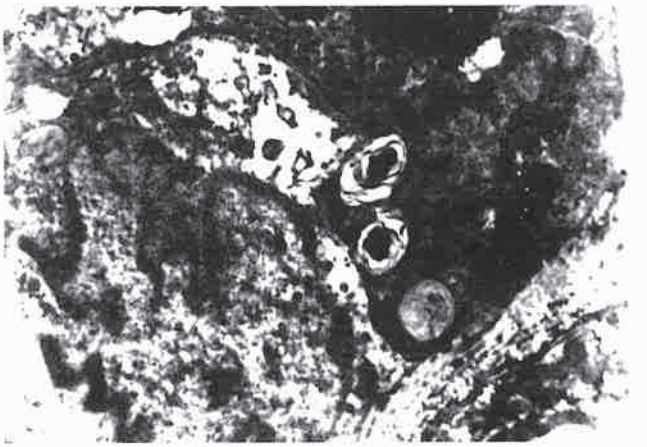

Figure 4: Experimental group. Leydig cells exhibiting lobulated nuclei (arrow) and osmiophilic inclusions enclosed by filamentous material (arrow head). X 7200.

Figure 5: Experimental group. Leydig cells possess a well-defined polygonal cell body. Gap junction (arrow head). Widened intercelluar space (star). Splited gap junctional area and dense membranous appearance (arrow); X 7200.

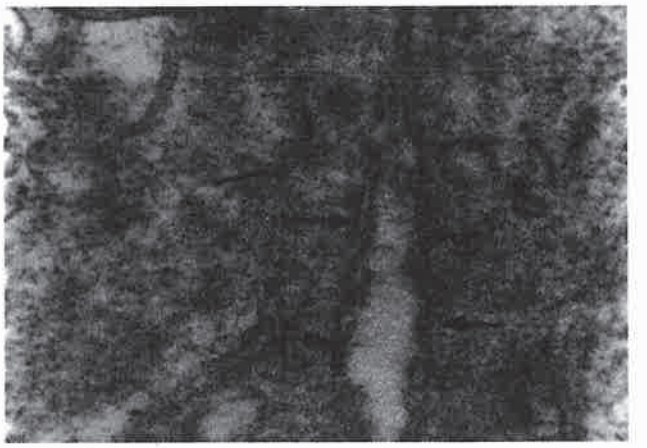

Figure 6: Experimental group. Expansion of the intercellular space (arrow); X 48000.

nuclei were present (Figure 2,3,4). The gap junctions of the affected cells were rare than the control cells. Some of the Leydig cells possesed a well-defined polygonal cell body, widened intercellular space, splited gap junctional area and dense membranous appearance (Figure 5,6).

DISCUSSION

A remarkable feature of the testis after administration of estrogens is the absence of typical Leydig cells as they transform into immature cells (9).

Exogenous estrogens inhibit the production of androgens through a direct influence on the Leydig cells and by the supression of gonadotropins (3,4,7,8,9). In the recent years there has been some evidence that gap junctions carry signals that regulate hormone secretion (6). Gap junctions in various tissues may be affected by a variety of treatments (2).

In our study under the effect of two-months estrogen treatment the typical Leydig cells were uncommon and the gap junctions that were seen numerously between control group Leydig cells were turned out to be rare. We support the previous results that as a result of estrogen administration there might be not only ultra structural changes in the Leydig cells but also functional defects in the stages of testosterone synthesis. Although Leydig cells have the ability to form clusters and to establish contacts in the form of gap junctions, in convenience with their dedifferentiation and degeneration they become smaller and this results in an expansion of the intercellular space. For this reason gap junctions might be decreasing.

In conclusion, after estrogen treatment, mature Leydig cells presumably dedifferentiate into immature cells and gap junctions between Leydig cells may be also affected because of the functional and structural disturbance.

REFERENCES

1) Bohrmann J et al: Gap junctions in ovarian follicles of Drosophila melanogaster inhibition and promotion of dye-coupling between oocyte and follicle cells. Cell-Tiss. Res. 273: 163-173, 1993.

2) Dermietzel R et al: The gap junctions family, structure, function and chemistry. Anat. Embryol 182: 517,518, 1990.

3) Jones TM et al: Direct inhibition of Leydig cell function by estradiol. J. Clin Endocrinol. Metab. 47: 1368-1373, 1978.

4) Kalla NR et al: Effect of estradiol on testicular testosterone biosynthesis. Endocrinology 106: 35-39, 1980.

5) Mikkelsen HB et al: Immunohistochemical localization of a gap junction protein in the muscularis externa of murine, canine and human intestine. Cell Tis., Res. 274: 249-256, 1993.

6) Perez EM et al: Characterisation of gap junctions between pairs of Leydig cells from mouse testis. Am J Physiol 267: 570-580, 1994.

7) Rodriguez-Rigau LJ et al: In vitro steroid metabolic studies in human testes. Steroids 29: 771-787, 1977.

8) Schulze C: Sertoli cells and Leydig cells in men. Embryology and Cell Biology 88: 1-56, 1984.

9) Schulze C: Response of the human testis to long-term estrogen treatment. Cell Tissue Res. 251: 31-43, 1988.

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GROUP PSYCHOTHERAPY WITH DELAYED TURKISH ADOLESCENTS*

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Gülsün Yavuzcan*** • Bedriye Öncü***

SUMMARY

This paper evaluates the group psychotherapy process of 8 delayed adolescents whose ages differ from 18 to 24, in a multidensional way. The group consisted of 2 males and 6 females and one male psychotherapist. Each week, the group process was observed by a team of 7 psychiatry residents for 6 months. The principles of dynamically oriented interactional group psyhotherapy were employed. Although the majority of the participants showed neurotic symptoms, it was observed that basically they had problems of separation from their families and establishing a stable identity. Some caharacteristics of the Turkish society and family life are discussed with relevance to symptom formation in these adolescents. The way how hese problems were handled in the group therapy sessions are discussed, with a particular emphasis on the importance of an eclectic stance on the side of the therapist.

Key Words: *Group Psychotherapy, Turkish Culture, Adolescence.*

Adolescence is a period between childhood and adulthood, where new developments occur, and as a result, different treatment approaches are needed for any psychological problem. Certain characteristics of the adolescent who is in a continous interaction with his social and physical environment, as well as some aspects of his family and the society in which he lives, play a role in the symptom formation. Since it is almost impossible to find the exact cause of a symtom, it would be wise to say that an eclectic and integrative approach which tries to cover all the problem areas may be the most pragmatic one.

In this paper, the group psychotherapy process of eight late adolescents, whom we preferred calling "delayed" adolescents for they were still struggling for separation and individuation problems beyond the age of eighteen, is discussed. The discussion included how the society, the families and the nature of adolescence itself interact and the way they were handled in the therapy process.

SEPARATION INDIVIDUATION IN TURKISH ADOLESCENTS

Mahler (13) stated that; the beninning of walking in the infancy is one of the first steps of separation and individuation. However, the emotional attachment continues until the adolescence period. According to her, the adolescent must get free from the infantile object bonds in order to become a member of the adult world. Blos (3), in his influential paper named this process as the "secondary individuation". The adolescent must succeed in his emotional separation from the objects which he internalized in his infancy in order to form a more stable personality. This process is a struggle for existence and development, at the same time it is fundamental in his identity formation (4, 12).

Separation and individuation grossly begins at adolescence, but when and how it will end varies from person to person. Since it is a separation from the long carried objects, a mourning period follows,

* This article was presented as a free communication on July 1992, at the 2nd International Congress of Eclectic Psychotherapy, Lyonnes, France.

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just like other loss experiences. At the same time, departure form the safe and protective setting of the childhood is another source of anxiety by itself. According to Berkowitz (1), the responce given by the family to the separation attempts of the adolescent, is also determinative on how this process will end. It is not uncommon for the family to try to interrupt this process, either implicitly or explicitly. From direct prohibitions, to subtle maneuvers that increase his dependency or guilt, a wide range of techniques may be used by the family, consciously or not.

Whatever the reasons are, any problem in the separation-individuation process may result in psychological problems and sometimes leave the adolescent passive dependent, as a child. Acording to Blos (3), the failure in separation from the infantile objects may reveal itself as ego problems, like; acting-out problems, learning disabilities, lack of initiative and negativism. Considering the process a mouming, if the adolescent has intensive ambivalence toward his family, the symptoms may further vary and be complicated (6).

Some aspects of the Turkish society also enhance the problems of individuation in adolescents. Although Turkey is progressing quite rapidly and the number of nuclear families is increasing day by day, Turkish society still has a large traditional population which retains many of its value systems and patterns of living, along with strong and wide family ties. The child is an important and valued part of the Turkish family. The boys are still valued more as a source of future economic support and security, plus they are supposed to promote the family name and increase the status of the mother and the family in his birth. There are no such expectations from the girls but to keep their virginity safe until they marry, thus not to bring a bad reputation to the family.

While the parents pay a lot of attention to the education of their children, they encourage dependency, conformity, submissiveness and passivity, instead of autonomy, self sufficiency, self control, creativity and initiative (10). The expectation of obedience, dependency and loss of one's own identity in relation to authority figures also show a similarity to old age security needs of the parents (11, 18). Independence of a growing child is not functional and may even be a threat to the livelihood of the family, since independent offspring may look after their own self interest rather than of the family origin. In urban areas, where education level and economic staus is much better, compared to rural areas, western features of social life and values are more or less established, but some traditional family characteristics, particularly the intergeneration dependencies, have been retained. Therefore, it is difficult to locate and define the existence of clear-cut traditional or modern groups (18,19,21). Özbek and Volkan (17), named these pseudo-modern, semi-traditional families as "satellite-extended". These families represent the majority of Turkish families. The term, satellite, was originally coined by Volkan and Corney (20) to describe a developmental compromise, a stable fixation in a psychological orbit around the central figure from whose representation the individual fails to separate and achieve true individuality. In a developmental sequence, the satellite state lies between a symbiotic relationship with the mother's representation and the ability to live intrapsychically apart from it without loss of identity. These families may react loosening of its ties with rage. The same writers also claim that, this problem is especially evident in girls, who, as a result, pause their separation individuation process by adopting their parents' values and laws, in another word by making foreclosure.

So, despite all the progress Turkey has achieved in recent years, it still has a great traditional population that makes adolescents' separation individuation process more difficult to solve. Both the rapid changes in society and the retaining of some traditional aspects, cause some problems when they attempt to form a steady identity (21). Now, a group therapy process of some adolescents, who became symptomatic because of issues mentioned above will be presented.

GROUP PSYCHOTHERAPY

The group was consisted of 8 people, 2 males and 6 females, all between 18-22 years old. All of them were outpatient clients and prior to our group therapy sessions, 3 of them had been hospitalized in the psycho neurotic disorders ward of the same hospital. After the detailed etiological questioning, it became obvious that all the patients, though varied in descriptive diagnosis (e.g. Obsesssive Compulsive Disorder [OCD], Anorexia Nervosa), had problems of separation from their families and various degrees of identity confusion.

The patients were included in a program of analytically oriented, interactional group therapy which was performed once a week for a period of six months. During this period no additional individual psychotherapy or pharmacotherapy was employed, except for one patient who took clomipramine for his OCD. Again, no formal family therapy was performed, while some of the families were consulted when necessary. The sessions were directed by an experienced male therapist and a session was limited by one hour. Following every session, which was observed by a team of 7 psychiatry residents, a discussion on the process for about 45 minutes took place.

DISCUSSION

It was not a coincidence to choose group psychotherapy as the therapy modality. It is already known that group psychotherapy has some advantages over individual psychotherapy when performed with the adolescents: Peer relations have a valued place for the adolecent who struggles to separate from his family. As the ties with his family loosen, he feels himself lonely and empty, fears of isolation and separation anxiety begins. At his period, friends become the new objects whom he can rely on (5). Berzonsky (2) named this situation as "resatellization". According to him, when the adolescent begins to separate from his family (desatellization process), he tries to make it easier by using peer relations. So, it is not unexpected for the adolescent to prefer group psychotherapy, where he can find some new friends. Additionally, it is evident that the adolescent, who tries to come over the pain of separation, devaluates the adults and as a result he can accept feedback coming from his peers more easily than form his individual adult therapist (9).

Although this was an analytically oriented group, the traditional interactional group phenomena based on interpersonal relations were used frequently. It is known that a rigid analytical orientation on the side of therapist might induce regression and thus pause the progress of the group (16). Besides, in this period the adolescent is mournful for the old objects and in search of the new ones which makes it harder to invest his libido to the therapist (8). As a result, the therapeutic relationship can become difficult to proceed, as can be seen by the increasing number of missing sessions. Odağ et al (16) particulary stressed that, the therapists who would deal with the adolescents had to be more flexible and patient.

During the process, several positive and negative aspects of an adolescent group were observed. Perceived not only an extension of the adult world, but also a representative of the father, the therapist faced with unwillingness to self disclosure and long silences in the first sessions. Even, they sometimes tried to devaluate the therapist. Here, the therapist's approach became similar to what Winnicott (22) mentioned long before; trying to create a "holding environment". He tried to accept and "survive" as Winnicott pointed, the instinctual assaults of the adolescents, without responding by retaliation or withdrawal. Such an approach provides the adolescent a different emotional experience. The therapist also tried to sustain as an identification object, who not only accepts them unconditionally, but also tries to keeps his neutrality in the face of their over-idealizations and devaluations. We can speculate that, with this neutral approach, the melting and integration of the aggressive and libidinal feelings could be achieved. This approach provided them a "new object", by which they had the opportunity to solve their separation-individuation problem smoothly in a healthy, universal manner. Here, "new object" does not mean solely a new person never met before, but rather, the novel experiences lived with him is what is meant. Such experiences have the power to open the obstructed developmental channels (7).

Limit testing by confrontation with the therapist was also observed in the group and it was reported as a common phenomenon of adolescent groups by numerous writers (14). One can speculate that it represents not only testing his limits, but also his therapist's limits too. Other common phenomena of the adolescent groups observed in our group include; setting up sub-groups to reduce group tension, using intellectualizations very often, giving direct advises and causing long silences, etc. We all observed such characteristics in the 20 weeks of the therapy.

The approach of the therapist became, providing process commentary in the here and now context. This was done in the light of psychodynamic rules, like monitoring transference and countertransference issues constantly.Given the characteristics of our culture and group, the therapist tried to become more active in the group, while paying

attention not to be misperceived as a domineering teacher or father.

In the beginning the therapist was perceived as an authority figure, like the representative of the father, and as a result they related to him in a distant manner. But as the group proceeded, he became a discussible and critizable authority figure and they felt closer to him. Following the group, some of the patients reported better relations with the authority figures, outside the group setting, which may implicate that their ego strenghts improved. This went parallel to their use of more mature defenses and the elevations in self-esteem.

In the first few sessions two girls dropped-out of the group. This 25% range is not unexpected for the adolescents who are infamous with their unfinished therapies (15). This group provided them a priceless emotioanal eperience with its interpersonal matrix. It also consisted an authority figure, the therapist, who represented one of the major conflictual persons in their life, namely the father. The adolescents, without being aware of it consciously or even gaining deep insights, lived almost the same separation-individuation problems with the therapist but this time without traumas, in a constructive way. In the termination stage both the clients and the team experienced grief and separation, so the adolescents recognized that it was a tolerable emotion. It could be speculated that, this recognition might have opened the doors of tolerance of ambivalence and accept their parents as a whole, and perceive them more realistically. Post session follow-up seemed positive and they still express the relief of feeling as an individual and not feeling guilty or scared.

CONCLUSION

Here, the process of group psychotherapy conducted with delayed adolescents is presented with a particular emphasis on the separation-individuation process of Turkish adolescents. It could be concluded that; group psychotherapy can be a powerful therapeutic instrument in dealing with adolescent problems and especially with separation-individuation problems which is generally provoked by the society.

REFERENCES

1. Berkowitz DA (1979) The disturbed adolescent and his family problems of individuation. J of Adolesc 2, 27-39.
2. Berzonsky MD (1981) Adolescent Development. McMillan Pub., New York. 299-302.
3. Blos P (1967) The second individuation process of adolescence. The Psychoanalytical Study of the Child. 22, 162-186, International Universities Press, New York.
4. Canat S (1988) The effect of family structure on separation-individuation process of the adolescents. Presented in the 14th National Psychiatry and Neurological Sciences Congress, Ankara.
5. Çevik A (1986) Liminality, developmental regression and cigarette smoking in the adolescents. Nöroloji, nörosirurji, Psikiyatri Dergisi. Vol 2; 1; 15-16.
6. Çevik A, Ceyhun B (1993) Psycho-political overview of the youth. (In print).
7. Çevik A, Söylemezoğlu Ü (1993) Minimal Need Frustrations. GATA Bülteni, 27, 435-443.
8. Freud A (1958) Adolescence. The psychoanalytical study of the child. 13, 255-278. International Unversities Press, New York.
9. Hill P (1989) Adolescent Psychiatry. Eds. Paykel E.S., Morgan G.H. Churchill Livingstone, London.
10. Kağıtçıbaşı Ç (1989) Cross-cultural psychology: current rch and trends. Annual Review of psychology. Alto CA.
11. Kağıtçıbaşı Ç (1990) Family and socialization in cross cultural perspective. Nebraska Symposium on Motivation, Vol 37, Univ of Nebraska Press, Lincoln.
12. Karpel M (1976) From fusion to dialogue. Family Process, 15, 65-82.
13. Mahler M (1963) Thoughts about development and individuation. The Psychoanalytic Study of the Child. 18, 307-324. International Universities Press, New York.
14. McLennan BW, Fensenfeld N (1968) Group Counseling and Psychotherapy with the Adolescnts. Columbia Univ Press, New York.
15. li 8) de to hi T ap
16. C H, r E (1 S basic principles of the adolescents. Tıp Dünyası. Vol 51, 378-385.
17. Özbek A, Volkan VA (1976) Psychiatric problems within the satellite extended families of Turkey. Am J Psychtherapy, 30; 577.
18. Öztürk MO (1991) Psychotherapy and Cultural Sensitivity. Paper presented at teh International Symposium on Cultural Psychiatry, Budapest, Hungary.
19. Timur S (1972) Family Structure In Turkey. Hacettepe Üniv Press, Ankara, 87-95.
20. Volkan VA, Comey R T (1968) Some considerations of satellite states and satellite dreams. Brit J of Med Psychol, 41, 283-290.
21. Volkan VA, Çevik A (1989) Fathers and their families. Eds. Cath S H, Gurwitt A, 347-364, The analytic Press, Hilsdale New Jersey.
22. Winnicott DW (1960) The theory of the parent infant relationship. International J of Psychoanalysis. 41, 585-594.

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GROUP PSYCHOTHERAPY, AS A PART OF A REHABILITAT ON PROGRAM WITH CHRON C PSYCHOTICS IN TURKEY*

Gülören Ünlüoğlu** • Aykut Özden*** • Çiğdem Soykan****

SUMMARY

Rehabilitation is clearly a major part of the treatment of chronic psychotic patients because of the rather deteriorating and debilitating nature of the illness. There are various rehabilitation programs throughout the world, using diverse modalities. Here, in Psychiatry Clinic of University of Ankara, we have a rehabilitation program in the form of a Day Hospital, where patients attend for about 7 months and then followed with group psychotherapy. In this paper, we want to share our experiences on this program with a particular emphasis on the group therapy process.

Key Words: *Rehabilitation, Chronic mental İllness, Group Psychotherapy, Day Hospital.*

It is well known that, psychotic disorders go on with periods of relapses and remissions. With the help of ever developing psychopharmacological strategies, one can hopefully reduce the rate of relapses and even the intensity of infamous "negative symptoms". Stemming from the medical model of the diseases, such results encouraged many clinicians that, one day, the "almighty antipsychotic drug" would come and heal them all. This raises the question; Are we waiting for Godot?

Not one single drug treatment has "cured" all of the pervasive problems of these patients yet, and we are afraid neither will do. Psychosis, with its chronic debilitating, stigmatizing and deteriorating effects need more aid, than a single pill. Patinets' self-esteem, self confidence, initiative, social compentence and relations, quality of life, and even self care, to count among a lot, all are affected in this disorder, someway or another.

This realization, decades ago, brought in some other treatment modalities, under the topic of "rehabilitation". Rehabilitation programs today, include as many diverse approaches as there are rehabilitation centers (2). Probably, the most preferred one is the day hospital approach, in which the patient receives various treatment modalities, while staying in his/her own environment. Here, we would like to present the rehabilitation program of our hospital, with a particular emphasis on the group psychotherapy process, that patients attend after they complete their day hospital program.

THE REHABILITATION PROGRAM

Psychiatry Clinic of University of Ankara, is located in a big metropalitan area with a seperate building from the main University Hospital. There are several inpatient departments and one outpatient unit. Various psychotherapy modalities, mostly individual and group therapies, has long been used. Patients mainly come from Ankara, where the clinic is located and generally, the cost of treatment is covered by the social security system of the govermment. Every year, we see approximately, 16000 patients (most of them are follow ups) in the outpatient unit and 600 a patients in the inpatient units. Usually, when a patient is dicharged from the inpatient unit, he/she is given an appointment for follow up. We believe that, this follow up procedure is

* This paper is presented at the 2nd International Congress on Psychiatric Rehabilitation, on June 1995, Barcelona.

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somewhat insufficient, especially for the chronic psychotic patients. Given the high number of patients and inappropriatly low number of doctors (15-16), a doctor can only give 15-20 minutes to such a patient, once a month or two! As a matter of fact, one can only write a prescription and "talk about" one or two very immediate problems of the patient... shortly.

In 1988, on realizing the urgent need for a rehabilitation program, we began our day hospital program (11), with two psychiatrists (one professor, head of the team and one resident), one clinical psychologist and two nurses. A social worker, also helped the team when needed. The program consisted of group psychotherapy (twice a week), individual psychotherapy (once a week), occupation therapy, music therapy, family meetings, discussion hours, psyhoeducation, social hours, outside facilities - going on picnics, museums and movies etc. And of course, drug therapy and education on drug maintenance. The program lasts about 8 months, between October and May and patients attend on week days, between 8:15 and 16:00 hours. We prefer to accept about 12-14 patients to our yearly program. The patients are refferred from inpatient and oupatient units.

In 1992 with growing experience, we as members of the therapy team, changed the name of our program from Day Hospital to Day Club, and launched into a very structured, token economy system, which was used by other clinicians perfectly, for a long time (6). On the other hand, we also witnessed the need for a post-rehabilitation activity, specially for the most withdrawn, troubled and unemplyoed patients. After a successful rehabilitation program, it was obvious that most of the patients could be reintegrated back into their social lifes, bu with some patients, it is quite unlikely to reach this point with a 7-months-therapy. although some problems could be solved and various ones could be covered successfully, some problems never die... so do solutions. Therefore, we decided to follow up some of our selected patients with the use of group therapy sessions.

GROUP PSYHOTHERAPY APPROACH

Group psychotherapy, has long been in the arsenal of psychiatry. When used properly, it is of great benefit both for the patients and the clinicians (10). For the clinician, it is indeed practical and cost-effective to reach 10-12 patients at the same time and place, not only having personal interaction, but also having the chance of close observation of their interpersonal interactions. Its benefit on the patients is known, for decades, by clinical observations and empirical researches made both in Turkey and abroad (8, 9, 12, 15).

Group therapies are also performed with chronic psychotics for decades (9,13) and its role on rehabilitation is noted by several authors (3,4,10).

Group therapy is not only a process of receiving treatment, but also a chance to socialize and stay socialized for the patients. Imagine a patient with long history of schizophrenia, living in a two-room-house, with his/her parent(s), day after day, and then take him/her to a place, where he/she could express feelings and thoughts, listen to others' coping mechanisms with the same problems and thus, make friends with whom she/he could drink a coffee or two afterwards.

THE PATIENTS

In the Fall of 1992, we started our follow up group therapy sessions, on a weekly basis. At present it is still continuing. The group starts at 13:15 and ends at 14:00 approximately, ever Wednesday. In the beginning, 11 patients (members) who had completed theri last Day Club program, were offered to join the follow up group therapy sessions. Four ot them left the group, after two years. One of them, a male patient who was employed by the department of post office, started working and felt that he did not need group therapy anymore. He was a relatively high functioning, delusional disoder patient with somewhat less cohesion to the group. Later on, another male dropped out without an obivous reason (who also had an Axis II personality disorder, which prevented his gains from the group because of frictions between fellow members and sometimes therapists). The other two patients were females, who left the group since they had to move out of town. One of them moved because she found a job and the other left because her husband was a police officer and he was assigned to a mandatory duty in South East Turkey. After these partly inevitable drop otus in 1994, the group left with 7 members. And we decided to take 6 more patients in, 3 from a previous 1989 program and 3 from 1993 program. One of these new patients, a Bipolar girl, was later discharged due to imrovement and

she started working as an arts and crafts teacher. At present she is on medication and comes back on individual basis when she thinks she needs consultation or medication. So, as a result, we still have 12 patients attending regularly; 7 of them since 1992 and 5 of them since 1994.

They are all chronic psychotic patients with 8 schizophrenics and 4 schizoaffectives, who receive various neuroleptics, antiparkinsonian drugs and lithium (the latter 4 patients). Six of the schizophrenic patients have, predominantly negative symptoms, while the other two have mixed symptoms. When they began the group therapy sessions, the mean duration of their illnesses was 11.6 years (between 3-26). During this time, they were hospitalized for 3.9 times (between 1-12), excluding the Day Club, which was not an inpatient facility. Nine of the patients are female and 3 of them are male, with mean age 38.6 years (between 24-51). Since the beginning of the group, only three of them had a regular job; a teacher in elemantary school who still works and two civil servants; one of them later resigned and the other retired. They all live with their immediate families, which is almost a rule among the psychotics, in our country. None of them is homeless or left alone. One of the patients is married, four are divorced and the others are single, yet. We learned that, 7 of them have lower - middle economic status, while the other 5 are somewhat better.

Common problems among the patients were; social withdrawal, low functioning in their homes, poor judgement, familial conflicts, occupational problems (again resulting from their low functioning and poor judgement) and inappropriate behaviors.

THE PROCESS

The group took place twice a week and the therautic approach of the therapists was, mainly supportive-didactic. Whe thought that, although none of patients were acutely psychotic, an expressive and highly confrontative style would harm their rather fragile egos. Instead, we tried to understand their feelings, thought processes and interactions with the world around. Trust is an important issue in psychotherapy. We tried to win their trust, so that we could open the doors to their minds. Cohesiveness, too, is an essential part of group therapy. Our work with psychotics showed that, the Day Hospital activites, clearly, increased the degree of cohesion in the group.

We could divide the group process into two periods: First period is, when the patients were attending the Day Club, where they were also receiving some other treatment modalities. At that time, the therapists (1 resident psychiatrist, 1 clinical psychologist and 2 nurses) were more active than they are now. We did not prevent questions about medication, causes of illness and extra-group material (whether it was asked directly to the therapist or not), nor did we insist on the "here and now" process or self-disclosure. However, it was our goal to make them feel free on discussing any subject, and this approach never turned out to bring in too abstract, illogical or irrevelant material. Rather, they gradually began to talk about interactions between them and their families. Maybe we could make things faster, but this would probably jeopardize some already inhibited patients, besides none of them was "expert therapy patients". In this period, the predominant therapeutic factors seemed to be cohesion, universality and instillation of hope. They were less motivated and more "advice oriented" than they are now and we had to give more counseling than we do now.

The second period is the two years after the completion of Day Club program. We took in six more patients and quite surprisingly, they showed great adaptation in a short period of time. In this period, we began to be more confrontative, but not interpretive and also, without forgetting to give the necessary support and verbal reinforcement, since we know that, explorative approaches may be noxious in psychotics (5). Issues like; responsibility taking, problem solving, disinhibition and socil skills became subjet more frequently. With established, strong alliance with the therapists, patients could face such confrontations on their problem areas, easily.

RESULTS

In this two and a half years, only two patients were needed to be hospitalized, but neither of them was in a full blown psychotic exacerbation. Instaed, one of them had become quite inhibited because of her family conflicts (she has a psychotic brother, who still terrorize their lives, an over-protective mother and a silent father), and the other had come to pre-relaps state, so she needed a time out. Other patients are, generally better or somewhat stable.

One of them could re-enter her previous job as an elemantary school teacher, after she had been retired for two and a half years because of her illness. The others were not in an occupation, but they also became more socially adaptive and well functioning. They began to help each other, which in turn improved their self esteem. They began to feel better and hopeful for the future. Eventually, they began to build and use more adaptive coping styles. Their compliance with the antipsychotics did not insist on being a problem, which is a big problem in psychotics universally (4). The relations with their families improved and this was enhanced by our occasional family meetings. Our patients usually, like to put the blame on their families or perceive them in a distorted fashion. With the help of groups, hey began to assess their families more objectively and tried to be in harmony with them. Families' role on rehabilition has long been documented in the literature (1, 4, 14), it could foster but also undermine the rehabilitation. By realising the importance of this issue, we planned to organize more structured and regular family meetings.

Such a long, slow, and less rewarding process might have caused negative feelings on the therapists, who also had some other duties in the hospital. It isnot so infrequent for a therapist to have negative countertransferance feelings when working with chronic psychotics (7), but with growing experience and cohesion to the group, we managed to overcomethem. We learned to be more modest in our goals, flexible and patient with their fluctuating needs and curse and tried to keep our concern and empathic capacity alive. Another important issue is the therapists' cooperation and working in harmony, that can otherwise undermine the hard earned benefits of the therapy. In fact, we did not have such a problem, but nevertheless, we tried to show them our respect, understanding, cooperation and open communication between each other with the hope of being a role model or guide.

For the last words, we could say that treatment of schizophrenia and other psychotic disorders need a pervasive approach, avoiding the earlier dichotomy between drugs and psychotherapy. The optimal treatment should therefore consist of preventing reapse and at the same time a soft promoting of social learning, thus it is a "rehabiltation". When a formal rehabilitation program is ended or unexistent because of various reasons, we could use group psychotherapy easily. We do not mean that it must be limited to off rehabilitation periods, since it is also, an effective, integral part of any rehabilitation program.

REFERENCES

1) Goldstein MJ, Rodnick EH, Evans JR, May PRA,Steinberg MR; Drug and family therapy in the aftercare of the acute schizophrenics. Arch Gen Psychiat, 35, 10, 1169-1177, 1978.
2) Honeycutt N, belcker JR; Clinical care update: social skils training. Community Mental Health J, Vol 27, No 1, 57-67, 1991.
3) Kurek OC; Group psychotherapy in an acute inpatient setting. Issues in Mental Health Nursing, 12 (1) 81-88, 1991.
4) Liberman RP, Eans CC; Behavioral rehabilitation for chronic mental patients. J Clin Psychopar, 5 (3 Supp), 8S-14S, 1985.
5) Linn MW, Caffey EV, Klett G; Day treatment and psychotropic drugs in the aftercare of zchizophrenic patients. Arch Gen Psychiatr, 36, 1055-1066, 1979.
6) Lukoff D, Wallance CJ, Liberman RP, Burke K; A holistic program for chronic schizophrenic patients. Schiz Bull, 12 (2), 274-282, 1986.
7) Sarti P, Cournos F; Medication and Psychotherapy in the Treatment of Chronic Schizophrenia. North America, VOl 13, No 2, 215-229, 1990.
8) Ünlüoğlu G; Ankara Üniversitesi Psikiyatri Kliniğinde grup terapilerinin başlatılma süreci ve psikotiklerle grup terapisi uygulamaları. 2. Grup Terapileri Sempozyumu, Ankara, Sempozyum Kitabı, Sayı 2, s. 1-12, 1977.
9) Ünlüoğlu G; Psikoz katlarında grup ağırlıklı terapötik yaklaşımlar. 6. Grup Terapileri Sempozyumu, Ankara, Sempozyum Kitabı, Sayı 6, s. 22-25, 1981.
10) Ünlüoğlu G, Sayıl I; Effect of group work with admitted psychotic patients' families on their readmission rate. J of Ankara med. School, 13; 331-337, 1991.
11) Ünlüoğlu G, Sözeri Z; AÜTF Psikiyatri Kliniğinde gündüz hastanesi uygulamaları. 26. Ulusal Psikiyatri ve Nörolojik Bilimler Kongresi, Balçova, İzmir, 1990.
12) Ünlüoğlu G, Tuncay V; Group work with patients' families. 4th Mediterrenean Congress of Social Psychiatry. Kongre kitabı, s.51-52, 1983.
13) Vaccaro JV, Young AS, Shirley G; Community based care of individuals with schizophrenia. North America, Vol 16, No 2, 387-399, 1993.
14) Waring EM, Carver C, Moran P, Lefcoe DH; Family therapy and schizophrenia: Recent developments. Can J Psychiat, 31 (2), 154-160, 1986.
15) Yalom ID; The Theory and practice of Group Psychotherapy. 3rd Ed., Basic Books, New York, 1985.

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GROUP THERAPY WITH MOTHERS OF AUTISTIC CHILDREN

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SUMMARY

Autism is a lifelong, chronic disorder. Therefore families of autistic children require help and support for their own well being as well. Austistic children are treated intensively whereas families, particularly mothers receive support, usually informative in content if ever. Most of the small number of studies on this subject stresses the socially reserved and secretive style of these families. Mothers who are continuously involved in the treatment of their children are found to be over burdened with responsibility and to present with feeling of weariness, hopelessness, unhappiness and anger for having a distressed child.

This study was designed to help mothers who share this same problem, by means of an interaction group therapy approach, which aimed to encourage the family in solving their problems and support their coping mechanisms.

The group consisted of 10 mothers and 2 co-therapists, which met on a weekly basis for 3 months, at the Center for Autistic Children, University of Ankara. Each session was of 1 hour duration. Seven mothers were asked to attend the groups regularly, to complete a Q-sort and to choose the therapeutic factors that they considered to be most helpful. Results showed that mothers found a group of factors, namely instillation of hope, catharsis, universality and learning to cope better with their problems, to be curative.

Instillation of hope in families dealing with chronic illness' disturbances has been found to be the main issue; catharsis which has a second place, suggests that an atmosphere of integration cooperation and mutual trust has been established, sufficient for the expres sion feelings. Universality permits the mother to understand that she shares similar problems with other members.

Key words: *Autism, child psychiatry, group therapy.*

Autistic disorder is one of the most disabling disorder of childhood. Beside its impacts on child, it could be a major source of stress to the family members. They have to deal with both management and care of their child which is generally percevied as an endless struggle with little success. Contact with medical staff usually provides no more hope and indeed, may result with disappointment on families. They learn that it is a serious, chronic illness and it is not possible to cure but rehabilitate it. Rehabilitation programs need to be long termed and largely depend on the participation of family members.

In Child Psychiatry Department of Medical School of Ankara University, a center for autistic children was founded at 1991. On working with autistic child the treatment team realized that most members of those children's family members has emotional problems and are in need of psychiatric intervention (1,2).

Mothers are the group whose responsibilites and at the same time, emotional difficulties seems to be the highest. Any approach to mother could help both the child and the family (3). In this context, the treatment team decided to do group therapy with the mothers of these children. Group approach aimed at being supportive and based on facilitating interaction of members. Although it is called as "therapy", this is not exactly true because the participants are seemingly healthy ones.

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Table I: The demographic characteristics of the mother and the child

Number of Mothers	N:	10
Age range Mothers		27-42
	X:	34
Education of Mothers		
Elemantary		2
Secondary		1
High school		7
Mothers occupation		
Occupied outside the home		4
House wife		6
Gender of children		Boy: 9
		Girl: 1
Age range of children		3^{4}-6^{11}
Time of diagnosis		
Diagnosed recently		6
Diagnosed previously		4

Mothers of 10 autistic child invited to the group sessions and 7 mothers were an to attended the groups regularly. The sessions were done from December 1992 to May 1993, once a week and for 60 minutes. There were two therapists experienced on both patient and family groups (Table I).

Yalom's Q sort test was used for comparisons and to evaluate group process (4,5). Test was given to the mothers after the 14th session. The rank order of mothers perception of curative factors are presented in Table II.

These groups are short-termed and done with realtively healthy subjects. Therapists had to adjust their therapeutic approach accordingly and applied techniques compatible with the features and the aims of the participants. Major aims of this group were not similar with patient groups and items such as understanding the dynamic basis of behavior. It was not an very important issue for the mother. However, issues concerning about ventilation, instillation of hope and guidance of mother are seemed to be appropriate approaches for this group. Facillitating group interaction for mutual feed-backs and helping them to see they are not the only one who has similar problems are other important issues. Indeed, mothers ranked curative factors related with those issues as the most beneficial items for them. It is better to consider curative factors as a whole, but to simplify the discussion they were taken separately.

Table II: Curative Factors of the Group

1- Instillation of hope
2- Catharsis
3- Universallity
4- Interpersonal learning-input
5- Guidance
6- Existential factors
7- Interpersonal learning-output
8- Cohesiveness
9- Self understanding
10- Family re-enachment
11- Altruism
12- Identification

Instillation of hope

Hope is an important motivation of therapy at all phases. Also, installation of hope is one of the most important goals of the therapist (2,6). This group consists of mothers who are really desperate about the features of their child, so, it is much more vital to emerge hope on the side of the mothers.

Catharsis

Catharsis consists of two interrelated but different set of items. Of those, while first set of items (eg. item 31) pertaining to the ventilation of patients, the second set covers both expressing feelings and positive attitudes towards the future. High cathartic activity in a group may represent altruistic attitudes, safety feelings, mutual trust and cohesiveness among the participants. These features are essentials of a working group. It is more essential in highly charged mothers of austistic child and usually after a cathartic activity, their group participation increase (7).

Universality

At the early phases of treatment, mothers realize that they are not the only one who has similar problems; that is called universality. Realizing universality generally accompanied by releasing feelings. When the mothers negative feelings towards the child becomes the issue of the group, most mothers talk about how they are suppressed and at the same time relaxed by learning that the others could also have similar feelings.

Interpersonal learning output and input

This curative factor emphasizes mutual interactions between patients and its effects on the patient. It covers, free expression of one-self in group situation, giving and getting feedback for these self-disclosures, and eventually elaboration those feedbacks for change.

Guidance

This curative factor covers all information provided by the therapist; such as, suggestion, advise, guidances for coping with daily problems of life and didactic information about autism. It has limited curative effects in patient groups but an important issue for the participating mother.

Existential factors

This curative factor emphasis the personal responsiblitiy of the mothers for their lives and problems (8). The mother is the one who has the responsibilty of her current individual problems, yet she also has the capability to help her child.

Cohesiveness

Group cohesiveness, on its own, is not usually considered as a curative factor that causally related to the changing process, but rather it provides a baseline for the utility of other curative factors. This factor cover issues related to the reciprocal acceptance and statisfying relationship between the therapy group members. The quality of this relationship provides a safety condition in which members act freely and other important curative factors, such as, catharsis, interpersonal learning can take place.

Self understanding

Intellectual components of therapy process included into self-understanding factor. Most of the candidates has been suffering from a free folating anxiety that they could not explain in any means. This factor is about providing explanations for the basis of unknown anxiety and increasing awareness of the sources of current problems. In regard wtih this, patients not only realize negative and weak parts of themselves towards their child and but positive and strong parts as well. It is technically very appropriate to bring into action self-understanding during the patients cathartic activity.

Family Re-enachment, Altruism and Identification

These curative factors were ranked at the lowest order and perceived as the least beneficial factors of all. This result seems to be similar with patient groups (5,7).

The participants of the group are relatively healthy subjects and the results of the group therapy have not controlled objectively. Indeed it is not very possible to apply any test prepared for the measurement of change of patients to these mothers. But subjectively both mothers and therapists share opinions about its usefulness. Not only the family but the child could also get beneficial effects from such an approach. This study should be considered as a preliminary one pointing out the importance and the need about such studies.

REFERENCES

1. Akçakın M.: Ailelerin psikiyatrik belirtiler yönünden incelenmesi. III. Ulusal Psikoloji Kongresi Bilimsel Çalışmaları. İstanbul, Sevinç Matbaası 359-367, 1984.
2. Akçakın M.: Otistik çocukların tedavisi. XXIV. Ulusal Psikiyatri ve Nörolojik Bilimler Kongresi. Ankara, Uzak Doğu Kültür Yayınları, Cilt 2, 54-58, 1990.
3. Akkök F.: Darvanışsal yaklaşıma dayalı aile rehberliğinin öğretilebilir çocukların öz bakım becerilerinin gelişimine etkisi. Ankara Üniversitesi Sosyal Bilimler Enstitüsü. Yayınlanmamış doktora tezi.
4. Yalom I.D.: The theory and practice of group psychotherapy, New York, Basic Books Inc. Publishers, 1985.
5. Yalom I.D., Vinogradov S.: Breavement groups: Techniques and themes. Int J Group psychother, 38(4): 419-446, 1988.
6. Akçakın M., Aysev A., Kerimoğlu E.: Kliniğimizde otistik çocukların aileleri ile yapılan çalışmalar. Otizm: Kerimoğlu E. Ankara Üniversitesi Basımevi, 127-135, 1993.
7. Çevik A. et al: Kısa süreli etkileşim grup psikoterapilerinde hastalarca belirlenen iyileştirici faktörler. XXVI. Ulusal Psikiatri ve nörolojik Bilimler Kongresi, Bilimsel Yayınlar Kitabı, 139-156, 1990.
8. Gerdtz J., Bregman J.: Autism A Practical Guide for Those Who Help Others By Van Ornum W. 67-116, 1990.

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CLOZAP NE V A FAM LY INTERVENTION PROGRAM N THE TREATMENT OF RESISTANT CHRON C SCHIZOPHREN A
A Preliminary Report

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SUMMARY

Clozapine is an atypical neuroleptic which has been shown in many open and controlled studies to have superior efficacy in the treatment of chronic resistant schizophrenia. On the other hand, the results of controlled studies have shown that family intervention program might improve the outcome of schizophrenia. Thus, the present study was started to examine whether an add-on therapy over clozapine with a family intervention program would elicit an add-on improvement on the status of chronic resistant schizophrenic patients.

Schizophrenic patients accepted to be treatment-resistant, participated in a oneyear program, carried out either with clozapine alone or clozapine via family intervention. The presented preliminary data cover the results of 20 patients under clozapine treatment (C1) and 14 patient under clozapine treatment with family intervention program (C2) of a 2.5 months follow up. All the patients were evaluated weekly using Modified Brief Psychiatric Rating Scale For The Assessment of Negative Symptoms (SANS), The Scale For The Assesment of Positive Symptoms (SAPS) and the Clinical Global Impression Scale (CGIS). Comparison of positive symptoms of both C1 and C2 groups did not display a significant difference throughout the treatment period. The improvement in negative symptom scores were found initiate after four week of therapy in the C1 group. Although the scatter plots of the negative symptom scores against weeks seemed to be different, a statistical significance could not be reached.

The results of the present trial are preliminary in nature, but promising. Thus, they have to be compared and discussed with the 1 year follow -up results.

Key Words: *Clozapine, family Intervention program, treatment resistant chronic schizophrenia*

Despite the proven efficacy of conventional neuroleptics in chronic schizophrenic patients, a substantial minority (15-20 %) derive little, if any, benefit from such medication (23,26), and, thus, therapeutic approach to this refractory subgroup represent a major challenge. The generally accepted criteria for treatment resistance is such: No significant symptomatic relief and/or good functioning with at least three six weeks period of neuroleptic treatment from at least two different chemical classes equivalent or higher to 1000 mg/day of chlorpromazine, in the preceding 5 years (17,18).

The re-emergence of clozapine, a dibenzodiazepine compound, as a highly effective and broad-spectrum antipsychotic, attracted a world wide attention due to several unusual characteristics such as an antipsychotic effect with minimal extrapyramidal side effects and hyperprolactinemia and the striking and significant improvement and rehabilitation it produces in the treatment resistant chronic schizoprenics (4,12).

Regarding the chronic treatment resistant schizophrenic patient as a biological/non-biological multilevel interactive system, it is not a naturalistic approach to only meditate the biological component for a gross treatment. Moreover, a considerable therapeutic outcome represent not only symptom-limited improvement but a significant improvement

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in social and individual functioning and quality of life and improvement and rehabilitation maintenance as well. Thus, it is very well known that care and treatment of chronic schizophrenic patients extend beyond pharmacologic interventions (11,13,14,15,20,31). But, the interactive relationship between pharmacological and psychosocial treatments with clozapine in chronic schizophrenic patients has scarcely been studied (32).

PATIENT SELECTION AND STUDY DESİNG

Thirty four chronic schizophrenic patients from two different psychiatry institutions who met the DSM IIIR criteria for chronic schizophrenia (3) but otherwise healthy were included. The demographic data for the patients are presented in Table 1. All the patients met the conventional criteria for drug-treatment resistance; no significant clinical improvement despite at least three periods of treatment in the preceding five years with traditional antipsychotic agents from at least two different chemical classes at doses equivalent to or greater than 1000 mg/day chlorpromazine for period of six weeks (patients with a total rating score of at least 45 in BPRS and over level 4 in CGI). History of drug abuse, chronic alcoholism, organic brain syndrome, mental retardation and any contraindication for clozapine treatment were accepted to be the exclusion criteria for participation in the trial. All patients and/or patient relatives gave their written informed consents.

Table 1: The Demographic data for the patients

	C1 Group	C2 Group
MEAN AGE	(27) 37.10 (59)	(19) 33.789 (50)
SEX	10 F (50)%	3 F (21.4 %)
	10 M (50 %)	11 M (78.6 %)
MARITAL STATUS	4 MARRIED (20%)	2 MARRIED (14.3 %)
	16 NON-M. (80%)	12 NON-M. (85.7%)
DURATION OF THE ILLNES (MEAN YEAR)	(5) 12.1 (30)	(4) 10.21 (15
PREVIOUS HOSPITALISATION (MEAN NUMBER)	(3) 8.4 (12)	(3) 7.71 (10)
THE DIAGNOSTIC SUBTYPES	P 15 (75%)	P 9 (64.2 %)
	D 3 (15 %)	D 3 (21.4%)
	I 2 (10 %)	I 2 (14.4 %)

P: Paranoid
D: Desorganised
I: Indefferentiated

The present study was designed as a two -center, open, comparative trial. The patients were all follow-up patients of chronic schizophrenia and were included into the study consecutively as they met the criteria for drug resistance. before all the patients entered the trial, they all had full physical and neurological examination and underwent a routine laboratory analysis.

While all the patients in one center (n=20) were given only clozapine treatment (C1), in the second center (n=14), they were given clozapine and an add-on family intervention program* was carried out. A one week wash-out period for conventional antipsychotics and a one month wash-out period for depot-antipsychotics were assessed before clinical trials.

For a close follow-up for agranulocytosis, all the patients underwent a total blood count analysis weekly, during clozapine treatment. Clozapine treatment was started at a dose of 25 mg/day and was gradually increased by 25 mg everyday until a dose of 300 mg/day was attained and if needed a final dose of 500 mg/day was given to patients by gradual increment of 50 mg everyday after a dose of 300 mg/day was achieved.

All the patients were weekly evaluated using Modified Brief Psychiatric Rating Scale (MBPRS) (30), The Scale for The Assessment of Negative Symptoms Scale (SANS)(9), The Scale for The Assessment of Positive Symptoms Scale (SAPS) (10), Simpson-Angus Rating Scale for The Assessment of E0trapyramidal Side Effects Scale (29) and Clinical Global Impression Scale (CGIS) (5) were evaluated before and after a 2.5 months treatment period.

* **Family intervention program** as a supportive and psychoeducational regimen was applied weekly for each family group therapy for relatives every two weeks. The duration of family interviews and group therapies for relatives were planned to be 45 and 90 minutes respectively. Family intervention program was based on the following characteristics (7,16):

- The establishment of a collaborative relationship between the treatment team and family members.
- The provision of information and support.
- Effort to create structured predictable environments in the treatment setting and in the home.
- Assessing the family unit itself to determine its own needs and resources.
- Assistance in daily living (problem solving training and management of stressful life events)
- Crisis intervention.

Statistical Analyses:

The improvement in rating scores in the two treatment groups has been given as the relative improvement with respect to the initial score of each patient. Results has been presented as the average values of such improvement in each group. Pointwise comparison of the two groups has been achieved by using Student's independent samples test. $p<0.05$ is considered significant, and such points are indicated on Figures.

RESULTS

Significant improvement in MBPRS and SAPS scores initiated after the 2nd week. Although there was found to be a significantly better improvement of MBPRS scores of C2 group during 4-5-6th weeks of treatment, the final effect achieved at the end of a 2.5 months treatment in both trial groups did not show any significant difference (Fig. 1).

Comparison of the improvement of positive symptoms of both C1 and C2 groups did not display a significant difference throughout the treatment period (Fig. 2).

The improvement in negative symptom scores were found to initiate on the second week in C2 group, but was found to initiate after four weeks of therapy in the C1 group. Although the scatter plots of the negative symptom scores against weeks seemed to be different statistical significance could'nt be reached (Fig. 3).

Comparison of the improvement in CGI scores, global improvement scores and side effect scores before and 2.5 months after the two treatment protocols, was fount to display a statistically significant difference as shown in figures 4 and 5. But this statistical significance was not considered to be meaningful, as, an at least 10 % difference in improvement between the two cilincal trial groups was initially validated.

The general side effect profile of both the treatment regimens has been shown in Table 2. there was a total of three drop-outs throughout a 2.5 months follow-up because of hypersalivation, seizure and leucopenia (3600/mm³).

Table 1: Side Effect profile of both treatment groups

	C1 Group	C2 Group
LEUCOPENIA	1 (5.5 %)	0 (0)
DROWSINESS	16 (88.8 %)	5 (35.7 %)
SEIZURE	1 (5. %)	0 (0)
ORTHOSTATIC HIPOTENSION	8 (42.2 %)	2 (14.2 %)
TACHYCARDIA	7 (38.8 %)	3 (21.4 %)
FEVER	2 (11.1 %)	1 (7.1 %)
HYPERSALIVATION	10 (50.5 %)	2 (14.2 %)
WEIGHT GAIN	3 (16.6 %)	2 (14.2 %)
NAUSEA/VOMITING	1 (5.5 %)	1 (7.1 %)
CONSTIPATION	5 (27.2 %)	4 (28.5 %)
LEUCOCYTOSIS	12 (66.6 %)	5 (35.7 %)

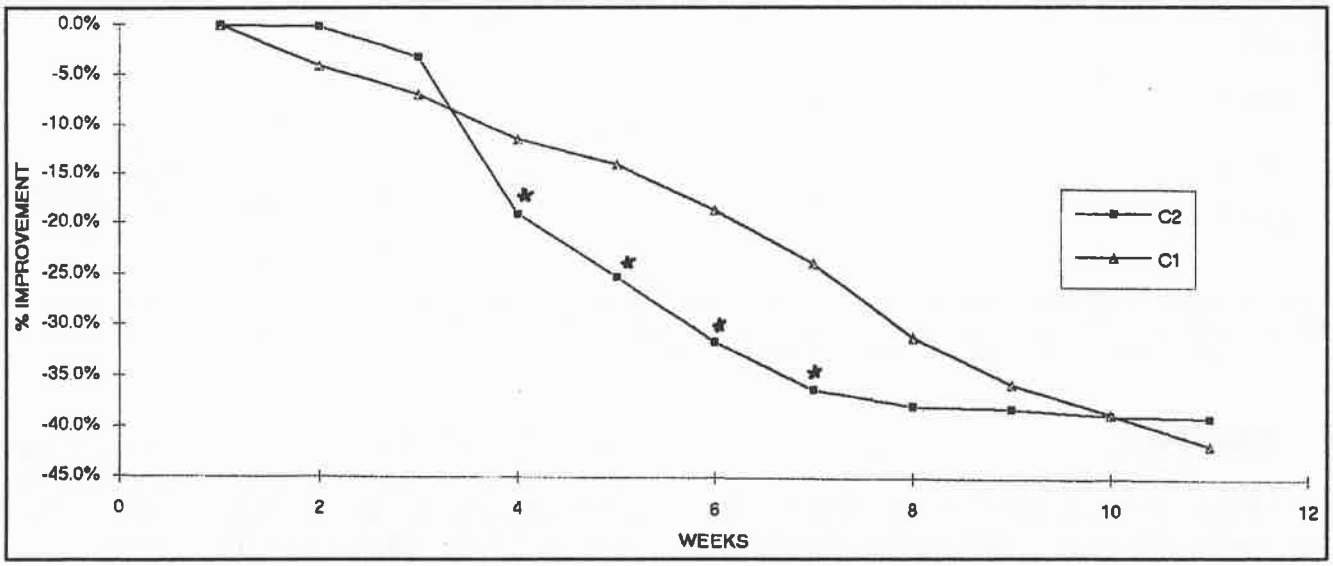

Fig. 1. Comparison of the improvementd in MBPRS scores of chronic schizophrenic patients treated by clozapine alone (C1) and clozapine treatment with an add-on family intervention program (C22)

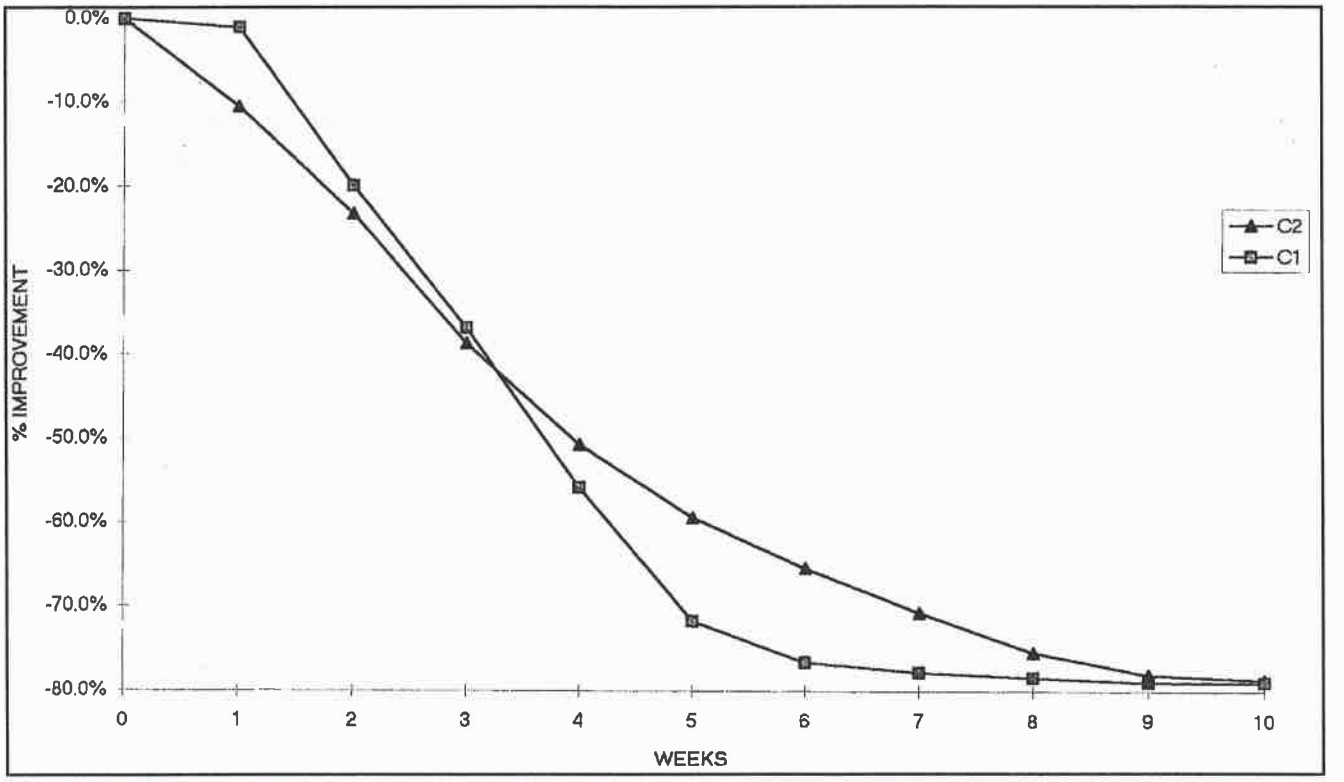

Fig. 2. Comparison of the improvementd in positive scores of chronic schizophrenic patients treated by clozapine alone (C1) and clozapine treatment with an add-on family intervention program (C2)

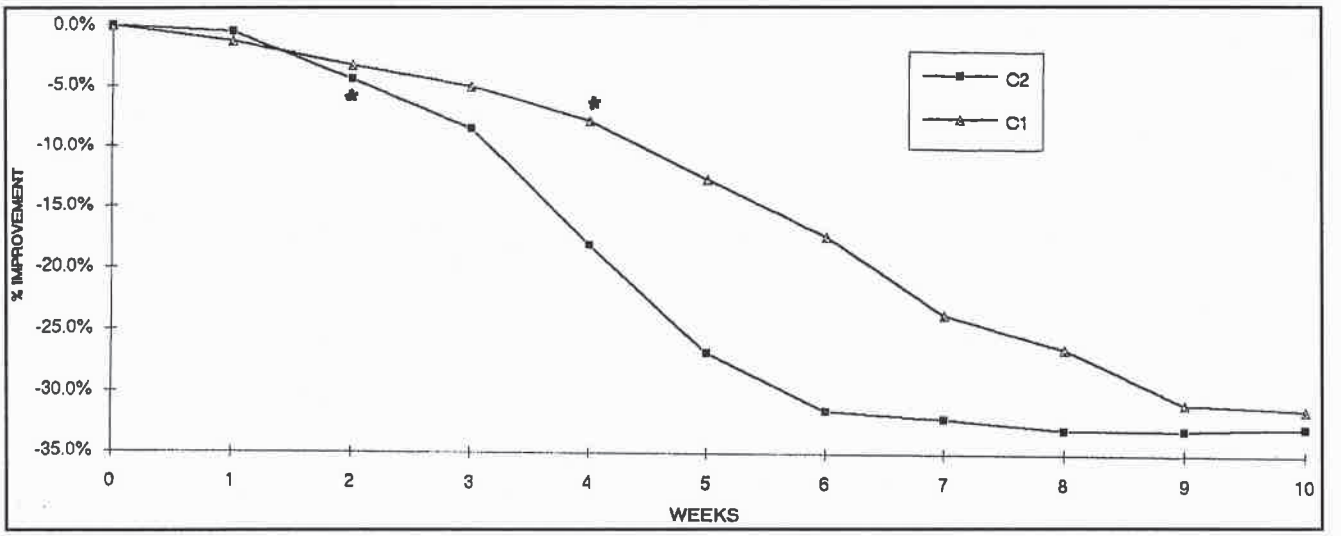

Fig. 3. Comparison of the improvementd in sans scores of chronic schizophrenic patients treated by clozapine alone (C1) and clozapine treatment with an add-on family intervention program (C2)

DISCUSSION

Clozapine was found to be significantly effective against both positive and negative symptoms of treatment-resistant chronic schizophrenic patients. While the improvement in positive symptoms was found to be 80 %, improvement in negative symptoms could only reach a 35%. As is known, there is not a consensus for the improvement of negative symptoms; it is suggested that the negative symptoms improvement by clozapine is partly due to a primary efficency and partly may be secondary to

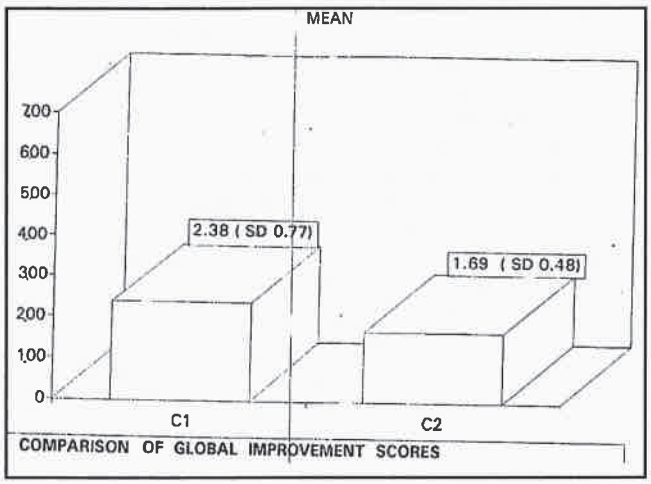

Fig. 4. Comparison of global improvement scores

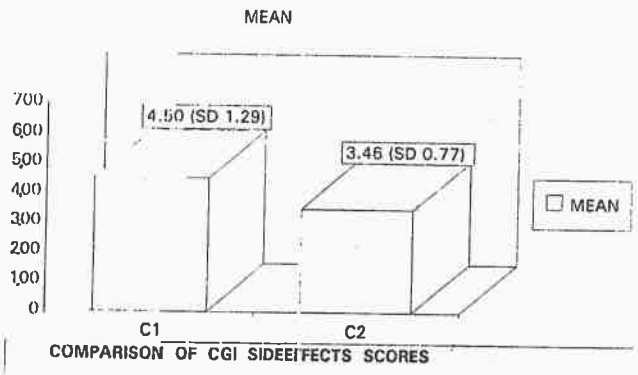

Fig. 5. Comparison of CGI sideeffects improvement scores

the improvement of positive symptoms. But, the discrepancy between the rate of improvement in positive and negative symptoms is not yet known (6, 8, 17, 21, 22, 24, 25, 27).

The aim of the present clinical trial was to explicate whether an add-on improvement could be achieved by an add-on psychosocial intervention. It is very well known that treatment and care for chronic schizophrenia extends beyond pharmacological interventions (11,13,15,20,31). Thus, several beneficial effects such as the prevention of relapses, rehospitalization and improvement in quality of life have been demonstrated by combined treatment of conventional neuroleptics and psychosocial regimens, but, have been scarcely evaluated with novel antipsychoitics such as clozapine (32).

The results of the present trial are preliminary in nature, but promising. Thus, an add-on psychosocial regimen, although not reaching a statistical significance, seems to produce a better improvement in resistant chronic schizophrenic patients particularly, in the sense of their well being.

The side effect profile of clozapine treatment indicates that it produces a wide range of side effects substantially different from calssical antipsychotics (1, 19, 28). A conservative approach was preferred for two patients exhibiting the severely potential side effects of clozapine treatment, seizure and leucopenia. No agranulocytosis and no extrapyramidal side effect could be assessed during the early 2.5 months treatment protocol, but this has to be discussed throughout a longer period, thus a one-year follow-up.

Consequently, the current results are the spot presentation of a 2.5 months treatment outcome, out of a one-year planned trial. We are looking forward to assess the long-term efficacy of combined treatment of clozapine and family intervention over clozapine therapy alone.

REFERENCES

1. Alvir AJ, Lieberman JA: A reevaluation of the clinical charasteristics of clozapine induced agranuloytosis in light of the United States experience. J Clin Psychopharmacology 14:87-89, 1994.
2. Andreasen NC and Olsen S: Negative-positive schizophrenia definition and validation. Arc Gen Psychiatry 39:789-794, 1982.
3. American Psychiatric Association: diagnostic and statistical manual of mental disorders, Third edit. revised, Washington D.C., American Psychiatric Press, 1987.
4. Baldessarini RJ and Frankerberg FR: Clozapine a novel antipsychotic agent. The N J Medicine 14:746-754, 1991.
5. Beneke M, Rasmus W: Clinical Global Impressions (ECDEU): Some critical Comments. Pharmacopsychiatrica 25:171-176, 1992.
6. Breier A, Buchanan RW, Kirkpatrich et al: Effects of clozapine on positive and negative symptoms in outpatients with schizophrenia. Am J Psychiatry 151:20-26, 1994.

7. Cole SA, JacobsJ: Family treatment of schizophrenia, Psychiatric therapies, Karasu TB, Edit, Volume 2, American Psychiatric Association, Washington D.C., 1543-1567, 1989.
8. Collins EJ, Lalonde P, Jones BD et al: Clozapine in the treatment of refractory schizophrenia: Canadian policies and clinical guidelines Can J Psychiatry 37 (7): 482-496, 1992.
9. Erkoç Ş, Arkonaç O, Ataklı C, Özmen E: Negative semptomları değerlendirme ölçeğinin güvenirliği ve geçerliliği. Düşünen adam 4(2): 16-19, 1991.
10. Erkoç Ş, Arkonaç O, Ataklı C, Özmen E: Pozitif semptomları değerlendirme ölçeğinin güvenirliliği ve geçerliliği. Düşünen Adam 4 (1): 16-19, 1991.
11. Falloon IRH- Boyd JL, Mcgill CW et al: Family management of in the prevention of exacerbation of schizophrenia: a controlled study. N Eng J Med 306: 1437-1440, 1982.
12. Fittion A, Heil RC: Clozapine: a review of its parmacological properties and therapeutic using schizophrenia. Drugs(40 (5): 722-747, 1990.
13. Goldstein MJ, Rodnick EH, Evans JR et al: Drug and family therapy in the aftercare of acute schizophrenics. Arch Gen Psychiatry 35: 1169-1177, 1978.
14. Goldstein MJ: Psychosocial (nonphamacolgical) treatment for schizophrenia. Review of psychiatry, Tasman A, Goldfinger SM, edit, volume 11, American Psychiatric Press, Washington D.C, 116-135, 1991.
15- Hogarty G, Anderson CM, Reiss DJ et al: Family education, social skills trainnig and maintenance chemotherapy in the aftercare of schizophrenia. Arch Gen Psychiatry 43:633-642, 1986.
16. Intagliata J, Willer B, Egri G: Role of the family in case-management of the mentally ill. Schizophr Bull 12 (4): 699-708, 1986.
17. Kane JM, Honigfeld C et al: Clozapine for treatment resistant schizophrenics. Arch Gen Psychiatry 45:789-796, 1988.
18. Kane JM: Clinical effica cy of clozapine in treatment refractory schizophrenic an overview. Br J Psychiatry, Suppl. 17:41-45, 1992.
19. Krupp P, Barnes P: Clozapine associated agranulocytosis: Risk and etiology. Br J Psychiatry, Suppl. 17:38-40, 1992.
20. Leff J, Kuipers L, Berkowitz R et al: A controlled trial of social intervention in the families of schizophrenic patients. Br J Psychiatry 141: 121-134, 1982.
21. Lieberman JA, Safferman SA, Pollack S et al: Clinical effects of clozapine in chronic schizophrenia: Response to treatment and predictors of outcome. Am J Psychiatry 151:1744-1752, 1994.
22. Lindenmayer JP, Grochowski S, MabugatL: Clozapine effects on positive and negative symptoms a six months trial in treatment refractory schizophrenics. J Clin Pharmacology 14:201-204, 1994.
23. Marder SR, Ames D, Wirshing WC et al: Schizophrenia, The Psychiatric Clinics of North America 16(3): 576-587, 1993.
24. Meltzer HY, Alpha LD, Bastani B et al: Clinical efficacy of clozapine in the treatment of schizophrenia, Pharmacopsychiatry 24:44-45, 1991.
25. Meltzer HY, Cola P, Way L et al: Cost effectivenes of clozapine in neuroleptics resistant schizophrenia, Am J Psychiatry 150(11): 1630-1638, 1993.
26. Meltzer HY: New drugs for the treatment of schizophrenia, The Psychiatry Clinics of North America 16(2): 365-385, 1993.
27. Miller DD, Perry PJ, Cadoret RJ et al: Clozapine's effect on negative symptoms in treatment refractory schizophrenics, Comprehensive Pscyhiatry 35:8-15, 1994.
28. Safferman A, Liberman JA, Kane JM: Update on the clinical efficacy and side effects of clozapine, schizophr Bull 17 (2): 247-261, 1991.
29. Simpson GM, Angus JWS: A Rating Scale for extrapramidal side effects, Acta Psychiatr Scand, Suppl. 212: 11-19, 1970.
30. Soykan Ç: Instutional differences and case typicality as related to diagnosis system severity prognosis and treatment, METU, The Inst. of Soc. Sci. Degree of Master of Science in the subject applied (clinical) psychology, 1990.
31. Tarrier N, Barrowclough C, Porceddu K et al: The community management of schizophrenia: a controlled trial of a behavioral intervention with families to reduce relapse, Br J Psychiatry 153: 532-542, 1988.
32. Viner MW, Escobar JI, Werick T: Clozapine plus psycoeducation in treament refractory schizophrenia, Neuropsychopharmacology, Suppl. Part 2, Oral communatications and poster abstracts of XIXth Collegium International Neuro-psychopharmacologicum Congress, Washington D.C. 10 (35): 207, 1994.

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LIPOPROTEIN (a) LEVELS IN TYPE II DIABETES MELLITUS: RELATIONSHIP TO LIPID PROFILE, METABOLIC CONTROL, MICROALBUMINURIA AND CORONARY HEART DISEASE

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SUMMARY

Lipoprotein (a) [Lp(a)] is an atherogen particle which structurally resembles low density lipoprotein and made of one molecule of abolipoprotein (a) and one molecule apobetalipoprotein B-100 linked with a disulfide bound.

Epidemiological studies showed Lp(a) as an independent risk factor for coronary atherosclerosis which is the leading cause of mortality in diabetic population. There are contradicting data for the serum Lp(a) levels and its relation with atherosclerosis in diabetes.

In this study serum Lp (a) levels and its relation with lipid profile, microalbuminuria and coronary heart disease (CHD) has been studied in 55 type II diabetic patients, whose median age was 54 (32-75).

Correlation was not found between serum Lp(a) levels and sex, age of DM, metabolic control,, CHD, microalbuminuria, obesity, body fat distribution, oral anti diabetic and insulin treatment. None of the lipid parameters (LDL, HDL, triglyceride, total cholesterol, LDL/HDL ratio) in daily clinical use showed a direct or reverse relation with serum Lp(a) levels.

In conclusion no evidence for Lp(a) as an additional risk factor for already increased atherogenesis in type II diabetes mellitus was found with the criteria used.

Key Words: *Diabetes Mellitus, Lipoprotein (a), Coronary Heart Disease.*

Individuals with DM have an increased risk for developing atherosclerotic diseases. This is partly a consequence of the association of DM with the other risk factors of atherosclerosis. Lipid disorders are more common in diabetic persons and are related to the degree of glycemic control (20,6). In diabetic dyslipidemias, usually characterized by hypertrygliceridemia and hypercholestrolemia, there is usually an increase in VLDL-triglyceride VLDL-cholesterol and LDL-cholesterol levels and a decrease in HDL-cholesterol levels.

Epidemiological studies examining the frequency of atherosclerotic manifestations in Diabetes have shown that an increased risk exists even when the corrections are made for total plasma cholesterol, HDL-cholesterol, arterial blood pressure and smoking. For these reasons the relationship between DM and atherosclerosis is a subject of common interest. A positive correlation between plasma Lp (a) levels and CHD and cerebrovascular accidents have been reported by both retrospective and prospective studies (4,19,10,34).

Lp(a) has been decribed by Berg in 1963 (1). It is made of cholesterol rich nucleus covered by apolipoprotein B-100 and apoprotein (a) complex proteins (7,35). Altough a high structural resemblance between plasminogen and Lp(a) exists, Lp(a) has no fibrinolytic activity. However competing with plasminogen for its endothelial receptors, Lp(a) may avoid plasminogen's trombolytic activity (17). Lp(a) also has a high affinity for the atherom plaques from wihch it has been isolated (2).

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Plasma level of Lp(a) is mainly genetically determined (40). However there are some environmental fatcors that can modify its plasma levels. For example, acute phase reactions (26), primary hypercholesterolemia (23) and nephrotic syndromes (41) are know to incraese plasma Lp (a) levels while weight loss (37) and alcohol intake (25) are responsible for the opposite.

Studies conducted on the relationship between Lp(a) and DM have shown that, especially, for type I DM metabolic control decreases Lp (a) levels and rising Lp(a) levels increase rate of atherosclerotic complications. Data for type II DM is controversial.

Our aim in this study is to investigate the relationship of plasma Lp(a) levels with lipid profile and CHD for type II DM.

MATERIALS AND METHODS

Fifty-five type II diabetic patients (24 male, 31 female) who were not using anti-lipemic medications and had no acute diseases or nephrotic syndrome were included in the study. The mean age was 54 (32-75). All the patients were examined. Body mass indices (BMI) were calculated. ECG and echocardiographic findings were studied and triglyceride, cholesterol, HDL - cholesterol, fasting and second hour postprandial blood glucose, HbA1c and Lp(a) levels were mesaured in blood samples. Twenty-four hours urinary microalbuminuria was also detected. Patiets were classified according to their duration of diabetes as; early DM (0-1 year), intermediate DM (1-5 years), and late DM (more than 5 years). The diagnosis of CHD was made according to the history, physical examination, ECG and stress ECG 2nd echocardiographic findings. Coronary angiography was not performed. Microalbuminuria was detected by RIA method from 24 hours' urine specimens and results over 30 mg/L were considered positive. Metabolic control of diabetes was determined according to the results of fasting, second hour postprandial blood glucose and HbA1c levels as; good, accepteble and poor using WHO criteria for type II DM.

Patients whose body mass indices were over 27 kg/height m2 were accepted as obese.

Blood samples for lipid measurements were taken after 12-14 hours' fasting. Lp(a) levels were studied by Solid Phase EIA (Macra, Enzyme Immunoassay Kit, Elkton MD 219-21 Cat D 306). 217 normal contols of our laboratory have shown that Lp(a) levels over 30 mg/dl were high and this is also the borderline value, which was declared to increase atherosclerotic phenomenon by some authors (28,5,29).

HbA1c levels were measured with column chromatography and statistical analyses were done using Chi-square, stundent's t-test and correlation analysis.

RESULTS

Our results are demonstrated in Table I, Serum Lp(a) levels of our 55 type II diabetic patients were found to be in a broad range (1-90 mg/dl) and the mean value of the group was 28±27 mg/dl. There was no correlation between these values and age or sex of the diabetic patients.

There was no correlation between the metabolic control and serum Lp (a) levels. Mean Lp(a) level of the good metabolic control group was 46±31 mg/dl and that of the poor metabolic control group was 18±18 mg/dl ($p > 0.05$). Twelve of our 55 patients had CHD and only 3 of these had Lp (a) levels over 30 mg/dl ($p>0.05$). Proteinuria over 30 mg/L was detected in 10 of our patinets, 2 of whom had Lp(a) levels exceeding 30 mg/dl. Twenty-three of our 55 patients were early (0-1 year), 17 intermadiate (1-5 years) and 15 were late (>5 years) cases. Forty-four percent of the early, 31% of the intermediate and 25% of the late diabetics had high Lp(a) levels (>30 mg/dl). Eight of the 26 obese patients (BMI > 27) had Lp(a) levels over 30 mg/dl. There was no statistically important relationship between the Lp(a) levels of 12 insulin using diabetics and the rest of the group who were on diet and/or oral anti diabetic ($p>0.05$).

According to our results we could not find a positive correlation between the metabolic control and the Lp(a) levels, on the contrary mean Lp(a) levels of our poor control group were lower than the acceptable and the good control group levels (46 > 25 > 18 mg/dl) (Table II). Correlation was not found between CHD and Lp (a) levels of our dibateics. Duration of the diabetes, proteinuria, obesity of the diabetic (BMI), insulin or oral anti diabetic treatment and lipid parameters (LDL-cholesterol, HDL choles-

Table I: The Relationship between serum Lp(a) levels and metabolic control, Coronary Heart Disease (CHD), proteinuria, duration of diabetes, Body Mass Index (BMI) and medication of type II diabetic patinets.

	TOTAL	of Patients Lp (a) < 30 mg/dl	of Patients Lp (a) > 30 mg/dl	mean Lp(a) mg/dl	P
Metabolic Control					
Poor	25 (%46)	22 (%56)	3 (%19)	18,1	> 0,05
Acceptable	15 (%27)	3 (%31)	3(%19)	25,4	
Good	15(%27)	5(%13)	10(%63)	46,3	
CHD					
No	43(%78)	30(%77)	13(%81)	29,1	> 0,05
Yes	12(%22)	9(%23)	3(%19)	24,8	
Microalbuminuria					
< 30 mg/L	45(%84)	35(%89)	10(%63)	178,0	> 0,05
> 30 mg/L	10(%16)	8(%11)	2(%27)	24,1	
Duration of DM					
0-1 Years	23(%42)	16(%41)	7(%44)	28,4	> 0,05
1-5 years	17 (%31)	12 (%31)	5 (%31)	29.1	
> 5 Years	15(%27)	11(%28)	4(%25)	30,7	
BMI					
< 27	29(%53)	21(%54)	8(%50)	27,8	> 0,05
> 27	26(%47)	18(%46)	8(%50)	29,6	
Medication					
OAD*	43(%79)	32(%82)	11(%69)	27,0	> 0,05
Insulin 12(%21)	7(%18)	5(%31)	36,1		

* Oral Anti Diabetic

terol, VLDL-Triglyserides, total cholesterol, tirglyserides and LDL/HDL ratio) that are in common clinical use showed no relation with serum Lp(a) level's ($p > 0.05$).

DISCUSSION

The first study about serum Lp (a) levels in DM was made in 1983 by Schernthaner et al. This study which included types I and II diabetes showed no significant difference in Lp(a) levels between diabetics and normoglycemic controls (36). Later on Ramirez et al published increased serum Lp (a) levels of the diabetic patients when compared with the normoglycemic controls. This study did not differantiate between the types of diabetes (32).

Bruckert et al in their study with 10 type 1 diabetic patinets found that mean Lp (a) concentrations decreased from 46 to 29 mg/dl by strict metabolic control in 21 days (3). Haffner and Nagoshima showed similar results with type I patients (16,30). Heller in his 61 type I diabetic patient group, found no statistically important difference in serum Lp(a) levels compared to 142 normoglycemic control (16). Gall et al supported him with his 152 type I DM patients (8). Haffner et al in their study with 68 type I patients and 18 controls, although they made corrections for Apo (a) phenotype and molecular weight and excluded patients with microalbuminuria, did not find any difference in serum Lp(a) levels. They stated that Apo (a) isoform distribution of type I diabetics was not statistically different from that of normoglycemic controls (11).

Table II: Table retaionship between lipid parametrs and metabolic control of dibaetes.

Lipoproteins	Metabolic Control		
	Poor	Acceptable	Good
Lp (a)	18 ± 3	25 ± 6	46 ± 8
HDL	37 ± 2	38 ± 3	39 ± 3
Triglceride	314 ± 64	331 ± 126	210 ± 33
T. Cholesterol	273 ± 12	268 ± 23	262 ± 19
LDL	116 ± 12	151 ± 17	180 ± 17
LDL / HDL	5,09	4,85	4,17

The results are in mg/dl and mean ± SE values

For type II DM,which is also the subject of our study Heller et al found no difference in Lp(a) levels among 100 patients on oral anti diabetic and normoglycemic controls. They also declared that patients treated with insulin have higher serum Lp (a) levels (18). In our patient group of 55 type II diabetes the mean Lp(a) levels where below 30 mg/dl, which is declared to be the borderline level for the risk of CHD by some authors (28,5,29), we found no difference between the Lp(a) levels of insulin using patients and oral anti diabetic using group.

Taskinen et al found lower Lp(a) levels in 116 oral anti diabetic using type II patinets compared to 95 controls. The same authors tested the effect of the metabolic control and could not find any difference for Lp(a) levels in strict metabolic control group (39). We coludn't find any statistically significant difference between good, acceptable and poor metabolic control groups as well. Haffner gives similar results for 260 type II dibaetics (12). In two other prospective, small, three week studies on type II DM, metabolic control did not change serum Lp(a) levels (33,13). In another prospective study, however, a decrease in Lp(a) levels was established with a strict metabolic control (9).

The most interesting and promising studies in the subject are about proteinuria and renal failure in diabetics. Tagekashi et al showed an increase in serum Lp(a) levels in a .stepwise fashion from microalbuminuria to macroalbuminuria and chronic renal failure (38). The type of DM was not mentioned in this study. Type I DM with increasing Lp(a) levels parallel to microalbimuniria (27), while in another no correlation colud be found (15). İn our study we colud not find any relation between microalbuminuria and serum Lp (a) levels.

As Lp (a) is considered to be a potent atherogenic particle studies were done to find out the relationship between CHD and serum Lp(a) levels for diabetics. In two different studies, with type I and II DM,using the same criteria with ours, no significant relation could be found (27,15). The subject is still yet to be defined. In two other studies a positive correlation between CHD and Lp(a) levels for type II diabetic was established (22,42). In our study, we found no correlation between CHD and serum Lp(a) levels for type II diabetics with the criteria used to diagnose CHD (coronary angiography. Similarly was not performed) we could not find any relation between Lp(a) levels and age, sex, other lipoproteins in routine clinical use.

Studies on this subject including ours are cross sectional. They don't have a prospective design in which mortality from CHD is the endpoint. Additionally Lp(a) has been mainly considered a risk factor for premature CHD but type II diabetes is a disease of the elderly. There may be an age bias at this point. However In this subject controlled, prospective and large studies with apo (a) phenotype and genetic variations, should be conducted for further investigation.

In conclussion, today we have no data to consider Lp (a), to be an additional risk factor for CHD in type II diabetics with the criteria used. Further on, we have no effective treatment that can decrease Lp (a) levels. For these reasons we believe that measuring Lp (a) levels has no place for the routine follow up of the type II diabetic patient.

REFERENCES

1. Berg K.A: A new serum type system in man: the Lp-system Acta Pathol Microbiol Scand. 59: 369-382, 1963.
2. Bihari-Varga M, Gruber E, Rotheneder M, Zechner R, Kostnerr GM: İnteractions of Lp(a) and low-density lipoproteins with glycosaminoglycans from human aorta. Arteriosclerosis 8:851-857, 1988.
3. Bruckert E, Davidoff P, Grialdi A, Truffert J, Giral P, Doumith R, Thervet F, De Gennes JL: Increased serum levels of Lp (a) in diabetes mellitus and their reduction with glycemic control (letter). JAMA 263:35-36, 1990.
4. Dahlen GH, Guyton JR, Attar M, Farmer JA, Kautz JA, Gotto AM: Associtaion of levels of lipoproein (a), pasma lipids and other lipoproteins with coronary heart disease documented by angiography. Cirulation 74:758-765, 1986.
5. Davidoff P, Bruckert E, Grimaldi A, Truffert J, Se Gennes K, Therwet F: Lp(a) in type I diabetes (abstract)., Diabetes 38 (Suppl 1): 70 A, 1989.
6. Dunn FL, Baskin P, Bilheimer DW, Grundy SM: The effect of diabetic control on very low-density lipoprotein-trygliceride metabolism in patinet with type II diabetes mellitus and marked hypertriglyceridemia. Metabolism 33: 117-123, 1984.
7. Eaton DL, Fles Gm, kohhr WJ, Mc Lean JW, Xu QT, Miller CG et al.: Partial aminoacid sequences of apolipopotein (a) shows that it is homologous to plazminogen. Proced Nat Acad Sci USA. 84: 3224-3228, 1987.

8. Gall MA, Rossing P, Hommel E, Voldsgard AI, Anderson P, Nielsen FS, Dyerberg J, Parvind HH: Apolipoprotein (a) in insulin dependent diabetic patients with and without nephropathy. Scand J Clin Lab İnvest 52: 513-522, 1992. 6.

9. Garber Aj, Jones PH, Ghanem KK, Morrisett JD: Response of plasma Lp (a) levels to diabetes contol therapy (Abstract). İn proced 9th international Symposium on Atherosclerosis Resomnt, II p.12, 1991.

10. Genest J Jr, Jenner JI, Mc Namara JR, Ordovas JM, Silberman SR, Wilson PWF, Schaefer EJ: Prevelance of Lp (a) excess in coronary artery disease. Am J Cardiol 67: 1039-1045, 1991.

11. Haffner SM, Frangos M, Williamson J, Santaiago J, Valdez R, Aldrete G, Mykkanen L, Grubber KK, Rainwater DL: Lp (A) concentrations and phenotypes in subjects with insulin-dependent diabetes mellitus. Chem Phys Lipids, 1989.

12. Haffner Sm, Morales PA, Stern MP, Gruber MK: Lp (a) concentaitons in NIDDM. Diabetes 41: 1268-1272, 1993.

13. Haffner SM, Tuttle KR, Rainwaer DL: Preliminary report: Lack of change of Lp (a) concentrations with improved glycemic control in subjects with type IIdiabetes. Metabolism 41: 116-120, 1992.

14. Haffner SM, Morales PA, Gruber MK, Hazua HP, Stern MP: Lack of association of lipids, lipoproteins and Lp (a) with microalbuminuria in NIDDM Arteriosclerosis 13:205-210, 1993.

15. Haffner SM, Klein BEK, Moss SE, Klein R: Lack of association between Lp(a) concentrations and coronary heart disease mortality in dibates: the Wisconsin Epidemiologic Survey of Diabetic Retinopathy Metabolism 41:194-197, 1992.

16. Haffner SM, Tuttle KR, Rainwater DL: Decrease of Lp (a) with improved glycemic control in IDDM subjects. Diabetes Care 14: 302-307, 1991.

17. Hajjar KA, Gavish D, Breslow JL, Nachmann RL: Lp (a) modulation of endotelial cell surface fibrinolyis and its potential role in atherosclerosis. Nature 339: 303-305, 1989.

18. Heller FR, Jamart J, Honore P, Derue G, Novik V et al: Serum Lp (a) in patients with diabetes mellitus. Diabetes Care 16: 819-827, 1993.

19. Hoefler G, Harnoncourt F, Paschke E, Mitrl W, Pfeiffer KH, Kostner GM Liportoein (a) a risk factor for myocardial infarction. Arteriosclerosis 8: 398-401, 1988.

20. Howard BV: Lipoprotein metabolism in dibaetes melitus. J Lipid Res 28: 613-628, 1987.

21. Jenkins AJ, Steele JS,Janus ED, Best JD: Increased plasma apolipoprotein (a) levels in IDDM patinets with microalbuminuria, Diabetes 40: 787-790, 1990.

22. Jenkins AJ, Steele JS, Janus ED, Santamaria JD, Best JD: Plasma apolipopotein (a) is increased in type II diabetic patinets with microalbuminuria. Diabetologia 35:1055-10569, 1992.

23. Kamboh MI, Ferrell RE, Kottke BA: Expressed hypervariable polymorphism of Lp(a). Am J Hum Genet 49: 1063-1074, 1991.

24. Kapelud H, Bangsted HJ,Dahl Jorgensen K, Berg K, Hansen KF: Serum Lp (a) lipoprotein concentrations in insulin dependent diabetic patients with microalbuminuria. Br Med J 303: 675-678, 1991.

25. Kervinen K, Savolainen MJ, Kaseniemi YA: A rapid increase in Lp (a) levels after ethanol withdrawal in alcoholic men. Life Sci 48: 2183-2188, 1991.

26. Maeda S, Abe A., Seishia M, Makino K, Noma A, KawadeM: Tansient changes of serum Lp (a) as an acute phase protein. Atherosclerosis 78: 145-150, 1989.

27. Maser ER, Usher D, Becker JD, Drash AL, Kuller LH, Orchard JT: Lp (a) concentratdion shows little relationship to IDDM complications in the Pittsburgh epidemiology of diabetes complications study chort. Diabetes Care 16:755-758, 1991.

28. Miles LA, Fless GM, Levin EG, Scanu AM, Plof EF: A potential basis for the thrombotic risks associated with Lp (a). Nature 339: 301-303, 1989.

29. Murai A, Miyahara T, Fujimoto N, Matsuda M, Kameyama M: Lp (a) lipoprotein as a risk factor for coronary heart disease and cerebral infarction. Atherosclerosis. 59: 199-204, 1986.

30. Nagashima K, Yutani S, Miyake H, Onigata K, Yagi H, Kuroume T: Lp (a) levels in Japanese children with IDDM. Diabetes Care 16: 846, 1993.

31. Niskanen L, Mykkanen L, Karonen SL, Uusitupa M: Apoprotein (a) levels in relation to coronary Heart disease and risk factors in type II. Cardiovasc Risc Factors 13: 205-210, 1993.

32. Ramirez LC, Arauz - Pacheco C, Lcackner C, Albrıht G, Adams BV, Raskin P: Lp (a) in DM relationship to metabolic control. Ann Intern Med. 117: 42-47, 1992.

33. Ritter MM, Richter Wo, Lyko K, Schawanelt P: Lp (a) serum concerntrations and metaboilc control (letter). Diabetes Care 15: 1441.

34. Rosengren A, Wilhelmsen L, Erikkson E, Riserg B, Wedel H: Lp (a) and coronary heart disease: A prospective case control study in a general population sample of middle-aged men. BMJ 301: 1248-1251, 1990.

35. Scanu AM, Fless GM: Lp (a). Heterogenity and biological relevance. J Clin Investigation 85: 1709-15, 1990.

36. Schernthaner G, Kostner GM, Dieplinger H, Prager R, Muhlhauser I: Apolipoproteins (A-I, A-II, B): Lp (a) lipoprotein and lechitin cholestrol acyl-transferase activity in diabetes mellitus. Atherosclerosis 49: 277-293, 1983.

37. Sonnichsen AC, Richler WO, Schwandt P: Reduction of Lp (a) by weiht loss. Int J Obes 14: 487-490, 1990.

38. Takegoshi T, Haba T, Hirai JL, Kioh C, Saga T, Yamazatei Y, Mabuchi: Alterations of Lp(a) in patients with diabetic nephropathy (Letter) Atherosclerosis 83: 99-100, 1990.

38. Taskinen MR- Enholm C, Jaubianen M, Kauppinen-Makelin R, Ykiwarvinen H, FINMIS group: The concentration of Lp (a) is not influenced by the degree of glycemic control in NIDDM (Abstract) Proc 9th International Symposium on Atherosclerosis Rosemont, IL, p. 196, 1993.

40. Utermann G, Menel NJ, Kraft HG, Duba HC, Kemler HG, Seitz C.: Lp (a) glycoprotein phenotypes. Inheritence and relation to Lp (a) lipoprotein concentrations in plasma. J Clin Invest. 80: 458-465, 1987.

41. Utermann G, Hoppichler F, Dieplinger H, Seed M, Thompson G, Boerwinkle E: Defects in the LDL receptor gene affect Lp (a) lipoprotein levels: multiplicative interactions of two gene loci associated with premature atherosclerosis. Proc. Natl Acad Sci USA 86: 4171-4174, 1989.

42. Velho GF, Erlich D, Turpin E, Neel D, Cohen D, Froguel P, Passa P: Lp (a) in diabetic patients and normoglycemic relatives in familial NIDDM Diabetes Care 16: 742-747, 1993.

43. Wincour PH, Bhatnagar D, Ishola M. Arrol S, Durrington PN: Lp (a) and macrovascular disease in type I (insulin-dependent diabetes Diabetic Med 8: 922-927, 1991.

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ELECTROENCEPHALOGRAPHIC CHANGES IN PATIENTS WITH PULMONARY TUBERCULOSIS

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SUMMARY

Study objective: To determine the incidence of electroencephalographic (EEG) abnormalities in patients with previously untreated pulmonary tuberculosis.

Design: A prospective study with electroencephalographic evaluations.

Setting: A university hospital-Department of Chest Diseases and Tuberculosis, Turkey.

Patinets: Seventeen patients with previously untreated pulmonary tuberculosis.

Measurements and results: Bacteriologic, radiographic and electroencephalographic evaluations were performed before and after antituberculosis treatment. EEG abnormalities was found in 8 patients (47%). After nine months of antituberculosis treatment, 6 of those 8 patients who had abnormal EEGs before treatment, showed normal or alleviated EEG findings.

Conclusion: EEG abnormalities can be detected in patients with previously untreated tuberculosis After antituberculosis therapy these abnormalites can be normalized or alleviated

Key Words: *Pulmonary tuberculosis. Electroencephalography*

Among systemic features of tuberculosis, neuropsychologic manifestations can be developed (7,9). Some investigators have suggested that the tuberculosis intoxication can cause these alterations in CNS (3). However, the mechanisms of CNS alterations in patients with tuberculosis are still not clear. Thus, further investigations which would elucidate the relationship between tuberculosis and CNS alterations are needed. This study was undertaken to determine the incidence of EEG abnormalities in patients with previously untreated pulmonary tuberculosis.

METHODS

Between June, 1994 and April, 1995, seventeen patients (n=17) with previously untreated pulmonary tuberculosis, referred to the University Hospital, were recruited for the study. None had a history of epilepsy, alcholism, drug abuse, severe head injury, cerebro vascular disease, migraine or other neurological or psychiatric disorders. Neurological examination was normal. No history of current or prior seizures was revealed. Blood chemistries were in the normal range.

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The diagnosis of tuberculosis was based upon clinical findings, demonstration of acid-fast bacilli (AFB) in smear or culture of sputum, and pulmonary tuberculous lesions on the chest roentgenogram.

The radiographs were independently interpreted by two experienced readers. Radiological classificaiton of disease extent was evaluated according to the National Tuberculosis Association of the U.S.A. (11).

Four-drug regimen [isoniazid (H)+rifampicin (R) + pyrazinamide (Z) + streptomycin (S)] (2SHRZ/7HR) for 9 months was given to the patients. At the end of ninth month control evaluation (clinical, bacteriologic, roentgenographic, and electroencephalographic) was performed for patients who had EEG abnormalities before treatment.

Eight-channel EEG registrations were made (Nihon Kohden EEG-5208). Ag/AgCl electrodes were applied to the scalp with collodion in accordance with the international 10-20 system. The EEG was recorded during at least 30-45 min. with the awake subject lying in a semidarkened room (eyes closed).

RESULTS

Table I shows the demographic data of the patients. All patients had smear and culture positivity for AFB. Radiologic findings of disease extent were as follows: minimal in 2 patients (11.8%), moderately advanced in 10 patients (58.8%), and far advanced in 5 patients (29.4%). Clinically, none of our patients had cyanosis and respiratory distress.

Out of 17 patients eight patients (47 %) had electroencephalographic abnormalities. Table II demonstrates the EEG findings before and after 9-month treatment of 8 patients who had abnormal EEGs before treatment. Six (75%) of them completed their treatment with clinical, bacteriologic and radiographic improvement. No side effects were obsered during the treatment. Control EEG recordings were not done for two patients because of their poor compliance during the treatment.

DISCUSSION

In this study we found the abnormal findings in patients with previously untreated pulmonary tuberculosis. It has been well recognized that abnormal EEG findings could be detected in patients with tuberculoma of the brain. These tuberculomas even can cause epileptic seizures (5, 6, 8). However, in a study, the abnormalities on EEGs have been found

Table I. Demographic data of enrolled patients.

No. of patients	17
Gender	
Male	10
Female	7
Age (years)	
mean ± SD	36.12 ± 18.01
range	17 - 71

Table II. Electroencephalographic changes in patients of the study

No.	Sex	Age (yr)	EEG findings	
			Before Treatment	After Treatment
1	F	17	Left temporal intermittent theta activity	Normal
2	M	38	Paroxymal generalized sharp wave bursts, most prominent in the temporoparietal region	Bitemporal paroxysmal sharp activity
3	F	38	Paroxymal generalized sharp wave bursts more prominent in the temporoparietal region	Bitemporo - parietal paroxysmal theta activity
4	M	32	Bitemporal paroxysmal theta activity	Normal
5	M	33	Paroxysmal generalized theta and sharp wave bursts	———
6	F	71	Generalized background activity, bitemporal paroxysmal slow and sharp activity	Normal
7	F	55	Bitemporal paroxysmal theta activity	Right temporal focal theta paroxysms
8	F	18	Bitemporal paroxysmal theta activity	———

also in chronic pulmonary tuberculosis patients without intracranial tuberculoma. They had been suffered from severe respiratory distress, and it has been shown that EEG abnormalities increased with lowered arterial blood pH, elevated arterial blood pCO2, and lowered oxygen saturation rate (10). In contrast, Chelnokova and coworkers (3) have suggested that the abnormalitieosn EEGs of patients with pulmonary tuberculosis are due to tuberculous intoxication process affecting CNS. They have demonstrated the abnormal EEG findings in 54.7 % of tuberculosis patients who had had extensive disease and severe symptoms; 25 % of those patients had epileptiform abnormalities (3). Broşteanu has reported that 13 % of the reactivated tuberculosis cases had marked EEG alterations (2). In our study, almost half of our patients had EEG changes. In general population, 5 % of abnormal (epileptiform) EEG findings have been reported (1).

A further interesting finding of the present study is normalization or alleviation of abnormalities on EEG after antituberculosis treatment.

In summary, in view that some antituberculosis drugs, such as ethionamide and cycloserine are neurotoxic and can cause abnormalities on EEGs (4, 12), the further investigations which would elucidate the mechanism of alterations of CNS in pulmonary tuberculoisis are required.

REFERENCES

1. Ansgar M: Epilepsien: Diagnostik und therapie für klinik und praxis, 4. ed. 1984 Stuttgart: Georg Thieme Verlag, page: 3.
2. Broşteanu R: The value of electrophysiological investigations in the rehabilitation of former tuberculosis patinets. Electroenceph Clin Neurophysiol 27: 632, 1969.
3. Chelnokova NV, Starostenko EV, Salpagarov AM, Kruglova EG: dysfunctions in the central nervous system in polmonary tuberculosis patients. Probl Tuberk 8:46-48, 1991.
4. Chelnokova NV, Starostenko EV, Salparagov AM, Simirnova NA, Kruglova EG: Biochemical mechaanisms of neurotoxic reactions to antibacterial preparations in pulmonary tuberculosis patinets. Probl Tuberk 1-2: 8-10, 1992.
5. Fegan D, Glennon J: Epilepsy and disappearing lesions: adapting a wait and see policy. BMJ 302: 1402, 1991.
6. Gorska-Kowalska J, Bukowska-Nierojewska D, Pawlukiewicz M: A case of tuberculoma of the brain in a young patient. Pneumonol Alergol Pol 59: 59-62, 1991.
7. Hopewell PC: Mycobacterial diseases. In: Murray JF, Nadel JA, eds. Respiratory medicine, 1988 Phidalephia: WB Saunders, pages: 856-915.
8. Kioumehr F, Dadsetan MR, Rooholamini SA, Au A. Central nervous system tuberculosis: MRI. Neuroradiology 36:93-96, 1994.
9. Moran MG: Psychiatric aspects of tuberculosis. Adv Psychosom Med 14:109-118, 1985.
10. Otomo E, Mikami R: Clinical studies on the relationship of the electroencephalogram to pH and pCO2 in arterial blood. Neurology 15:1063-1070, 1965.
11. Seaton A, Seaton D, Leitch AG: Crofton and Douglas's respiratory diseases, 4th ed. 1989 Oxford: Blackwell Scientific Publications, page: 409.
12. Swash M, Roberts AM: Reversible pellagra-like encephalopathy with ethionamide and cycloserine. Tubercle 53:132-136, 1972.

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RADIOLOGICAL JOINT DAMAGE IN RHEUMATOID ARTHRITIS: RELATIONSHIP WITH CERTAIN VARIABLES

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SUMMARY

This cross-sectional study, in a group of 50 rheumatoid arthritis patients, was designed to elucidate the relationship between radiographic joint damage and various factors such as age, disease duration, seropositivity, hand deformity, gip strength, hand disability, functional capacity and general disability.

Our results showed that radiographic scores, reflecting the joint damage, was significantly correlated with the disease duration, hand deformity and grip strength. Additionally, an association between radiologic status and current functional health status as measured by Stanford Health Assessment Questionnaire, Hand Disability Index and Steinbrocker Functional Index was demonstrated. When we studied the contribution of the above factors to the variation of the radiologic scores by multiple regression analysis, we found that hand deformity, grip strength and disease duration were the primary variables explaining the variation in the total radiographic score. Seropositivity was a significant factor only in the exp;lanation of the variation in radiographic erosion scores.

These data suggest that radiographs of hands and wrists are deflection of disease nature. It is appropriate to use this tool in the assessment of long term outcome and disability in rheumatoid arthritis.

Key words: *Disability, functional ability, outcome, radiological damage, rheumatoid arthritis.*

Destruction of bone and cartilage is a regular consequence of persistent, active synovitis in rheumatoid arhritis (RA). Because of the predilection for this destructive pathology in the small joints of hand and wrist, a number of investigators have proposed that in these joints would represent an index of disease outcome (22). Consequently, plain radiographs of hands and wrists have been widely used in clinical practice to diagnose rheumatoid arthritis (11), to assess severity and progression of disease (15), to make decisions about medical and surgical interventions (6,8,11) and to evaluate pharmacotherapeutic efficacy (18). Additionally, early in the disease, this tool is used as a prognostic indicator of future progression and risk of deformity (21), serios joint damage (2) and poor outcome (3).

Decreased functional status is the final common result of uncontrolled RA so the measurement of the outcome both in short and long term is very important. According to Fries, outcome is the end result of the disease whereas the process is merely what happens along the way to a certain outcome (7) Radiographic joint damage is a result of the disease which may ultimately effect joint alignment, joint function and cause disability (12).

Herein, we designed this study, in a group of RA patients to assess to what extent radiographic joint damage was related to the current functional health status. The correlation between the radiologic status and various factors such as age, disease duration, seropositivity, hand deformity, functional capacity, hand disability and general disability was determined.

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PATIENTS AND METHODS

The study population included 50 consecutive patients (39 women, 11 men) seen at Physical Medicine & Rehabilitation Department at Ibni Sina Hospital. All the patients met the criteria of American Rheumatism Association (ARA) 1987 revised criteria for rheumatoidt arthritis (1).

All patients received an extensive evaluation including seropositivity, hand deformity, single posteroanterior (PA) radiographs of both hands and writsts, grip strength, functional capacity, hand disability and general disability all within the same week. The assessment of all patients was done by the same observer.

Seropositivity was searched by latex agglutination test and defined as rheumatoid factor positive or negative.

Both hands of all patients were examined to detect the presence of uncorrectable ulnar deviation, swan neck and button hole deformities. Uncorrectable ulnar deviation was considered to be present if the deformity coult not be corrected by the patient. Each deformity on every finger was recorded and a hand deformity index of each hand was formed by the mean of the total number of all deformities in that hand.

Grip strength of both hands was measured by a vigorimeter (kPa/cm2).

General disability was assesed by Stanford Health Assessment Questionnaire (SHAQ) (9). In this questionnaire, functional ability was measured in 8 general component categories; dressing and grooming, arising, eating, walking, hygiene, reach, grip strength, and outside activities; by a total number of 21 questions. The difficulty in performing each activity was scored on a scale 0 to 3 (0 = without and difficulty, 2= with much difficulty, 3 = unable to do). Hand disability was evaluated by a special hand disability index which was formed by the seven items included in SHAQ (5,14) Both instruments are widely used for functional assessment in rehabilitation medicine and the appropriate modifications were made so as to adapt them to Turkish conditions. Questions included in hand disability index are shown in Table I. The total score of SHAQ was calculated as the mean of all answers (range = 0-3) and hand disability was calculated as the sum of scores of the seven items (range = 0-21).

Functional capacity was evaluated by Stein brocker index (24). Details of this index is shown in table II.

Radiographs of the hands and wrists were assessed by the same radiologist. The hand and wrist joints were evaluated for joints space narrowing, erosion and malalignment by the method explained by Kaye et al (13). Schema of hand joints which were evaluated for the above indices are shown in Figure I. Scoring options for joints pace narrowing were 0=normal, 2=mild, 3=moderate, 4=severe, 5=ankylosis. Scoring options for erosion were 0=normal, 2=mild, 3=moderate, 4=severe. Scoring options for malalignment were 0=normal, 2=subluxation and 4=dislocation. No equivocal results (=1) were used. Overall, 40 readings were recorded for each hand, including 14 joints space narrowing scores, 11 erosion scores and 15 malalignment scores. Joints that could not be evaluated for any of the 3 radiographic findings (e.g., joints with dislocation or subluxation that could not be read for joint space narrowing) were recorded as missing in that category of evaluation and were not included in the computation of mean scores. Joints

Table I: Questions included in Hand Disability Index.

ARE YOU ABLE TO
Dress yourself, including trying shoelaces and doing buttons?
Cut your meat?
Lift a full glass to your mouth?
Open a new milk or juice carton?
Open room doors?
Open jars which have been previously opened?
Turn taps on and off?

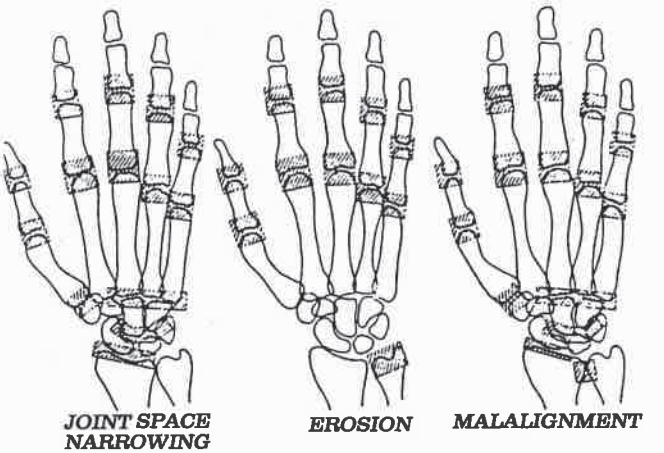

Figure 1. Schema of hand joints, evaluated quanhtitatively for joint space narrowing, erosion, or malalignment.

Table II. Steinbrocker Functional Index

Grade	Definiton	Description
I	Fit for all activities	Complete ability to carry out all usual duties without handicap
II	Moderate restriction	Adequate for normal activities, despite handicap or limited motion at one or more joints
III	Marked restriction	Limited only self-care and little or none of the duties of normal occupation
IV	Confined to chair or bed	Incapacitated, largely or wholly bedridden or confined to wheelchair or no self-care

From Steinbrocker et al. (24)

Table III. Demographic, clinical and radiological characteristics of the patients.

	MEAN ± SD	RANGE
Age 48.2 ± 15.1	16-80 years	
Disease duration	8.3 ± 7.2	1-30 years
Grip strength	24.81 ± 22.25	0-91
R-	26.12 ± 22.55	
L -	24.16 ± 22.43	
Hand deformity	0.40 ± 0.50	0-2
R-	0.41 ± 0.54	
L-	0.38 ± 0.50	
Hand disability	8.08 ± 5.55	0-21
General disability	1.18 ± 0.79	0-3
Total radiographic score	1.36 ± 0.66	0-4
R-	1.39 ± 0.66	
L-	1.35 ± 0.64	
Joint space narrowing	2.25 ± 0,98	0-5
R-	2.22 ± 1.01	
L-	2.32 ± 0.98	
Erosion	1.88 ± 0.89	0-4
R-	2.01 ± 0.86	
L-	1.84 ± 0.88	
Malalignment	0.26 ± 0.49	0-4
R-	0.29 ± 0.52	
L-	0.24 ± 0.54	

with the evidence of prior articular surgery were presumed to be severly effected, and were assigned erosion and joint space narrowing scores of 4, but malalignment was assessed for subluxation and dislocation as above. The mean of all scores were determined. The total radiographic score calculated was the mean of the 40 individual scores. The mean, rather than the total, was used in the analysis, to adjust for joints that could not be evaluated.

Storage and the analysis of the data were accomplished using the Statistical Package for the Social Sciences (SPSS) software program. Tests used were simple correlation analysis, stepwise multiple regression analysis, chi-square and t-test.

RESULTS

Demographic, clinical and radiologic characteristics of patients are shown in Table III. The mean age was 48 years and the mean disease duration was 8.3 years.

27 patients (54 %) showed deformity. Almost all patients showed erosion and joint space narrowing in their hand and wrist joint radiographs but malaligment was seen in 21 patients (42%) only. 9 patinets were in steinbrocker functional grade III or IV whereas 41 patients were in grade I or II. 39 patients showed seropositivity.

Table IV. Correlations of total radiographic score and joint space narrowing, erosion, malalignment scores with various factors.

	Total radiographic scone correlation coefficent (r)	Joint space narrowing (r)	Erosion (r)	Malalignment (r)
Age	0.28***	0.22	0.30***	0.13
Disease duration	0.50*	0.56*	0.44*	0.34**
Grip strength	-0.58*	-0.55*	-0.48*	-0.42**
Hand deformity	0.63*	0.62*	0.48*	0.55*
Hand disability	0.51*	0.48*	0.35*	0.25
General disability	0.50*	0.55*	0.36**	0.42***

*p < 0.001, ** p < 0,01, *** p < 0.05

All the patients were right handed and no siginificant difference was found between the right and left hand regarding grip strength, hand deformity, joint space narrowing, erosion, malalignment scores and total radiographic scores ($p>0.05$). So mean scores of the right and left hand for the above indices, were used in the statistical analyses.

Table IV. represents the correlations of total radiographic score and joint space narrowing, erosion, malalignment scores with various factors. The total radiographic score and joint space narrowing, erosion, malalignment scores were significantly correlated with the disease duration.

A significant correlation between total radiographic score and age was found although the correlation coefficient was low ($r=0.28$), showing a weak correlation. The strongest factor correlating-with the total radiographic score was hand deformity ($r=0.63$) The other correlating factors with the same varible were grip strength ($r=-0.58$), hand disability ($r=0.51$), general disability ($r=0.50$) and disease duration ($r=0.50$).

We found that patients in worse functional garde showed more radiological deterioration. Thus, total radiographic score the patients in functional grade III, IV and in grade I, II were 1.85 ± 0.32 and 1.26 ± 0.61, respectively ($p < 0.01$).

Multiple stepwise regression analysis were performed to assess the relative contribution of age, disease duration, hand deformity, grip strength, hand disability, functional grade, seropositivity to explain the variation in radiological status. The analysis revealed that the best set of powerful predictor variables of radiographic scores were hand deformity, grip strength and disease duration which colud explain the 54 % (R^2: 0.54, $p < 0.001$) and 56 % (R^2: 0.56, $p<0.001$) of the variation in total radiographic score and in joint space narrowing score, respectively. Variation in erosion scores was explained significantly by grip strength, disease duration and seropositivity (R^2: 0.43, $p < 0.001$). Hand deformity could explain 39% of the variation in malalignment scores (R^2:0.39, $p<0.001$).

DISCUSSION

Radiographs represent a biologic end point resulting from inflammatory and enzymatic destruction of cartilage and subchondral bone (17). The principal radiographic changes-bone erosions and cartilage loss-are mainly related to rheumatoid pannus and possible mechanisms involve enzymes such as collagenase, soluble factors such as catabolin, chondrocyte dedifferentiation and mesenchymal cell proliferation which are regarded as the chronic phase of RA and are only indirectly related to the mechanisms of the acute synovitis in the acute phase (19).

Rheumatoid arthritis extends over an average course of 25 years so the health status at a selected time point is significantly effected by the accumulated past damage (7). It is of paramount importance that we have to minimize the overall impact of the disease overtime without neglecting the potential longterm difficulties.

The current study is cross-sectional, correlating the degrees of abnormalities seen on hand and wrist radiographs with various factors including contemporaneous functional health status. Disease activity was not taken into consideration depending on the previous reports stating that radiographs are not expected to reflect current imflammatory activity adequately (16).

Almost all our patients had radiological changes reflecting the disease nature. Radiologic changes and hand deformity were somewhat higher for the rihgt hand than the left hand, but the differences were not statistically significant neither for deformity nor for the radiological status, as reported before (10).

Rheumatoid arthritis is a chronic disease with major impact on functional ability which is usually concerned with the performance on activities of daily living and functional outcome assesses this disability. Sherrer reported that 90% of 681 RA patients with a mean disease duration of 22 yeras had functional disability by SHAQ score of greater than zero and he also found that the best predictors of disability in the population were age, radiologic grade, sex and initial functional class (23). An association of radiographic scores with impaired funciton as measured by SHAQ has also been observed by Sharp (20). In another study, it was emphasized that radiographic joint space narrowing and anklyosis was a relatively common feature of RA, and a marker of patients whose disease was clinically and functionally more severe (13). In our study, we demonstrated a correlation between radiological status and SHAQ scores, functional index, supporting the above studies. Regan and cowokers reported a lack of correlation between the severity

of abnormalities observed on hand radiographs and funcitonal health status (17) but in that study, the authors used a method of radiological evaluton which is the oldest in this filed and the changes were not quantitatively assessed.

Prevention of hand disability as well as general disability must be one of the chief aims of RA therapy since manual dexterity is crucial in our daily life. It was reported that there was some loss of hand function associated with increasing radiographic joint damage. In the same study, grip strength correlated with the jonit damage strongly (18). The present study revealed significant and strong correlations of total radiographic score with hand disability and grip strength. Also regression analysis showed that grip strength, an indicator of hand function, was a significant variable explaining the variation in the radiologic status.

Fuchs reported their finding of a relationship of radiographic scores with the disease duration and deformity which also had the most predictive power for the explanation of the variation in radiologic scores (10). In another research, it was emphasized that there was an association between radiographic damage and disease duration, hand function, hand and wrist deformities (21). The results of our study support the findings of the both studies.

Seropositivity appeared to be a significant variable contributing to the explanation of variation in erosion scores confirming the suggestion of Burns and Calin (4).

Overall, our data suggest that radiographs of hands and wrists reflect the history of the joint pathology in rheumatoid arthritis and do relate to disease duration and hand deformity. The association between radiological status and disability strongly support that it is appropriate to use hand and wrist radiographs to assess the disaese severity and the impact of RA on the life and functional capacity of the individual patient.

REFERENCES

1. Arnett FC, Edwarth SM, Bloch DA, Mchhane DJ, et al.: The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 31: 315-324, 1988.
2. Brook A, Corbett M: Radiograph changes in early rheumatoid arthritis. Ann Rheum Dis 36:71-73, 1977.
3. Brook A, Fleming A, Corbett M: Relationship of radiological change to clinical outcome in rheumatoid arthritis. Ann Rheum Dis 36: 274-275, 19877.
4. Burns TM, Calin A: The hand radiograph as a diagnostic discriminant between seropositive and seronegative rheumatoid arhtritis; a controlled study. Ann Rheum Dis 42: 605-612, 1983.
5. Eberhart K, Johnson PM, Rydgren L: The occurence and significance of hand deformities in early rheumatoid arhtritis. Br. J Rheumatol 30: 211-213, 1991.
6. Edwards JCW, Edwards, SE, Huskisson EC: The value of radiography in the management or rheumatoid arthritis. Clin Radiol 34: 413-416, 1986.
7. Fries JF: Toward an understanding of patinet outcome measures. Arthritis Rheum 26: 697-704, 1983.
8. Fries JF, Bloch DA, Sharp JT, MC Shane DJ, et al: Assessment of radiologic progression in rheumatoid arthritis: a randomized controlled trial. arthritis Rheum 29: 1-9, 1986.
9. Fries JF, Spitz P, Kraines RG, et al: Measurement of patinet outcome in arthritis. Arthritis Rheum 23: 137-145, 1980.
10. Fuchs HA, Callahan LF, Kaye JJ, Brooks RH, et al: Radiographic and joint count findings of the hand in rheumatoid arthritis; related and unrelated findings. Arthritis Rheum 31: 44-51, 1984.
11. Hartley RM, Liang MH, Weismann BM, Sasman JL et al: The value of conventional views and radiographic magnification in evaluating early rheumatoid arthritis. Arthritis Rheum 27: 744-751, 1984.
12. Heide A, Jacobs JWG, Dinant HJ, Bijlsma JWJ: The impact of end point measures in rheumatoid arthritis clinical trials. Semin Arthritis Rheum 21: 287-294, 1992.
13. Kaye JJ, Callahan LF, Nance EP, Brooks R, et al: Bony ankylosis in rheumatoid arxhritis; Associations with longer duration and greater severity of disease. Invest Radiol 22: 303-309, 1986.
14. Küçükdevci AA, Dalyan M, Gök H, Ergin S: Hand disability in rheumatoid arthritis. J Rheum Med Rehab 6(1): 6-10, 1995.
15. Larsen A: The value of individual joints for radiologic assessment of rheumatoid arthritis. Scand J Rheumatol 5: 119-123, 1976.
16. Pinals RS, Masi AT, Larsen RA: Preliminary criteria for clinical remission in rheumatoid arthritis. Arthritis Rheum 24: 1308-1315, 1981.
17. Regan-Smith MG, O'Connor GT, Kwah CK, Brown LA, et al: Lack of correlation between the Steinbrocker staging of hand radiographs and the functional health status of individuals with rheumatoid arhritis. Arthritis Rheum 32: 128-133, 1989.

18. Scott DL, Coulton BL, Bacon PA, Popert AJ: Methods of X-ray assessment in rheumatoid arthritis; a re-evaluation Br. J Rheumatol 24: 31-39, 19856.
19. Scott DL, Dowes PT, Fowler PP, Grindulls KA, et al.: Anti-rheumatic durgs and joint damage in rheumatoid arthritis. Quart J Med 54: 49-59, 1985.
20. Sharp JT: Radiologic assessment as an outcome measure in rheumatoid arthritis. Arthritis Rheum 32: 221-229, 1989.
21. Sharp JT, Lidsky MD, Collins LC, Moreland J: Methods of scoring the progression of radiologic changes in rheumatoid arthritis: correlation of radiologic, clinical and laboratory abnormalities. Arthritis Rheum 14: 706-720, 1971.
22. Sharp JT, Young DY, Bluhm GB, Brook A, et al.: How many joints in the hands and wrists should be included in a score of radiologic abnormalities used to asssess rheumatoid arthritis. Arthritis Rheum 28: 1326-21335, 1985.
23. Sherrer Ys, Daniel AB, Donald MM, Donald YY, et al.: The devolepment of disability in rheumatoid arthritis. Arthritis Rheum 29: 494-500, 1986.
24. Steinbrocker O, Traeger CH, Batmann RC: Therapeutic criteria in rheumatoid arthritis JAMA 140: 659-662, 1949.

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URINARY TUBERCULOSIS: HOW DID WE DIAGNOSE AND MANAGE GENITO-URINARY TUBERCULOSIS?

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SUMMARY

This study was designed to show our experience of urinary tuberculosis in Gülhane Military Medical Academy and Faculty, Department of Urology. It was a retrospective study involving 60 patients (51 male, 9 female). The study period was between 1982-1992. The mean age was 30.4 (7-80). Cases were identified by:

1) Review of diagnosis on discharge during the study period

2) Review of consultations performed by urology department

3) Review of all cases in which Mycobacterium Tuberculosis organisms were cultured from sites other than sputum and gastric washings

4) Review of all cases in which the histologic diagnosis were extrapulmonary tuberculosis.

The charts of patient swith suspected genitourinary tuberculosis were reviewed. Management always included appropriate chemotherapy and surgery when indicated. The complete recovery rate was 70%, while acceptable results were shown in 13.3%.

It is concluded that genitourinary tuberculosis remains an important infectious disease problem in our country and given appropriate treatment, patients can be cured. But we must investigate genitourinary tuberculosis with other infections.

Key Words: *Tuberculosis, Genitourinary System.*

Genitourinary tuberculosis is secondary to hematogenous spread from pulmonary tuberculosis and remains a problem in areas of the world where health conditions are poor and adequate chemotherapy is not available. Urinary tuberculosis is a disease of young adults (60% of patients are between the ages of 20-40). The kidney and posibly the prostate are the primary sites of tuberculosis in the genitourinary tract (2,6). All other genitourinary organs become involved either by ascent (prostate to bladder) or descent (kidney to bladder; prostate to epididymis). The testes may become involved by direct extention from epididymal infection (1).

There is no classic clinical picture for genitourinary tuberculosis. Tubercle bacilli may invade one or more of the organs of the genitourinary tract and cause chronic granulomatous infection that shows the same characteristcs as tuberculosis in other organs. If you evaluate the patients with chronic, unexplained symptoms of urinary system and with present or past history of tuberculosis, you see that many cases of urogenital tuberculosis can be discovered and it is not, as sometimes quoted "a once in a lifetime diagnosis"(1).

PATIENTS AND METHODS

The study population includes the patients with genitourinary tuberculosis seen in Gülhane Military Medical Faculty, Urology department from 1982 to 1992. Cases were identified by:

1) Review of diagnosis on discharge during the study period

2) Review of consultations performed by urology department

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3) Review of all cases in which Mycobacterium Tuberculosis organisms were cultured from sites other than sputum and gastric washings.

4) Review of all cases in which the histologic diagnosis were extrapulmonary tuberculosis.

The charts of patient with suspected genitourinary tuberculosis were reviewed. Criteria for the diagnosis of genitourinary tuberculosis were strict. Isolation of M. tuberculosis was the evidence of active tuberculosis. Positive urine cultures indicated infection of kidney ureter or bladder. Adequate cultures were not obtained for all patients, with inadequate or negative cultures were still classified as having genitourinary tuberculosis if they had histologic proof of granulomatous inflamation plus compatible clinical roentgenographic and skin test findings.

Sixty patients with genitourinary tuberculosis were identified. They ranged in age from 7 to 80 years (mean 30.4 years). The group included 9 women and 51 men. The anatomic locations of infection in 60 patients with genitourinary tuberculosis were at table 1.

Table 1: The Locations

LOCATION	NUMBER OF CASES	PERCENTAGE
Kıdney	25	42
Ureter	2	3.3
Bladder	8	13
Prostate	2	3.3
Epididymis	15	25
Testes	8	13

For 9 women, the site of infection was the kidney. We didn't find any sign of female genital tract tuberculosous infection. Three women and fifteen men had active tuberculosis with positive cultures. Twenty patients had past history of tuberculosis. But they had never received chemotherapy. In all of 20, infection was pulmonary tuberculosis. Twenty patients (10 were the cases with the past histories of tuberculosis) had scarring or calcification on their chest roentgenograms compatible with previous clinically silent tuberculosis.

RESULTS

The presenting symptoms focused largely on the genitourinary tract (77% of cases) (Table 2).

Table 2: Presenting symptoms and signs.

SYMPTOMS and SIGNS	NUMBER	PERCENTAGE
Edididymitis	12	20
Frequency, burning	24	40
Hematuria	18	30
Renal colic	6	10
Albuminuria	6	10
Hematospermia	3	5
Painless mass in scrotum	8	13
No genitourinary symptom	14	23

Symptoms of urinary irritation was the commonest initial symptom of genitourinary tuberculosis in our group. Hematuria was the next most common symptom, and painless, total hematuria. Epididymitis was more commonly at rigth side. Renal colic, albuminuria and hematospermia were all found occasionally.

Elapsed time between the first symptom and the diagnosis of urinary tuberculosis varied from 1 month to 24 years after the patient had brief, period of symptoms, which then subsided and remained quiescent for many months or years, before recurring and causing the patient to seek medical aid.

The patients who had no genitourinary symptoms and in whom a diagnosis of renal tuberculosis was made, were a heterogenius group. In three patinets, culture of a draining sinus finally made the proper diagnosis. One of these had a pyelolithotomy sinus, another a suprapupic fistula. In the others, urine smear was positive while the chest signs and symptoms were being evaluated. Vague generalized malaise, fatigability, low grade but persistent fever and night sweats were some of the non-specific complaints. Physical examination was rarely diagnostically helpful. In thirty-two cases there were no abnormalities related to tuberculosis. Five patients had signs of active tuberculosis and four had stigmas of old tuberculosis. A thickened, nontender or slightly tender epididymis was discovered in 10 of cases. In 2 cases, a chronic sinus through the scrotal skin was pathognomonic of tuberculous epididymitis. In four of them, the epididymis could not be differentiated from the testis with palpation. In four cases, hydrocele accompanied tuberculous epididymitis. In four of them, the epididymis could not be differentiated from the testis with palpation. In four cases, hydrocele accompanied tuberculous epididymitis. In 4 of 15 cases with epididymitis, ipsilateral seminal vesicle was indurated, enlarged and fixed.

Laboratory findings: Proper urine analysis afforded the most important clue to the diagnosis of genitourinary tuberculosis. Ninety percent of cases had abnormality of the sediment.

1) Persistent pyria without organisms on culture or on smear staint with methylene blue meant tuberculosis until proved otherwise (At 17 cases). Acid-fast stains done on the controlled sediment from a 24 hour specimen were positive in at least 50% of cases.

About 12 of patients with tuberculosis had secondary pyogenic infections, the clue (sterile pyuria) was thereby obscured. If clinical response to adequate treatment failed and pyuria persisted, tuberculosis had to be ruled out by bacteriologic and roentgenologic means. We did this and obtained positive culture results.

2) Culture for tubercle bacilli form the first morning urine were positive in a very high percentage of cases of tuberculous infection. M. tuberculosis was isolated from at least one urine specimen in 34 patients.

Only ten patients were anemic, and renal function, however, was well preserved. Five patients had azotemia. In three, this was due to other causes where as in two azotemia couldn't be explained only by tuberculosis.

The diagnosis of tuberculosis was established clinically in 45 patients. In nine patients, tuberculosis was an unexpected pathologic finding (discovered at operation). Intradermal skin tests were positive in 20 of 21 patients tested. Urine cultures were of even great diagnostic significance. M. tuberculosis was isolated from at least one urine specimen in 50 patients. In 9 cases, only post-operative specimens were cultured and antituberculous therapy had already been started.

Intravenous pyelograms were obtained in 34 patients and were abnormal in 32. In 8 patients, the abnormalities were mild, consisting of calyceal on pelvic dilation or deformity limited to one kidney with normal excretion of contrast material and normal ureters and bladder.

Ten patients had moderate abnormalities or unilateral destructive changes including focal calcification, dilatation or unilateral destructive changes including focal calcification dilatation or unilateral destructive changes including bilateral calyceal dilatation, small cavities or filling defetcs, cortical scarring or nonvisialization of one calyx. At 12 patients, intravenous pyelograms showed advanced disease at the time of diognosis, including destructive lesions in both kidneys or major unilateral damage, such as large cavities or autonephrectomy. These advanced changes reflected ongoing tuberculous infection for substantial periods of time prior to diagnosis. Retrograde pyelograms and renal arteriograms corraleted well with intravenous pyelograms and were not diagnostically helpful. At some cases for the management of therapy renal scanning gave us information of functional renal tissue and information as to the extent of the disease. Cystoscopy was really of little importance genitourinary tuberculosis. We used cystoscopy to assess the extent of the disease in the bladder and the response of the bladder to chemotherapy. Bladder biopsy was used when tubercles were seen in the bladder of when an ulcer was present some distance from a normal, uteric orifice. Ultrasound was used to monitor kidney lesions and the volume of a contracted bladder during treatment. CT Scan was used in the early management of tuberculosis, because intravenous urography gave us accurate pictures (4,5). PROCEDURES ADOPTED IN ESTABLISHING THE DIAGNOSIS are shown at Table 3.

Table 3: The Procedures.

PROCEDURES	NUMBER DONE	POSITIVE FINDINGS	%
3 Direct Urine Smear	50	30	60
Plain X Ray of Chest	50	20	40
Plain X ray of Abdomen	40	22	55
Bilateral Renal Cal.		3	7.5
Unilateral Renal Cal.		15	37.5
Calcification Along-The Ureter		4	10
Intravenous Pyelogram	34	32	94
No Abnormality Detected	2		0.6
Mild Abnormality Detected		8	24
Moderate Abnormality Detected		10	29
Advanced Abnormality Detected		12	35
Cystoscopy	20	8	40
Normal Bladder		12	60
Patchy Cystytis		4	20
Small Capacity		2	10
Ulceration		1	5
Tubercles and Granulation Disease	1	5	
Biopsy During Cystoscopy	15	4	27
Renal Scanning	20	8	40
CT Scan	8	6	75

Treatment: Therapy was directed by numerous physicans and was not uniform. 25 patients were treated with chemotherapy alone; 30 patients were treated with both chemotherapy and surgery. No follow - up data was available in nine.

There was no uniformly recommended chemotherapeutic program. Patients with positive urine cultures but negative findings on urine analysis and normal urograms usually treated with isoniazid (200-300 mg oralliy once daily) and rifampin for one year. Patients with clinically manifest tuberculosis were usually treated with three antituberculous drugs such as isoniazid, etambutol (25 mg/kg daily for two months, then 15 mg/kg orally once dailly), and rifampin (600 mg orally once dailly) for two years. If the patient's initial urinary isolate was M. tuberculosis resistant to isoniazid or was one of the nontuberculous (atypical) myobacteria, isoniazid therapy should be continued, but two other drugs were chosen on the basis of invitro susceptibilities.

If, after 3 months with triple chemotherapy, cultures still positive and gross involvement of the affected kidney was radiologically evident, nephrectomy was performed. Twenty patients were treated with chemotreapy completely. The urine was studied bacteriologically every 3 months during treatment and then every year for 10 years. We determined that after 3 months of chemotherapy, the urine was sterile and at the end of one year-two years course chemotherapy, there were some signs of recovery radiographically. Five had persistently positive urine cultures on therapy, but all of them took medications erratically. After 6 months no follow-up data were available in these five patients.

Surgery continues to play an important role in the modern philosophy of the management of genitourinary tuberculosis. Fifty percent of our patients required some operative procedures.

The indications for nephrectomy were a nonfunctioning kidney, extensive disease involving the whole kidney, together with hypertension and pelviureteric obstruction. If it was decided that surgical treatment was essential, nephrectomy was performed between 3-6 months after the start of chemotherapy, so that we saw whether there was any well being with chemotherapy alone and the organisms were destroyed. We performed 15 nephrectomy and 3 partial nephrectomy. The indication for partial nephrectomy was a localized polar lession containing calcification which was slowly increasing in size and threating to destroy gradually the whole kidney (2).

There were two patients with stricture of the lower third of the ureter. A normal chemotreapy regime was started. If there was no deterioration or no improvement after three weeks of chemotreapy, corticosteroids, 20 mg t.i.d. was given together with other chemotherapy. but we didn't have any improvement and we performed surgical reimplantation (8).

The main indication for epididymectomy was a caseating abcess that was not responding chemotherapy. We performed epydidymectomy at two cases with fistulectomy for this indication. Another indication was a firm swelling that had remained unchanged or slowly increased in size, despite antibiotics and antituberculous chemotherapy because unsuspected malignancy of the epididymis might be present (9). We performed epididymectomy in five patients for this indication. And we performed orchidectomy at three patients; unsuspected malignancy of the testis might be present.

All patients were seen 3, 6 and 12 months after the course of chemotherapy had been completed. Every time, three consecutive early morning specimens of urine were examined. Intravenous urography was performed also. If the radiological appearences remained unalthered and the urine was persistently sterile, the patient is discharged with instructions to report back if there was any recurrence of the previous urinary symptoms. Results are shown at Table 4.

Table 4: Results of Treatment

RESULTS	ONLY CHEMO-THERAPY	SURGERY COMBINED WITH CHEMO-THERAPY	%
Complete Disappearance of Signs And Symptoms	20	22	70*
Partial Ameloration of Signs and Symptoms	—	8	13*
Failure of Treatment or Recurrence	5	—	8
No Follow-Up Data	5 Without Any Therapy		8

(*): Total

DISCUSSION

Tuberculosis is an acute or chronic infectious disease, which is usually caused by Myobacterium tuberculosis in Turkiye. Mycobacteria, customarily gain access to the human body by inhalation, although the bovine organisms may be acquired by ingestion of unpasteurized milk. After initiation of the tuberculous infection, a primary pathologic focus develops which usually heals spontaneously. In addition, the primary infection frequently results in an initial silent bacillemia that is responsible for systemic spread of mycobacterium with latent infection of many organs. These latent foci of tuberculous infection may break down and result in overt tuberclosis of the kidney or other part of genitourinary system. Bacillemia and seeding of the genitourinary system may also occur from a focus of progressive primary or reactivation tuberculosis in the lung or from clinically evident secondary tuberculosis in any other organs. Therefore any individual with previous tuberculous infection is at risk for development of genitourinary involvement(2).

Genitourinary tuberculosis is rarely an acute disease. And usually does not initially present with any severe episode. Urologist should thus consider the possility in patients who have presented on several occasions with vague urinary symptoms, usually combined with a lower urinary tract infection for which there is no obvious cause. Males predominant over females and 20 to 40 is the predominant age group (4,5). The urine is normally sterile on routine culture, and most patients have a high proportion of pus cells in the urine (6).

It is apparent that any patient with epydidymitis, hematuria or persistent urinary sympotms should be investigated for possible tuberculosis of the urinary tract. Lesions diagnosed before the disease had progressed were always easiest to treat. If the diagnosis is missed, the kidneys will bedestroyed in spite of our ability to control the disease with modern chemotherapy. Tuberculosis is a great imitator and any patient with unexplained symptoms in the urinary tract should be investigated for tuberculosis.

REFERENCES

1) Bortwick WM. Present position of urinary tuberculosis. Br. J. Urol. 42:642, 1970.
2) Emil AT. Specific infections of the genitourinary tract. Smith's General Urology. 12: 240-246, 1992.
3) Gow JG, Barbosa S. Genitourinary Tuberculosis. A study of 1117 cases over a period of 34 years. Br. J Urol 54:449-455, 1984.
4) Gow JG. Results of treatment in large series of cases of genitourinary tuberculosis and the changing pattern of the disease. Br. J. Urol. 42:647, 1970.
5) Gow JG. Genitourinary tuberculosis. Postgrad. Doctor. 8:37, 1985.
6) Gow JG. The current management of patients with genitourinary tuberculosis. AUA Update Serise. 26:202-207, 1992.
7) Harvey BS, Allan JW. Genitourinary tuberculosis. American J. of Medicine. 63:410-417, 1977.
8) Kerr WK, Gale GL, Peterson KSS. Reconstructive surgery for genitourinary tuberculosis. J. Urol, 101:254, 1969.
9) O' Flynn D. Surgical treatment of genitourinary tuberculosis. Br. J. Urol. 42:667, 1970.

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THE SELECTION OF ANTIBIOTICS IN DEEP NECK INFECTIONS

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SUMMARY

Although the advent of antibiotics has reduced the overall number of deep neck infections (DNI), they still occur with a definite potential for significant morbidity and even mortality. In the years between 1992 and 1995, 21 patients hospitalized at Ankara Numune State Hospital with DNI are enrolled in this study.

Eight were managed with surgical drainage and antibiotic treatment and the rest received only antimicrobial therapy. Drainage was performed in those with abscess formation.

Penicillin G was administered to 18 patients and 14 of these patients responded well only to penicillin therapy. As no clinical improvement was seen in 4 patients after 48 to 72 hours, the parenteral therapy was changed. So 77 % of the patients who had received penicillin initially go on well with this treatment

As a result we can say that; if the patients are not compromised or systemically ill and has not got the infection in the hospital then only penicillin therapy still remains a good choice when it is used in appropriate dosage.

Key Words: *Deep neck, antibiotic, infection*

The infection between the superficial and deep parts of the deep neck fascia is called deep neck infection. Infection occurs in deep cervical fascia by the secondary invasion of the organisms.

Before antibiotics came into use, DNI mostly originated from the pharynx and tonsil infections. DNI can occur as a result of infections of the pharynx, tonsils, salivary glands, temporal bone, paranasal sinuses, deep lymph nodes, oesophagus and from upper respiratory tract infection. Recently reports of DNI about injection of illicit drugs have been appearing in foreign countries and have become the major source in some of them(10).

Trismus, swelling of the neck, dysphagia, fever, neck paint that limits the motion of neck are to most frequently seen symptoms. There are life threatening complications of infections in this region. Acute upper airway obstruction, rupture of the abscess into the pharynx or trachea resulting in asphyxiation, lung abscesses or empyema, pneumonia, suppurative descending mediastinitis, thrombophlebitis with thrombosis of the internal juguler vein; and erosion of the carotid or vertebral arteries resulting in hemorrhage are the most important ones among them.

If these life-threatening complications are taken into account, it becomes appearent how it is important to early diagnose and treat these infections with appropriate antibiotics.

In the treatment of deep neck infections, besides antimicrobial treatment surgical drainage is also advised. Dzyak and Zide (4) had reported that with antimicrobial therapy only 10-15% of the paitents were trented and all the others had needed surgical drainage.

On the other hand Broughton (3) have recomended that more than 50 % of the patients were treated only by medical therapy. In the years between 1992-1995, of the 21 patients with deep neck infecitons hospitalized at Ankara Numune State Hospital, 8 were managed with surgical drainage and antibiotic treatment and the other 13 patients were given only medical therapy. Surgical drainage was administered to those with abscess formation.

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MATERIALS AND METHODS

The 21 patients ranged in age from 14 to 44 years, with the average of 23 years. 14 were male and 7 were female. Symptoms had begun before admission to hospital with a mean of 4.8 days and all of the patients had been treated with an oral or IM. antibiotic before hospitalization (mean 2.4 days).

All patients received parenteral antibiotic therapy with hospitalization. Parenteral therapy was continued for a mean of 8 days (range, 6 to 11 days). Eighteen patients were begun penicillin G 16-20 million units/day. Since no clinical improvement was seen, 3 of them received sulbactam-ampicillin (SAM) 4x1.5 gr/day after 48-72 hours and one was begun ceftriaxone 1.5 gr/day according to the results of bacterial culture. One patient was allergic to penicillin and treated with cefoxitin and 2 patients received SAM as they were systemically ill. The etiologies, parenteral therapy and results are shown in Table 1.

Reduction in fever and neck swelling, improved range of motion of the neck with decreased pain, improved oral intake were considered to be clinical improvement. All the patients received orl therapy after parenteral treatment andthey were given amoxicillin 3x1 gr/day, amoxicillin-clavulanate 3x625 mg/day, SAM 4x375 mg/day and cefuroxim axetil 2x500 mg/day.

Table 1: Clinical Profile of 21 Patients With Deep Neck Infections

CASE	ETIOLOGY	SURGERY	ORGANISM	DRUGS	CHANGE IN THERAPY
1	URI			Pen G	
2	Per. Abs			Pen G	
3	Unknown	(+)	An.GNR, alpha strep.	Pen G	
4	Tooth Exraction			Pen G	
5	Tonsillitis			Pen G	
6	Unknow (DM)*	(+)	S.aureus, An. GPC	SAm	
7	URI			Cfx.	
8	Tonsillitis			Pen G	
9	Unknown	(+)	AN.GNR	Pen G	(+) Cftrx.
10	URI			Pen G	
11	Unknown			Pen G	(+) SAM
12	URI	(+)	GPC	Pen G	
13	Tooth Extraction			Pen G	
14	A. Parotitis	(+)	GPC, alpha strep.	Pen G	
15	Unknown (DM)*	(+)	S. aureus, alpha strep.	SAM	
16	Per. Abs.	(+)	No growth	Pen G	
17	Unknown (P)**			Pen G	
18	URI			Pen G	
19	URI			Pen G	(+) SAM
20	Tonsillitis			Pen G	
21	Unknown			Pen G	(+)SAM

* Diabetes Mellitis ** Pregnant Ceftrx. : Ceftriaxone SAM: Sulbactam-ampicilin
Cfx: Cefoxitin, URI: Upper respiratory tract infection, Per. Abs.: Peritonsiller abscess, GPC: Acrobic,gram-positive cocci. An.GPC: Anaerobic gram-positive cocci, An.GNR: Anaerobic gram-negative rods.

RESULTS

The mostly seen symptoms at the time of preesntation were; fever (100%), limitation of motion of the neck and pain (90%), dysphagia (52%) and sore throat (38%).

The most common physical findings at the time of admission were swelling of the neck (100%), stiffness of the neck at the time of movement (85%), dental cares (38%) and tonsillitis/pharyngitis (28%). Leukocytosis was present in all patients (mean 16.100/mm3).

Of the 21 patients, 8 were managed surgically and specimens were collected for bacteriologic examinations .Except one, all of the specimens yielded bacterial growth. The patients who were managed with surgical drainage and the bacterial isolates are shown in Table 1.

DISCUSSION

Aerobic and anaerobic pathogens are often the causes of deep neck infections together (1,2,5). The most common isolated aerobic organisms in the literature are alpha and gamma hemolytic streptococci, group A beta hemolytic streptocci and Staphylococcus aureus. Neisseria species, Moraxella catarrhalis, Haemophilus species are isolated occasionally. The predominant anaerobes have included Bacteroides species, Peptostreptococcus species and Fusobacterium species(8). The treatment should be directed towards these pathogens.

It is now recognized that DNI, caused by beta-lactamase producing organisms are not unusual (1,2). This is consistent with the 3 patients that we could not cure with penicillin monotherapy. These 3 patients received SAM as no clinical improvement was seen after 48 to 72 hours. In the study by Brook, results of the cultures from his patients yielded, all of S. aureus, 33% of Bacteriodise melaninogenicus and 67 % of Bacteriodes oralis were betalactamase producing. In the same study, from 71% of the patients penicillin-resistant organims were recovered(2). In another study, it has been found that 41 % of the areobes were producing beta-lactamase(4).

Anyhow, if the patient is not compromised, systemically ill and has not got the infection in the hospital, then only penicillin therapy still remains a good choice when it is used in appropriate dosage. Of our series, 5 patients had tonsillitis and peritonsiller infections. These patients responded to penicillin monotherapy dramatically. Also the choice of specific antibiotics for the treatment of odontogenic infections requires not so much the results of bacterial culture as many of these organisms, including both anaerobes and areobes are sensitive to penicillin (6,9).

Two patients had diabetes mellitus and one of them received ceftriaxone and the other SAM according to the results of the cultures and a pregnant patient in her first trimester was administered penicillin G.

Life threatening complications of DNI, may happen much more easy in systemically ill patients such as diabetes mellitus and leukemia, so it would be weise to select antibiotics active against beta-lactamases and gram negative bacilli (e.g. SAM). Penicillin allergic patients may be treated with an antianareobic cephalosporin like cefoxitin or with clindamycin at high doses (4x600 mg) if gram-negative pathogens are not considered to be the cause of the sepicific infection.

Metronidazole, although highly active against anaerobic gram - negative bacilli, it is only moderately active against anaerobic cocci and is not active against aerobes including streptococci (6,7). For that reason it should not be used as a single agent in deep neck infections. Imipenem have been recently come into use in DNI but it should be spared for the serious hospital infections in order to prevent early resistance.

CONCLUSION

In our opinion, if the source of the infection is outside the hospital and the patient has no other disease, then penicillin monotherapy is really an effective choice for the treatment of deep neck infections.

Since gram-negative bacilli and beta-lactamase producing organisms are found at a higher ratio in comprimised and systemically ill patients, it would be appropriate to start therapy against these pathogens.

Of the 21 patients hospitalized with deep neck infections, 18 were administered only penicillin G and 14 of these (77%, overall 66%) responded well to the treatment.

Especially, when it is compared with the other antimicrobial drugs, the low incidence of the side effects and the low price of the drug still make it the first choice although lots of new antibiotics are administered to the market everyday.

REFERENCES

1. Asmar BI. Bacteriology of retropharyngeal abscesses in children. Pediatr Infect Dis J 9: 595-596, 1990.
2. Brook I. Microbiology of retropharyngeal abscesses in children. Am J Dis Child 141:202-204, 1987.
3. Broughton RA. Nonsurgical management of deep neck infections in children. Pediatr Infect Dis J 11(1)/: 14-18, 1992.
4. Dzyak WR, Zide MF. Diagnosis and treatment of lateral pharyngeal space infections. J Oral Maxillofac Surg 42:243-249, 1984.
5. Heimdahl A, Konow LV, Satoh T, et al. Clinical appearance of arofacial infections of odontogenic origin in relation to microbiological findings. J. Clin Microbiol. 22(2): 299-302, 1985.
6. Hill MK, Sanders CV. Principles of antimicrobial therapy for head and neck infections. Infect Dis North Am. 2:57-58, 1988.
7. Hood FJC. The Place of metronidazole in the treatment of acute orofacial infection. Antimicrob Agents Chemother 15:71-72, 1978.
8. Shumrick KA, Sheft SA. Deep Neck Infections. Michael M. Paparella, Donald A. Shumrick (ed): Otolaryngology, vol 3 (ed 3). 1991 Philadelphia, PA, Saunders, page:% 2545-2563.
9. Tomi TA, Parker GS. Eikenella corrodens and emerging pathogen in head and neck infections. Arch. Otolaryngol. 110:752-754, 1984.
10. Tom MB, Rice DH. Presentation and management of neck abscess: A retrospective analysis. Laryncoscope 98(8):877-880, 1988.

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NONINVASIVE POSITIVE PRESSURE VENTILATION

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SUMMARY

Although mechanical ventilation via endotracheal intubation is usually a lifesaving method in conditions associated with respiratory failure, many efforts have been spending to provide sufficient support avoiding endotracheal intubation for many years. Approaching positive pressure on both inspiration and expiration separetely (Bilevel positive airway pressure-BEEPUP) via a nasal or full face mask can reduce the need for endotracheal intubation. During the past few years noninvasive ventilation via a mask have been used for the treament of both acute exacerbations of chronic obstructive respiratory disease and the acute respiratory failure wih alveolar hypoventilation. Although many of the studies on noninvasive ventilation reported that the satisfactory results have been obtained, some suspected results have been reported. Since the noninvasive ventilation has several advantages, more investigations should be done to find out the certain indications.

Key Words: *BEEPUP, Epap, Ipap, COPD, Respiratory failure, noninvasive ventilation.*

Mechanical ventilation has been successful in supporting ventilation in patients with respiratory failure. The mechanical ventilation through endotracheal intubation are not optimal for the comfort of the patients and ancilliary care. For purposes of improving comfort and while providing ventilatory support without the physical and psychological trauma associated with tracheal intubation, ventilatory support can be administered through a tight-fitting nasal or face mask. The treatment of sleep apnea (18), acute respiratory distress(9), nocturnal muscle fatigue (20) and chronic obstructive pulmonary disease (6,17).

The noninvasive pressure ventilatory support system is based on a standard nasal CPAP (Continuous positive airway pressure) flow generator. A pressure controlling valve maintains pressure at one of two different levels, the expiratory positive airway pressure (EPAP) level (equivalent of PEEP of conventional mechanical ventilation) or the inspiratory positive airway pressure (ıpap) level (equivalent to pressure support), even in the presence of rapidly changing flows. (1,11).

Historical Perspective

Although the first mechanical ventilators were described in the late 1700s, invasive mechanical ventilation could be introduced hundred years later. But it was not extremely used until the late 1950s, when experience using anesthesia for surgery led to the development of positive pressure that reliably delivered preset pressures and volumes. These early positive pressure ventilators were used almost exclusively with artificial airways (3,8,10). Noninvasive administration of intermittent positive pressure became popular during the 1950's through the 1970s for several respiratory disorders with the use of intermittent positive pressure breathing through a mouthpiece.

During the 1960s and 1970s, a few centers used noninvasive positive pressure ventilation to provide ventilatory support to patients with chronic respiratory failure, but the technique required cooperative, motivated patients and considerable patience and coaching from medical staff. During the mid 1980s, investigators began applying intermittent positive

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pressure ventilation through nasal interfaces and rapidly discovered that it augmented ventilation in patients with chronic respiratory failure, particularly during sleep. Most recently, small, relatively inexpensive, easily portable ventilators were developed to be used specifically with noninvasive positive pressure ventilation using a nasal mask.

Noninvasive Ventilation in Acute Respiratory Failure

Acute respiratory failure has been primarily treated with mechanical ventilation through endotracheal intubation for several years. Many complications including upper airway trauma, nasocomial infections, barotrauma, etc. and the difficulties on patient care associated with this type of mechanical ventilation. To avoid tracheal intubation and its attendant complications, investigators recently began administering noninvasive ventilation to selected patients with acute respiratory failure. The theoretical advantages of this ventilation are to improve patient comfort, to reduce the need of sedation, and to maintain airway defense, speech and swallowing. Of course there are some limitations to use this system extensively including the need for patient cooperation, the lack of direct acces to airway, which could promote mucus plugging or atelectasis in patients with copious secretions, facial skin ulcers caused by mask pressure and aeorophagia. Results of the treatment of the patients with acute respiratory failure in some studies are shown in Table 1.

Patients in most studies used noninvasive positive pressure ventilation for 8 to 20 hours per 24-hour period, but in one study patients were given 1-hour rest rest periods after 2 or 3 hours of use, amounting to approximately 18 hours of use per 24-hours period. (14,15). Although most studies reported a 60% or more success rate for noninvasive ventilation in patients with acute respiratory failure, some studies reporting the minimal no success in patients with acute respiratory failure, caused by COPD exacerbation (2,4) were present. However most of the recent studies reported the very high success rate for the treatment of patients with acute respiratory failure caused by COPD exacerbation by nonivasive ventilation. (7,13,16). In these studies, it is reported that in 70-85 % of the patients were applied nonivasive ventilation, endotracheal intubation was avoided. The selection guidelines for noninvasive positive pressure ventilation use in acute respiratory failure are listed in Table 2.

Use of Noninvasive Positive Pressure Ventilation in Chronic Respiratory Failure

There have been several studies reporting the results of the treatment of the patients with chronic respiratory failure secondary to neuromuscular diseases, thoracic wall deformities, obstructive sleep apnea, etc. by intermittent positive pressure ventilation (5,12,19). These studies showed that noninvasive positive pressure ventilation support in patients with chronic respiratory failure due to disorders mentioned above, alleviation of day time symptoms of hypoventilation and improvement in daytime gas exchange. However most of the studies were uncontrolled cohort studies, in which success rates depend on the patients' severity of illnesses. Some studies on the use of noninvasive positive pressure ventilation were listed in Table 3. Despite convinc-

Table 1: Studies on the use of noninvasive Positive Pressure ventilation in Acute Respiratory Failure

	Arterial Blood Gases				Duration of Use
Years of Trials	Baseline		After NPPV		Hours per day
	pH	pCO2	pH	pCO2	
1991	7.38	49.2	7.40	44.3	6.8
1991	7.28	73.0	7.41	48.1	7.3
1992	7.33	73.5	7.37	60.0	4.0
1992	7.28	69.5	7.34	63.2	-
1993	7.35	64.5	7.38	54.3	7.6

Table 2: Selection Guidelines for Noninvasive Positive Pressure Ventilation Use in Acute Respiratory Failure

Respiratory Failure or insufficiency without need for immediate intubation with the following:
- Acute respiratory Acidosis
- Respiratory distress
- Use of accessory muscles or abdominal paradox
Cooperative patient
Hemodynamic stability
No active cardiac arrythmias or ischemia
No active upper gastrointestinal bleeding
No excessive secretions
Intact upper airway function
No acute facial trauma
Proper mask fit achieved

Table 3: Studies on the use of Noninvasive Positive Pressure Ventilation in Chronic Respiratory Failure

	Arterial Blood Gases				Duration of Use	Symptom Relief
Years of Trials	Baseline		After NPPV		Trial Time	
	pO2	pCO2	pO2	pCO2		
1990	48.0	69.2	64.0	46.0	24 hrs	Yes
1990	-	61.0	-	50.1	2.0 wk.	Yes
1991	52.0	64.0	68.0	51.0	2.0 wk.	Yes
1991	7.28	69.5	7.34	63.2	5.8 mo.	Yes
1992	-	58.3	-	46.3	14.0 mo.	Yes

ing evidence that intermittent positive pressure ventilation is effective in treating certain forms of chronic respiratory failure, patients must be carefully selected to optimize chances for success (Table 4). The patients with obstructive sleep apnea, central hypoventilatory disorders and stabilized COPD are usually suitable candidates for the chronic use of noninvasive ventilation. The patients with very slowly progressing neuromuscular disorders are also good candidate for this ventilation. But the patients with rapidly progressing muscular disease, such as Duchenne type muscular dystrophy, applying noninvasive ventilation may not a feasible approach for its very short term use. Although noninvasive ventilation can be used uninterruptedly, some authors recommends permanent tracheostomy in the patients who required positive pressure ventilation more than 16 hours per day.

Table 4: Selection Guidelines for noninvasive Positive Pressure Ventilation Use in Chronic Respiratory Failure

Slowly progressive respiratory Failure due to following:
- Neuromuscular disease
  - 1- Muscular Dystrophies
  - 2- Postpolio syndrome
  - 3- Multiple sclerosis
  - 4- Amyotrophic lateral sclerosis
- Thoracic wall deformities
  - 1- Kyphoscoliosis
  - 2- Postthoracoplasty
- Obstructive sleep apnea
  Obesity hypoventilation
- İdiopathic hypoventilation
- COPD

Intact upper airway function
Minimal secretions
Cooperative and motivated patients

Conclusions

It is obvious that, noninvasive positive pressure ventilation offers many advantages comparing with the alternative methods, such as endotracheal intubation and negative pressure ventilation. With acute respiratory failure, noninvasive ventilation may obviate the need for endotracheal intubation, thus possibly decrease the length of stay in the intensive care unit. With chronic respiratory failure, it reverses nocturnal hypoventilation and improves daytime symptoms and gas exchange.

Noninvasive ventilation is easier to apply and usually better tolerated by the patients. Despite all the advantages of the noninvasive ventilation, patients must be selected carefully. Patients with acute respiratory failure must be sufficiently cooperative and to coordinate their breathing with the ventilator and the patients must not have excessive secretions.

Respiratory failure is a life threatening condition. So the patients with respiratory failure must be carefully managed. Many controlled studies are needed to compare the various types of ventilation.

REFERENCES

1) Bernard E. Pennock, Kaplan M., Carlin B. Pressure support ventilation with a simplified ventilatory support system administered with a nasal mask in patients with respiratory failure. Chest: 1991: 100; 5:1371-76.

2) Brochard L, Isabey D, Piquet J, Amaro P, Mancebo J, Messadi AA, et al. Reversal of acute exacerbations of chronic obstructive lung disease by inspiratory assistance with a face mask. N Engl J Med. 1990; 323: 1523-30.

3) Bryant LR. Mechanical respirators. Their use and aplication in lung trauma. JAMA. 1967; 199: 149-54.
4) Chevrolet JC, Joillet P, Abajo B, Toussi A, Louis M. Nasal positive pressure ventilation in patients with acute respiratory failure. Difficult and time consuming procedure for nurses. Chest. 1991; 100:775-82.
5) Di Marco AF, Connors AF, Altose MD. Management of chronic alveoler hypoventilation with nasal positive pressure breathing. Chest. 1987; 92:952-4.
6) Driver AG, Blackburn BB, Maraiard SP. Nutritional assesment of patients with chronic obstructive pulmonary disease and acute respiratory failure: Chest 1982: 82:568-571.
7) Foglio C, Vitacca M, Quadri A, Scalvini S, Marangoni S, Ambrosino N. Acute exacerbations in severe COLD patients. Treatment using positive pressure ventilation by nasal mask. Chest, 1992; 101:1533-8.
8) Goldstein RS, Molotiu N, Skrastins R, Long S, de Rosie J, Contreras M, et al. Reversal of sleep induced hypoventilation and chronic respiratory failure by nocturnal negative pressure ventilation in patinets with severe ventilatory impairment. Am Rev Respir Dis. 1987; 135:1049-55.
9) Greenbaum DM, Miller JE, Eross B, Snyder JV; Continious positive airway preesure without tracheal intubation in spontaneously breathing patients. Chest 1976; 69: 615-19.
10) Hill NS. Clinical applications of body ventilators. Chest. 1986; 90:897-905.
11) Hurst JM, Deltaven CB, Branson RD, Use of CPAP mask as the sole mode of ventilatory support in trauma patients with mild to moderate respiratory support. J. Trauma 1985: 25; 1065-68.
12) Leger P, Lennequin J, Gerard M, Robert D. Home positive pressure ventilation via nasal mask for patients with neuromuscular weakness or restrictive lung or chest wall deformities. Respiratory Care. 1989; 34:73-7.
13) Marino W. Intermittant volume cycled mechanical ventilation via nasal mask in patinets in respiratory failure due to COPD. Chest. 1991; 99:681-4.
14) Meduri GU, Aboi Shala N, Fox RC, Jones CB, Leeper KV, Wunderink RG. Noninvasive face mask mechanical ventilation in patients with acute hypercapnic respiratory failure. Chest. 1991; 100, 445-54.
15) Meduri GU, Conoscenti CC, Menashe P, Nair S. Noninvasive face mask ventilation in patients with acute respiratory failure. Chest. 1989; 95:865-70.
16) Pennock BE, Kaplan PD, Carlin BW, Sabangan JS, Magovern JA. Pressure support ventilation with a simplified ventilatory support system adminitered with nasal mask in patients with respiratory failure. Chest 1991; 100:1371-6.
17) Petrof BJ., Legare M., Goldberg P., Milic-Emili J., Gottfriend Sb. Contunious positive airway pressure reduces work of breathing and dyspnea during weaning from mechanical ventilation in severe chronic obstructive pulmonary disease. Am. Rev. Respir. D 1990; 141: 281-89.
18) Sanders MH, Moore SE, Evasluge J.; CPAP via nasal mask: a treatment for occlusive sleep apnea, Chest 1983; 83: 144-45.
19) Strumpf DA, Millman RP, Hill NS. The management of chronic hypoventilation. Chest. 1990; 98: 474-80.
20) Strumpf D, Carlisle CC, Millman RP- Simth KW, Hill NS. An evaluation of the Respironics BIPAP Bi-level CPAP device for delivery of assisted ventilation. Respiratory Care 1990; 35: 415-22.

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ENDOVASCULAR COIL EMBOLIZATION OF BASILAR ANEURYSMS: REPORT OF TWO CASES

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Celal Bağdatoğlu* • Umman Şanlıdilek****

SUMMARY

In cases of cerebral aneurysms in whom surgical therapy, fails or for aneurysms of surgically inaccessible anatomic locations, interventional techniques that make use of coils may be a useful therapeutic alternative. In this report, the endovascular coil embolization therapy for a incompletely surgically clipped basilar aneurysm case with subarachnoid hemorrhage is discussed.

Key Words: *Basilar Aneurysm, Endovascular Therapy, Coil Embolization.*

Morgagni in 1761 was probably the first person to recognize an intracranial aneurysm at the time of autopsy. The first clinical diagnosis of aneurysm that was proven later at autoppsy was made by Hutchinson (10). Subsequent to the use of carotid angiography by Moriz in 1927, aneurysms recognized as a definite clinical entity. Intracranial aneurysms are more common in 1% of the general population (11). They are more common in females. The youngest case of an aneurysm recognized and treated successfully is a 4 week old infant (10). Of intracranial aneurysms, 85 to 90 percent are in the anterior portion of the circle of Wills and 3 to 15 percent in the posterior or vertebral basilar system (13,14). Interventional treatment of complex intravascular disorders, including arteriovenous malformations and fistulas was first reported in the early 1970's by Serbinenko (15). Since then, continued advancements in microballoon and catheter technology, steerable guide wires, permanent solidifying materials, and high resolution Digital Substraction Angiograpy with road mapping capability have allowed access to nearly all cerebrovasscular territories (2,7). The combination of partial surgical clipping followed by endovascular treatment of the remaining aneurysm may prove to be new theraphy for difficuilt aneurysm that can not be treated by either modality alone(5).

CASE REPORT

CASE 1:

A 44 year old-man was transferred to department of Neurosurgery, University of Ankara. He was in a severe disabled condition with a GCS of 4 points. From his past medical history, it was learned that 3 months ago, the same patieent was admitted to an another neurosurgical center with the complaints of headache, nausea and vomiting. Except from the neck stifness, no profound neurological abnormalities was detected. After diagnostic work-up, he was operated for a giant-basilar aneurysm via pterional approach. The aneurysm was tried to be clipped and because of premature rupture and bleeding during operation, also wrapping was employed. The patient had no extra neurologic deficit in the early post operative period. He was readmitted to the same center after a month from discharge with a sudden loss of consciousness. Hydrocephalus was revealed by cranial CT scans and V-P Shunting procedure was performed. Respiratory distress began after the second operation and the patient was sent to our clinic.

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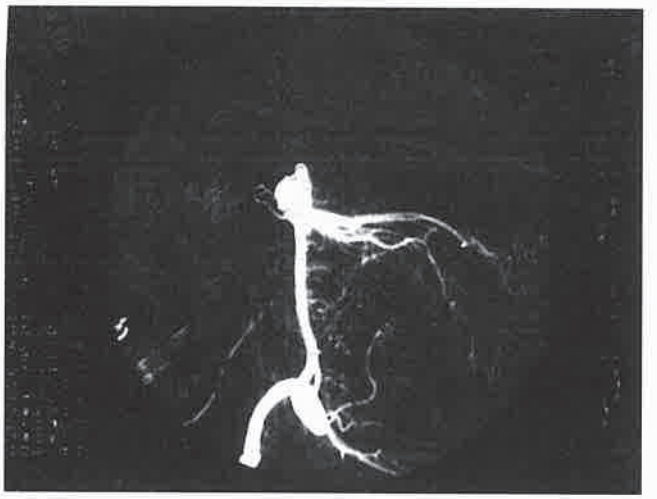

Fig. 1. Vertebral angiography in lateral view demonstrated basilar tip aneurysm.

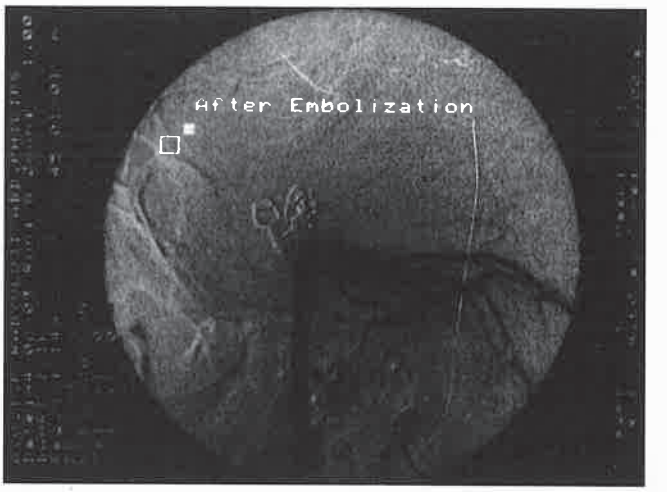

Fig. 2. After coil embolization, total aneurysm occlusion was demonstrated.

On admission, the patient was unconscious and had no response to painful stimuli. He had anisocoria, with the right pupil beign more dilated than the left. The V-P shunt device was found to be nonfunctioning. His CBC and blood biochemical analysis were normal. After 4 vessel DSA, a basilary tip aneurysm without involvement of both posterior cerebral arteries was detected (Fig. 1) The two clips which had been employed in the previous operation were not located on the neck of the aneurysm. After these, coil embolization of the aneurysm (Fig.2) and a MP-VP shunt revision was performed. On control DSA, the aneurysm was found to be entirely filled with coils and on control CT Scans hydrocephalus was decreased. In the post operative period, the patient improved neurologically. He was obeying verbal commands, trying to speak with ongoing left hemiplegia in the first postoperative month. He is still in the rehabilitation program of our clinic.

CASE 2:

58 year old woman was admitted to University of Ankara, Department of Neurosurgery complaints of headache and vomiting. From her past medical history, it was learned that 15 years ago she had operated for right posterior communican arteria aneurysm in another neurosurgical center. After this operation she had left hemiparesia. Her physical examination was normal. Neurological examination was normal except left hemiparesia, (+) neck stifness and slightly increased deep tendon reflexes. CBC and biochemical analysis were normal. Metallic aneursym clip artefact and subarachnoid hemorrhage was seen on cranial tomography. Digital substraction angiography revealed a basilar tip aneurysm. The patient was hospitalized, 1 week later her neurological condition was stabil, and through femoral catheterization, aneurysm was obliterated by microcoils without any complication. Control DSA showed obliteration of aneurysm. 1 month later, on control neurological examination, she had no neurological deficit except left hemiparesia.

DISCUSSION

Two percent of the entire population of the United States will have an intracranial aneurysms. In North America, 25000 intracranial aneurysm rupture every year followed by bleeding into the subarachnoid space or cerebral tissues(16). The primary purpose of treatment for ruptured intracranial aneurysms is to prevent rebleeding which in most cases would be catastrophic.

We don't have enough information about statistical analysis of aneurysms in Turkey. Interventional treatment of complex intracranial vascular disorders including arteriovenous malformations and fistulas was first reported in the early 1970's by Serbinenko. Since, then, continued advancements in microballoon and catheter technology, steereable guide wires, permanent solidifying materials and high resolution digital subtraction angiography with road-

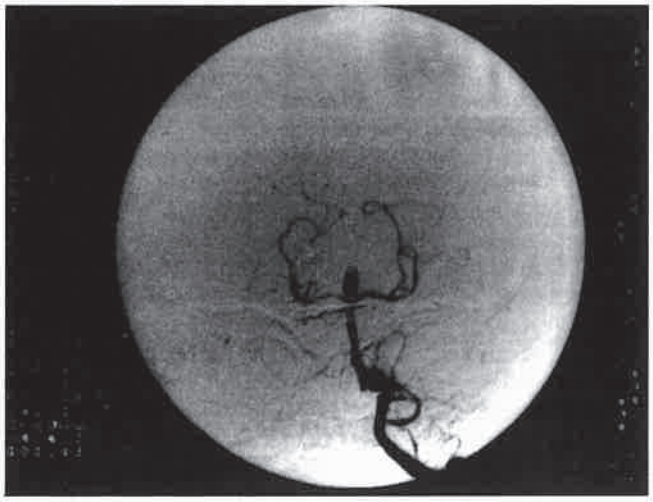

Fig. 3. Vertebral angiography of the second case showed basilar tip aneurysm.

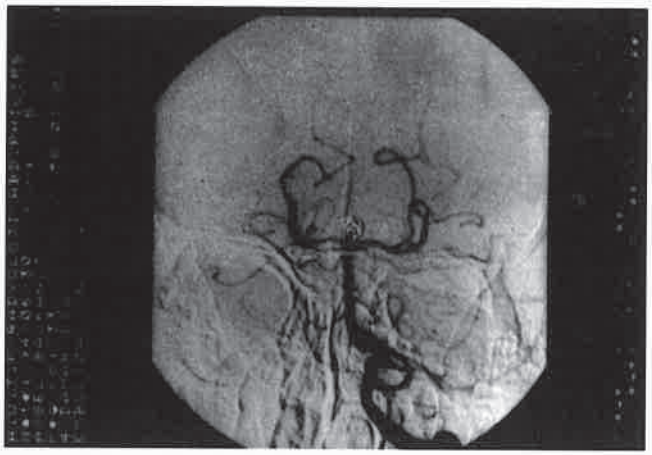

Fig. 4. After coil embolization, total aneurysm occlusion was demonstrated.

mapping capability have allowed access to nearly all cerebrovascular territor ies (7). Aneurysm occlusion with coils was first reported by Hila (9) in 1988. Coils of various sizes and shapes can be deposited inside the sac, allowing more homogenous filling of the lumen and a stable occlusion (3).

The indication for endovascular treatment was based on a consensus between interventional neuroradiologists, neurosurgeons and anesthesiologist. Endovascular treament was considered primarily for anatomical reasons (giant , most posterior circulation aneurysms), clinical reasons (Hunt and Hess grades 3 and 4, anesthetic contraindications) or when surgery was refused by the patient or the patient's family(2).

Most reports have discussed remnant aneurysm filling below the clip with regard to 'regrowth or rehaemorrhage'. The management of incomplete clipping of an aneurysm neck with contrast filling of its residual aneurysm cavity above the clip have been a clinical situation rarely reported in the literature (1). The issue of how to manage a residual aneurysm should be surgical. Drake et al. have recommended reoperation and reclipping to obtain complete aneurysm occlusion (4,12). Endovascular treatment should be considered when surgery has a great risk. The endovascular approach to aneurysm occlusion has previously been limited to ballon embolization (6). The main disadvantages that the fragile wall of the aneurysm undergoes stress while adapting to the the acute post-hemorrhagic phase. In a series of 84 inoperable patients treated by balloon embolization with preservation of the parent arteria. Higashida et al.(8) reported a 17.9 % mortality rate and a 10.7 % morbidity rate directly related to the embolization procedure. We didn't use balloon embolization because we believe that detachable coils are less traumatic than balloons and also carries less risk of rupturing an aneurysm, especially in the acute phase of SAH. In conclusion, we would like to emphasize that endovascular therapeutic procedures may complete the insufficient surgical interventions in cases with cerebral aneurysms.

REFERENCES

1- Black SP, German WJ: Observations on the relationship between the volume and size of the orifice of experimental aneurysms. J., Neurosurgery 17:984-90, 1960.

2- Casasco EA, Aymord Aa, Gobin P, Haudart E, Rogopoulas A, Geoorge B: Selective endovascular treatment of 71 intracranial aneurysms with platinium coils. J. Neurosurgery 79:3-10, 1993.

3- Dowd CF, Halbsch VV, Higoshida RT: Endovasculer coil embolization of unusual posterior inferior cerebellar artery aneurysms. Neurosurgery 27:954-961, 1990.

4- Drake CG, Friedman AH, Peertess SJ: Failed aneurysm surgery; reoperation ni 115 cases. J. Neurosurgey 61:848-56, 1984.

5- Fraser WK, Halboch VV, Teitelbaum GP, Smith TP: Endovasculer platinium coil embolization of incom-

pletely surgically clipped cerebral aneurysms. Surgical Neurology 41:4-8, 1984.

6- Guglielmi G, Vinuella F, Dion J, Duckwiler G: Eelctrothrombosis of sacculer aneurysms via endovasculer approach: Part 2 preliminary clinical experience. J. Neurosurgery 75:8-4, 1991.

7- Higoshida RT, Halbock VV, Hieshimo GB: Treatment of complex intracranial aneurysms by interventional techniques. In: Margulis AR, Gooding CA, eds. diagnostic radiology 1989. San Fransisco: Universty of California Printing Services, 357-360; 1989.

8- Higoshida RT, Halbock VV, Baunell SC: Treatmant of intracranial aneurysms with preservation of the parent vessel; results of percutaneous balloon embolization in 84 patinets. AJNR: 11:633-640, 1990.

9- Hilal SK: Synthetic fiber coated platinium coils successfully used for the endovascular treatment of arteriovenous malformations, aneursyms and direct arteriovenous fistulae of the central nervous system. Radiology 169 (supply) 28-29, 1988 (abstract).

10- Jones RK, Shearburn EW: Intracranial aneurysm in a four week old infant. Diagnosis by angiography and successful operation. J. Neurosurgery 18:122-124, 1961.

11- krayenbuhl HA, Yaşargil MG, Flamm ES, Tew JM Jr: Microsurgical treatment of intracranial sacculer aneurysms. J. Neurosurgery 37:678-686, 1972.

12- Lin T, Fox AJ, Drake CG: Regrowth of aneurysm sas from residual neck following aneurysm clipping. J. Neurosurgery 70, 556-60, 1989.

13- Mc Cormick WF, Nafzinger JD: Sacculer intracranial aneurysms J. Neurosurgery 22; 155-159, 1965.

14- Mc Kissock W, Paine KWE, Walsh LS: An analysis of the results of treatment of ruptured intracranial aneurysms. Report of 772 consecutive cases. J. Neurosurgery 17:762-776, 1960.

15- Serbinenko FA: Ballon catherization and occlusion of major vessels. J. Neurosurgery 41:125-145, 1974.

16- Weir B. Intracranial aneurysms and subaracnoid hemorrahge an overview, in Wilkins RH, Rengachary SS (eds). Neurosurgery New York: Mc Graw-Hill. vol. 2:1308-1329, 1985.

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THE COEXISTENCE OF HEMORRHAGIC CYSTITIS AND ENGRAFTMENT FAILURE AFTER ALLOGENEIC BONE MARROW TRANSPLANTATION FOR CHRONIC MYELOGENOUS LEUKEMIA: OVERCOMING OF PROBLEMS WITH ALLO PERIPHERAL STEM CELL TRANSPLANTATION

Muhit Özcan* • **Önder Arslan**** • **Haluk Koç***** • **Meral Beksaç******

SUMMARY

A 19 year-old-woman underwent an allogeneic bone marrow transplantation for chronic myelogenous leukemia (CML). She had both early and late onset haemorrhagic cystitis (HC) developed on the infusion day and the 28th day, respectively. Gross haematuria persisted up to day +97. haematopoiesis became granulocyte-colony stimulating factor factor (G-CSF) dependent during this period. No viral etiology was identified for HC or poor graft function. HC was treated by formalin instillation and engraftment failure was overcome by second allogeneic peripheral blood stem cell transplantation. We report here a very rare coexistence of two major complications of bone marrow transplantation.

Key Words: *Hemorrhagic cystitis, engraftment failure*

Hemorrhagic cystitis (HC) refers to the syndrome of hematuria and symptoms of lower urinary tract irritability. The incidence of hemorrhagic cystitis which is seen after bone marrow transplantation (BMT) varies considerably according to conditioning regimen and the preventative measures (1). HC which has two main patterns of onset, can occur at any time after BMT. Early onset HC is due to drugs such as cyclophosphamide used in conditioning. Late onset HC occurs weeks to months after the transplantation and its pathogenesis is more complex. Early onset HC is a well-known risk factor for late onset HC. Most of the cases are associated with viruria or graft versus host disease (GVHD). We present here a patient having both early and late onset HC and subsequent graft failure with no documented GVHD or viruria.

CASE REPORT

A 19-year-old woman with chronic myelogenous leukaemia underwent BMT from her HLA-matched sister using busulfan (16 mg/kg) and cyclophosphamide (200 mg/kg) conditioning. MESNA, forced diuresis and urine alkalinization were used as prophylaxis for HC. A total of 1490 cc bone marrow was harvested under general anesthesia. Mononuclear cells separated with a cell separator (COBE Spectra). 1,1 x 10^8/kg mononuclear cells and 3,26 x 10^6 CD34 (+) cells/kg were transplanted. She received cyclosporine and short-term methotrexate for GVHD prophylaxis and acyclovir for herpesvirus, fluconazole for candida. G-CSF (Neupogen, Roche) were given to fasten the haematopoietic recovery. On the infusion day, she presented with urinary frequency and dysuria with microscopic haematuria. The culture of urine was negative for bacteria. The amount of hydration was increased to seven liters per day. The symptoms and signs disappeared on the 6th day. The urinary discomfort with gross haematuria reappeared on the 28th day. This time, the culture of the urine revealed the Klebsiella as causative agent, thus imipenem and amikacin were started. Although the CMV IgM was negative, iv Ig 500 mg/kg weekly were added. Gross haematuria decreased by the time. One week later, the urinary symptoms and haematuria were minimal and urine culture was again negative for bacteria. The neutrophil count reached to 0.5 x 10^9/L on day 34. İmipenem and amikacin treatment were stopped on day 37. But the haematuria aggravated within 24 hours after the cessation of the ther-

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apy. On the 40 th day, complete blood count showed a leukocyte of 2.1 x 10^9 /L, platelet of 19 x 10^9/L and Hb 8.4 g/dl. G-CSF was stopped on day 43 and ciprofloxacin po was added to treatment for prophylaxis.. Electron microscopy showed no inclusion body for virus in urine. The neutrophil count decreased to 0.5 x 10^9/L on day 47. Anti Parvovirus B19-IgM and CMV-IgM were negative on the same day. Staphylococcus (coagulase negative) was isolated in culture of urine on day 51. (Sulbactam + ampicillin) treatment was started according to the drug sensitivity test. Histopathologic examination of bone marrow revealed advanced hypocellularity with marked oedema. But platelet counts reached to >20 x 10^9/l and >100 x 10^9/L on day 50 and 59, respectively. Vesicular washes were started. Cytogenetic examination of bone marrow resulted in Ph (-) karyograms, which was confirmed by (FISH). Haematuria persisted with deep fluctuaitons during this period. Although the findings indicating viral etiology were negative, ribavirin capsule which is used successfully in adenovirus associated haemorrhagic cystitis after intravenously (3), (VirazideR, Cilag) 1200 mg/day per oral were started because of unavailability of parenteral form in our country. Hb level decreased to the nadir of 4.6 g/dl due to haematuria. Leukocytes became G-CSF dependent and decreased to 0.8 x 10^9/l without G-CSF on day 87. Patient's sympoms did not improve with ribavirin treatment. A large haemorrhagic area and some large clot formation were seen and removed by cytoscopy. Formalin instillation was the treatment of choice on day 97. On the same day compleete blood counts were as follows: neutrophil 0.4 x 10^9/L platelet 19x10^9/L, Hb 6.6 g/dl. It was decided to perform an allo PSCT to overcome the secondary engraftment failure. The donor's leukocytes were stimulated with G-CSF 30 MU/day. A total of 7.1 x 10^8/kg mononuclear cells and 5.7 x 10^6/kg CD34 (+) cells/kg were harvested and infused immediately on day 6 and 7. There were no platelet requirement and only two packs of erythrocytes were given after the allo infusion up to the discharge of patient. On day 134, after 27 days from the alloinfusion, she was discharged with hematological values as follows: WBC 2.2 x 10^9/L, neutrophil 1.6 x 10^9/L, platelet 65X10^9/L, Hb 9.2 g/dl. She has been alive and well for a year.

DISCUSSION

A number of variables have been associated with graft failure. Included among these are inadequate conditioning regimen, inadequate number of stem cells, damaged stem cells by prior chemotherapy and infections (2). A vairety of infectious agents including bacteria, fungi, viruses have all been associated with haematopoietic suppression. Certain CMV isolates also appear to affect stromal cells. But there is no known, common etiologic agent both for engraftment failure and (HC). CMV IgM and anti-HCV were negative in our patient in several situation. Although the influence of the number of infused progenitor cells on the engraftment is controversial, transfused (MNC) and CD34 (+) cells number were within the acceptable limits in our patient. Also, inadequate conditioning regimen was not a contributing factor in this case. She had been transplanted within 1 year after the initial diagnosis of CML. So, she had not received prior chemotherapy which may damage to stem cells. Finally, there were no HLA-disparity and ABO-incompatibility. Although an association between hepatitis and incomplete recovery after syngeneic transplant has been reported and treated successfully with second transplantation(4), we report this case because both for the rare coexistence of HC and poor graft function and also the overcoming of these complications by allogeneic stem cell transplantation.

REFERENCES

1. Grigg A. Hemorrhagic cystitis. In: Clinical Bone Marrow Transplantation. Atkinson K. (ed.). Cambridge: Great Britain, 1994; pp372-377.
2. Holmberg L, Torok-Storb B. Mechanisms of failure of sustained engraftment. In: Clinical Bone Marrow Transplantation. Atkinson K. (ed.). Cambridge: Great Britain, 1994, pp26-30.
3. Juradao M, Navarro JM, Hernandez J, Molina MA, DePablos JM. Adenovirus-associated haemorrhagic cystitis after bone marrow transplantation successfully treated with intravenous ribavirin. Bone Marrow Transplant 1994, 14:651-652 (letter)
4. Niki T, Nakao S, Ueda M, et al. Incomplete marrow recovery associated with hepatitis after syngeneic bone marrow transplant for aplastic anemia: successful treatment with second marrow transplants without preconditioning, Br J Haematol 1990, 75:285-286.

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MALAKOPLAKIA OF THE PROSTATE MIMICKING MALIGNANCY: A CASE REPORT

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SUMMARY

Malakoplakia is a rare granulomatous disease most commonly affecting the urinary tract, mainly the bladder.

A 71-year old man with a history of recurrent urinary tract infection, urinary frequency and nocturia was referred with a diagnosis of infravezica obstruction. Both physical examination and laboratory findings were suspicious for prostate cancer. Transrectal needle biopsy was performed and pathology revelaed histopathologcal features of malakoplakia.

Key Word: *Malakoplakia, prostate, malignancy.*

A prostatic malakoplakia that mimics prostate cancer is presented. Malakoplakia of the prostate is a rare granulomatous disease. And it is found that Malakoplakia is seen more often in the bladder than the other part of the urinary tract.

In this report, we describe both physical examination and laboratory findings.

The synchronous presentatism of prostate cancer and prostatic malakoplakia is also discussed under the view of literature.

CASE REPORT

A 71-yearold man with a history of recurrent proven Escherichia coli urinary tract infection, urinary frequency and nocturia was referred with a diagnosis of bladder outlet obstruction. Prostate Spesific Antigen level was found significantly elevated as much as metastatic prostate cancer. Digital examination and transrectal ultrasound of the prostate were most compatible with carcinoma. On the other hand, isotope bone scan showed no evidence of bony metastases. Transrectal needle biopsy was performed and pathology revealed histopathological features of malakoplakia (Fig.1). the patient was then treated with long-term use of trimethoprim-sulfamethoxazole and ascorbic acid. After a 27-month-follow-up period the patient remained well without urinary tract infection.

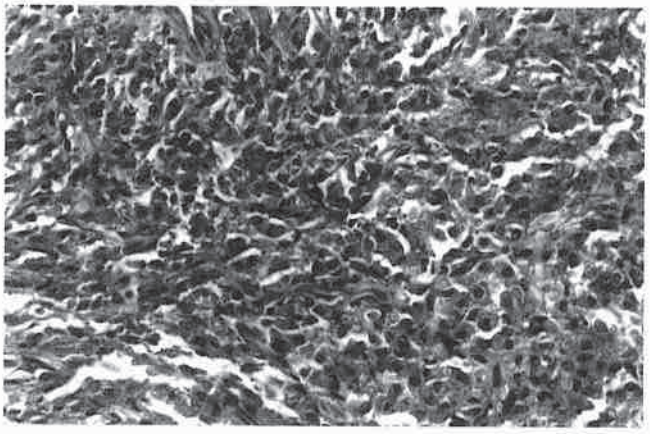

Fig. 1: Histiocytes (so called von Hansemann cells) which include intracytoplasmic inclusion known as Michaelis-Gutmann bodies (arrow) are seen (x100, H-E).

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DISCUSSION

Malakoplakia is a rare granulomatous disease most commonly affecting the urinary tract, mainly the baldder (6,7). Less frequently the condition affects the genital tract and retroperitoneum, and sporadic cases have been reported involving the lung, brain, conjunctiva, pancreas, skin, tonsils, adrenal gland and skeleton (6,7).

The etiology and pathogenesis of malakoplakia of the prostate are unsettled. The first case involving the prostate was reported by Carruthers in 1959(1). Twentynine additional cases have been reported in the more recent literature (2). The patients, who range in age from the fifth decaded to the ninth decade, most commonly have urinary retention or dysuria (9), and has been frequently reported to be associated with recurrent E. Coli Urinary tract infections (8), as in the present case. The diagnosis is histological, with the classical Michaelis-Gutmann bodies as its pathognomic finding (4).

As in other locations, malakoplakia of the prostate has been mistaken for carcinoma (2,3). On the other hand two cases of malakoplakia associated with prostatic carcinoma has been reported previosly (5). Additionally , there have been four previously reported cases of malakoplakia misdiagnosed histopathologically as carcinoma of the prostate (2,3,8,10). So, one must be alerted for the presence of malignancy when come across malakoplakia of the prostate.

REFERENCES

1. Carruthers NC.: Malakoplakia: report of a case. Canad J Surg, 2: 213, 1959.
2. Coup AJ.: Malakoplakia of the prostate. J Pathol, 119: 119, 1976.
3. Ferreira AA, Alvarengo M.: Malakoplakia of the prostate confused with clear cell carcinomas. J Urol, 116: 828, 1976.
4. Klaaborg KE, Bennedbaek J and Staklint H.: Two cases of malakoplakia of the prostate. Eur Urol, 11:137, 1985.
5. Liu S Christmas TJ and Kirby RS.: Malakoplakia and carcinoma of the prostate. Br J Urol, 72: 120, 1993.
6. Long JP, and Althausen AF.: Malakopakia: a 25-year experience with a review of the literature. J Urol, 141: 1328, 1989.
7. Mc Clure J.: Malakoplakia J Path, 140: 275, 1983.
8. Mc Clure J.: Malakoplakia of the prostate: a report of two cases and a review of the literature. J Clin Pathol, 32: 629, 1979.
9. Petersen RO.: Urologic Pathology, JB Lippincott Company, Philadelphia, 1993, pp 588-590.
10. Rubenstein M Bucy JG.: Malakoplakia of the prostate. South Med J, 70: 351, 1977.