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GENE MAPPING USING LINKAGE ANALYSIS*

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SUMMARY: Sanal O, Foroud T, Gatti RA. (Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey, and Departments of Biomathematics and Pathology, University of California, (UCLA), Los Angeles, California, USA). Gene mapping using linkage analysis. Turk J Pediatr 33: 1-12, 1991.

Linkage analysis is a recombinant technology used for gene mapping. If two genetic loci segregate together in a pedigree more often than by random chance, they are said to be linked, that is they lie close on the same chromosome. What makes the detection of linkage between two markers on a chromosome possible, are the recombination events which occurred during meiosis. Thus, information can be obtained for the location of a mutant gene by using markers with known locations.

Since the first published reports of linkage over thirty years ago, the use of the "lod score" method to determine the chromosomal location of a disease gene has become widespread. With the continual production of new RFLPs, the mapping of new loci will continue to become faster and more efficient. The power of the linkage method has spawned the development of several new techniques which utilize marker data to graphically represent the most likely location of a disease gene. Such advances, however, can best be utilized only after initial chromosomal localization of the particular gene through the lod score method. *Key words: linkage analysis, gene mapping, restriction fragment length polymorphism, southern blotting.*

Linkage analysis is an important tool for genetic mapping of polymorphism loci. By this approach, many disease genes have been localized to a specific chromosomal region. In at least one case, cystic fibrosis, this approach has played a direct role in the isolation of the gene. We have a similar interest in trying to "fine map" and eventually, to isolate the gene(s) for ataxia-telangiectasia[1-3].

A human cell contains 23 pairs of homologous chromosomes; one chromosome per pair is inherited from the mother and the other from the father. During the first phase of meiosis, the homologous chromosomes in a progenitor cell are duplicated and distributed to the germ cells, each of which contains 23 single chromosomes. The parental chromosomes, however, are not transmitted intact.

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In the course of meiosis, homologous chromosomes exchange segments in a process termed recombination or crossing-over. Thus, each chromosome that is transmitted to a germ cell generally carries segments from both parental chromosomes. Chromosomes are covered with loci, which are like signposts along a road. Loci can be functional genes or RFLPs (Restriction Fragment Length Polymorphism). Any two loci from a given parent that appear to segregate together more than half the time are considered to be linked. Linked loci lie on the same chromosome. The concept of linked loci has been widely used in the study of inherited disease in order to establish linkage between a disease gene and another locus (marker).

Figure 1 illustrates the theory behind linkage with a disease gene. In this example, homologous chromosomes carry different alleles at two markers (A and B)[4]. One chromosome also bears a mutant allele causing disease (m) and the other chromosome bears the normal allele (+). In the precursor cell, the disease is associated with allele 1 of both marker A and marker B. After replication, the homologous chromosomes cross-over. Here crossing-over takes place between loci A and B. As a result of this exchange, two germ cells (a, d) carry the parental combinations of alleles, and two (b, c) contain recombinant chromosomes. In cell b, the mutant gene is still found with allele 1 at locus A but is now also on the same chromosome as allele 2 at locus B. After studying many instances of meiosis, if the frequency of cross-over is low between the disease gene and the marker A, then the disease gene and the genetic marker are closely linked. The probability that a cross-over will occur increases as the distance between the two genes increases.

One percent recombination corresponds to approximately one cento Morgan (cM) or 1×10^6 nucleotides. In other words, the genetic distance between two markers is defined as one cM when the markers have a probability of one in 100 of recombining at each generation. If a marker and a disease gene lie well apart on a chromosome, the recombination frequency will approach 50 percent. The marker and the gene are then unlinked. The same probability may be seen when a marker and a mutant allele are on different chromosomes since 50 percent approximates random chance.

An inheritable phenotype can serve as a marker (e.g HLA antigens or ABO blood groups). In recent years RFLPs have been used as markers for linkage analysis. A good marker for linkage studies should have high informativeness, codominant expression and simplicity of use and interpretation in the laboratory[5]. Here informativeness means the ability to determine if a recombination event has occurred between the two markers being studied. For example, if one of the alleles of a marker is present at a very high frequency in the population, the probabilty that the two parental chromosomes will have the same alleles at one locus is high. Since all of their offspring will have only that one allele at that locus

it will not be possible to follow the segregation of paternal and maternal chromosomes; the results will be uninformative. Thus, to detect a recombination event between a marker locus and the disease gene, it is necessary to be able to distinguish between the two chromosomes at the marker locus.

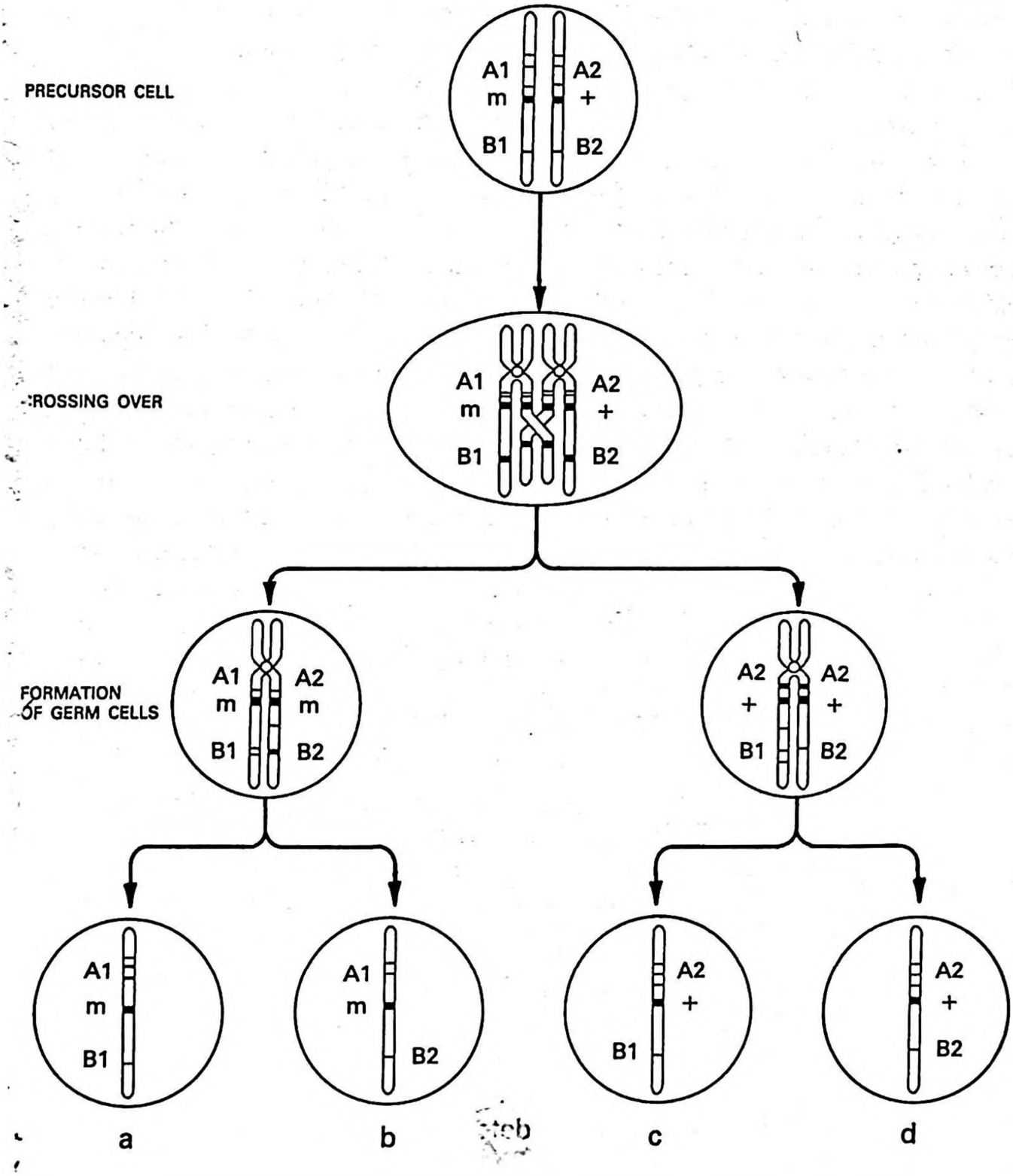

Fig. 1: The recombination event; exchange of segments of equal length between homologous chromosomes during meiosis (Reprinted with the permission of White R, Lalouel JM *Scientific American* 258:40, 1988).

The most informative markers are the ones that show many alleles in the population, none of which is present at a very high frequency. The following example illustrates the segregation of an autosomal dominant disease and a marker in a three generation pedigree (Fig. 2). Individual I-1 has both affected and unaffected children; therefore, she must be heterozygous for the disease gene. She is also heterozygous for the RFLP. If we follow the segregation of these two loci, it is clear that the affected offspring in the second generation (II-2, II-7 and II-8) do not have the same genotype at the marker locus. Since the father is homozygous (has the same two alleles at the marker locus), the affected mother has donated marker allele b along with the disease gene to two of her offspring; she has also donated the disease gene with marker allele a to the third offspring. If we consider the unaffected offspring in generation II, three children have received marker allele a with the mother's unaffected gene; however, one normal child received marker allele b. Therefore, either three of her children (II-4, II-5 and II-8) are recombinant and the other four nonrecombinant or these three children are nonrecombinant and the other four are recombinant. Since it is not known whether she carries RFLP allele a or allele b on the disease bearing chromosomes, we can not tell which is true. The situation is similar for the children of II-2. It would appear that individual III-1 and III-2 are recombinant. If we assume in this pedigree the minimal number of recombinant events, we can determine the recombination fraction as:

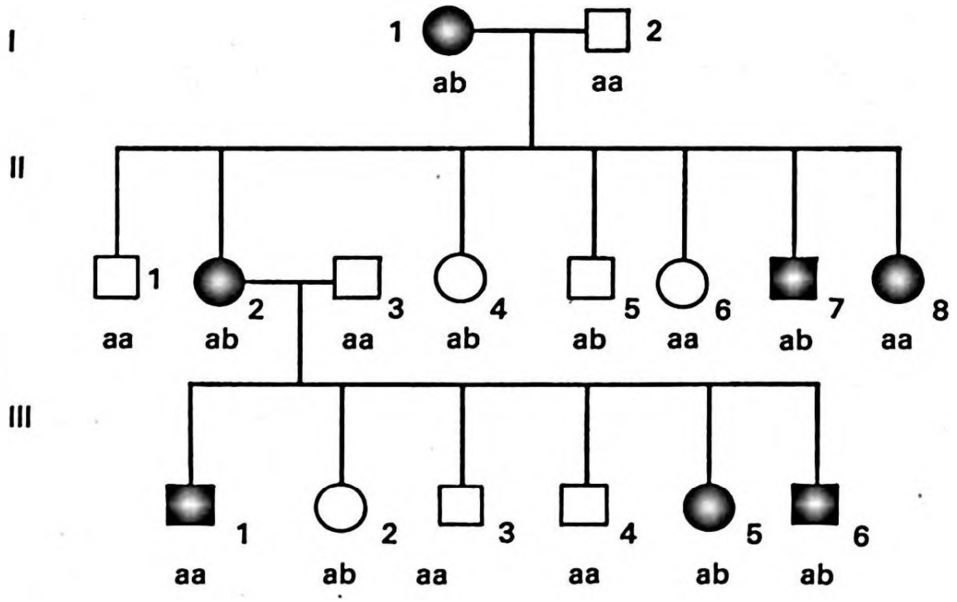

Fig 2: Segregation of an autosomal dominant disease and possibly linked marker.

$$\text{recombination fraction} = \frac{\#\text{ of recombinant chromosomes}}{\text{total number of chromosomes}} = \frac{3+2}{13} = \frac{5}{13} = < 0.50$$

It would appear that there is weak linkage between the marker and the disease gene.

Closely linked markers provide information about the location of a mutant gene and can be used for carrier detection and prenatal diagnosis[6]. Eventually, the information from linkage can be used to isolate the defective gene that causes the disease. However to be able to do all of this, markers linked to the disease of interest must be detected. Molecular biology has provided the polymorphic markers that are needed for linkage studies.

Very high levels of variation, i.e. polymorphism; found in the sequence of nucleotides of DNA allows linkage analysis to be possible. Approximately one in every 400 nucleotides is different between homologous chromosomes. These allelic variants provide a limitless number of markers scattered throughout the human genome.

RFLPs are recognized by detecting size differences between fragments obtained by cutting the DNA with restriction enzymes. RFLPs show Mendelian inheritance. The restriction endonucleases are bacterial enzymes that exist in nature to protect the host DNA from exogenous DNA. Each restriction enzyme cleaves DNA molecules whenever it meets a short, specific nucleotide sequence. The DNA fragments produced by this cleavage are very reproducible and are called restriction fragments. Any alteration in the primary sequence of the DNA will eliminate or create a cutting site. RFLPs are revealed by differences in the banding patterns shown by Southern blotting analysis between individuals for the same enzyme[7]. An example is given in Fig. 3.

A single restriction enzyme finds millions of cutting sites in the total human DNA. To detect one or two variant fragments among millions, the fragments are first separated by electrophoresis through a gel. The mobility of a fragment is inversely proportional to its length. Therefore, short fragments will travel more quickly through the gel, while large fragments will move proportionately shorter distances in the same time interval at the same voltage. Southern blotting is a sensitive technique used to detect these fragments. Double stranded DNA can be separated when heated or exposed to a high pH. The nucleotides along the single strands of DNA can then pair hybridize with a complementary DNA sequence. This feature is the essence of DNA hybridization techniques.

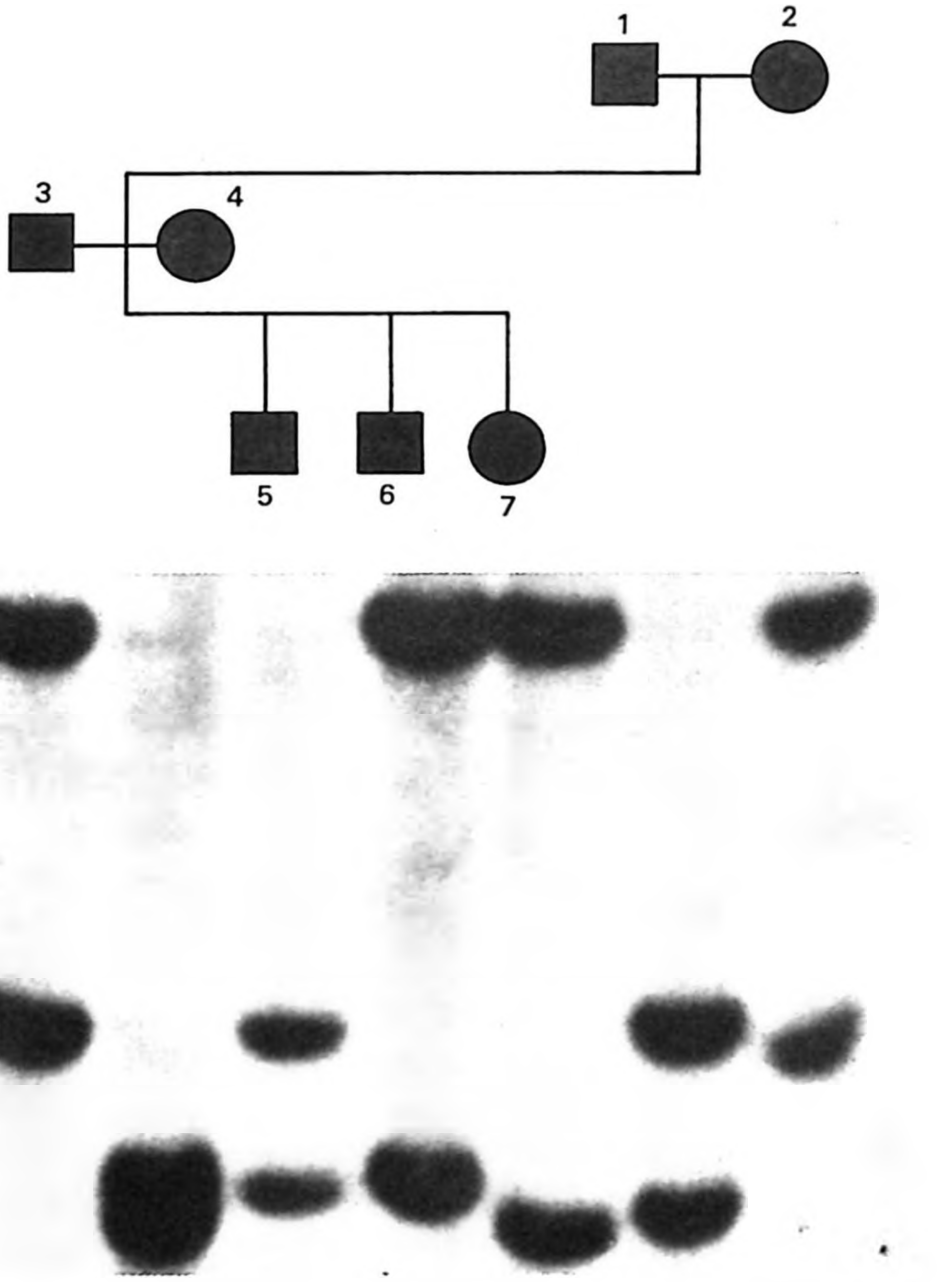

Fig. 3: A DNA marker displaying Restriction Fragment Length Polymorhism (RFLP).

In Southern blotting (Fig. 4), human genomic DNA is digested with a restriction enzyme and the fragments produced are separated by gel electrophoresis. The DNA is unwound and the single strands are blotted onto a nylon membrane. The probe, a single strand of DNA that is complementary to the piece of DNA of interest, is labelled by incorporating radioactive nucleotides and the nylon membrane is exposed to this probe. The probe will bind only to the DNA fragments complementary to this base sequence. A special film is exposed to this membrane to allow detection of the positions and patterns of bands that result from the DNA polymorphism. If the probe reveals a RFLP, then DNA from

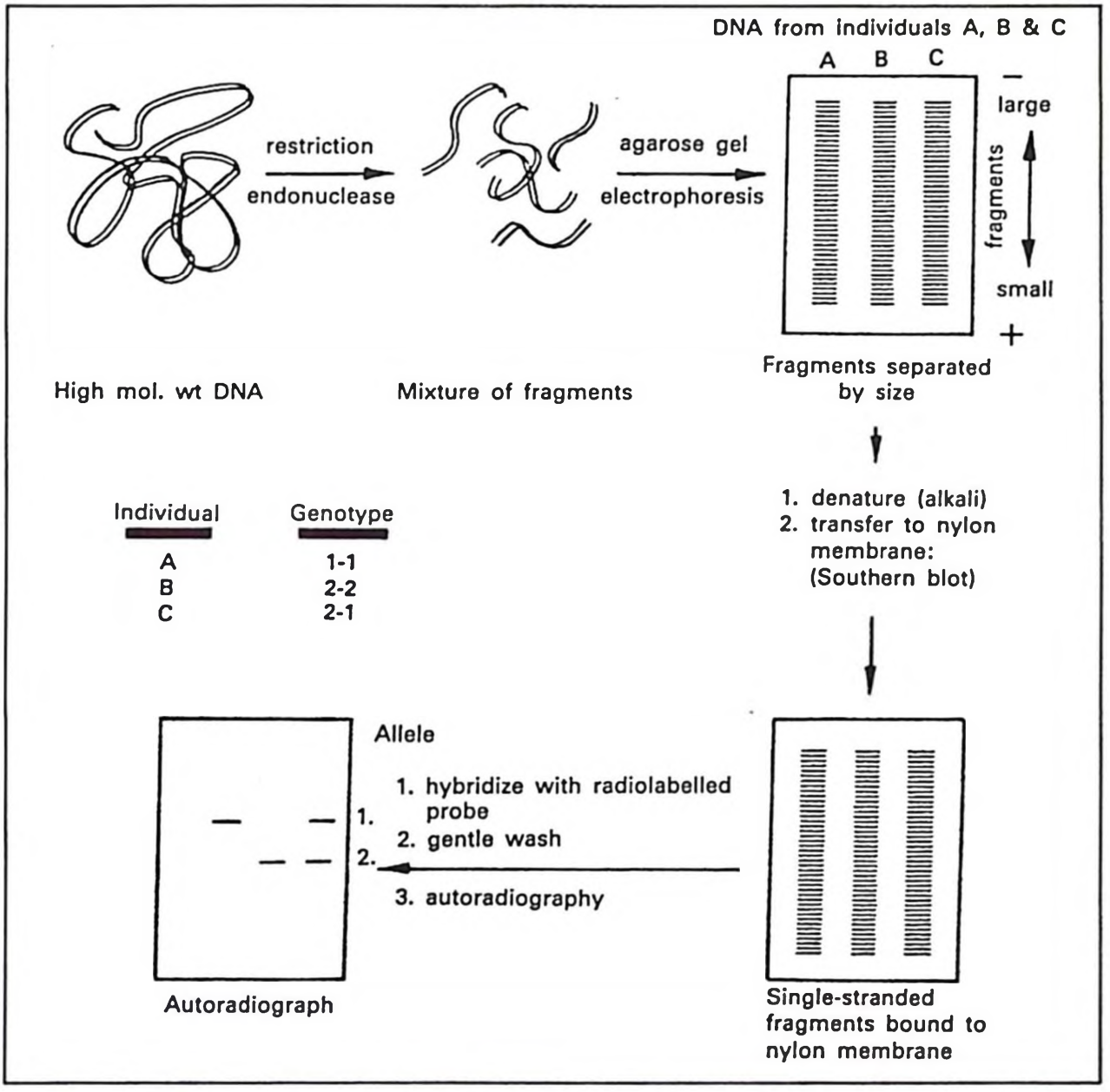

Fig. 4: Southern blotting technique for detecting RFLP.
(Reprinted with the permission of Davies KE, Read AP. *Molecular Basis of Inherited Disease*, 1988, p.8).

different individuals will show hybridization signals (bands) at different places on the blot. To detect a RFLP, a probe complementary to the DNA near the restriction enzyme cutting site should be found. These probes are chosen from a collection of cloned DNA fragments, representing the full human genome. The number of genes and anonymous DNA segments (uncoding or arbitrarily cloned DNA sequences) that detect RFLPs has increased continuously[8]. The total number of RFLPs described for each of the last four Human Gene Mapping Workshops (HGM) and the number of identified polymorphic loci per chromosome by June 1989, are shown in Fig. 5 and 6, respectively.

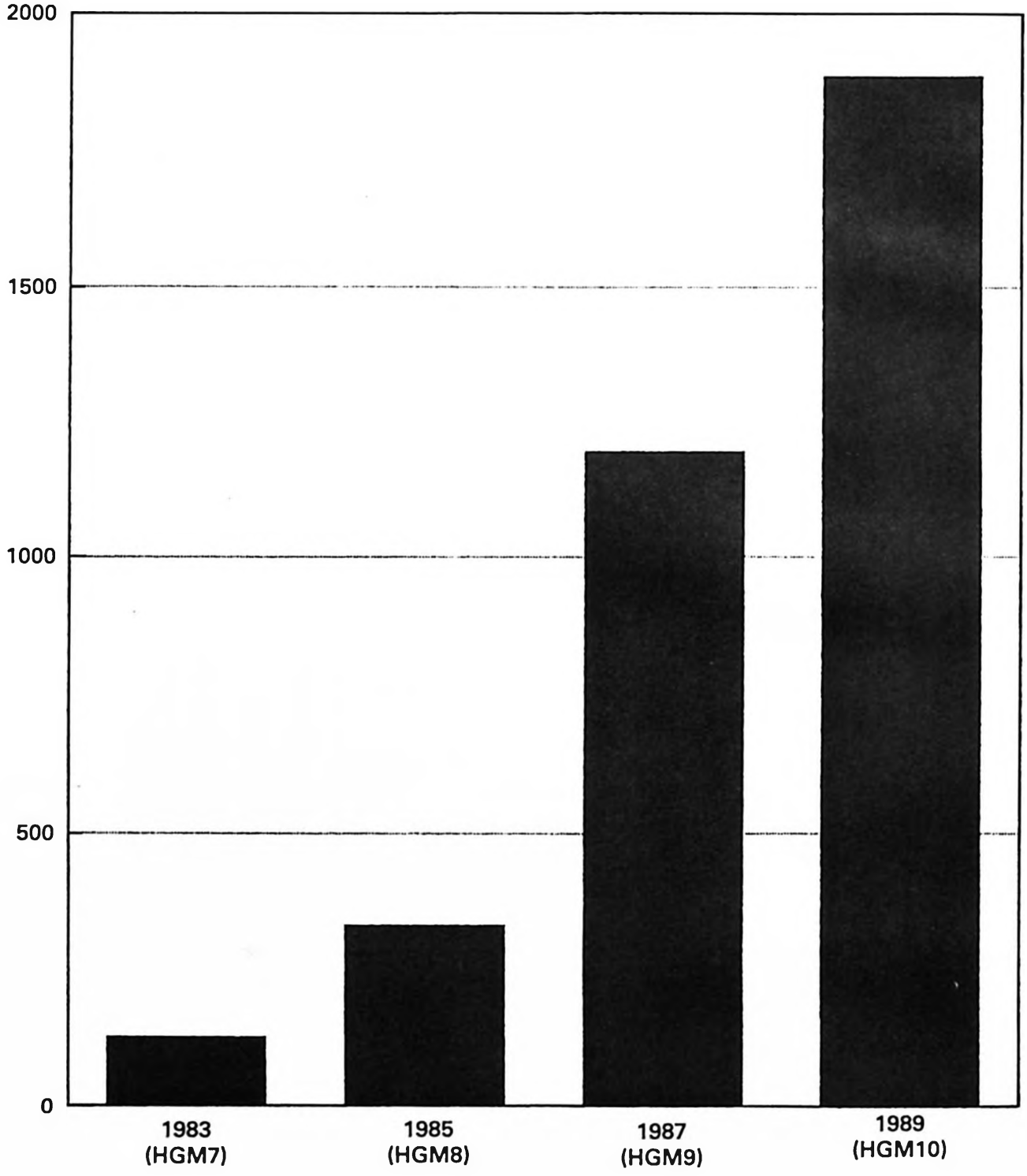

Fig. 5: The total number of RFLPs that have been assigned to specific chromosomes at each of the last four Human Gene Mapping Workshop (HGM).

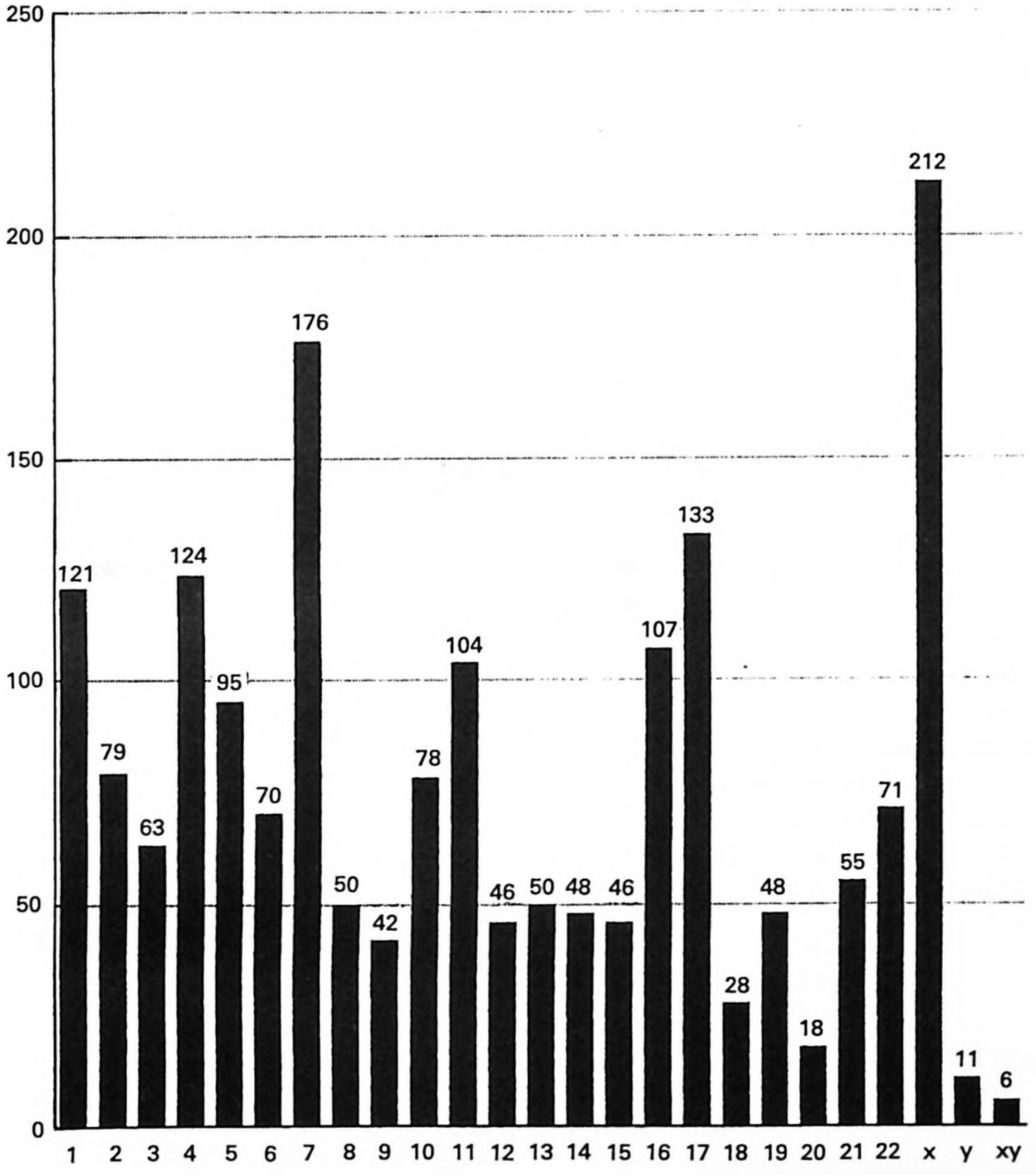

Fig. 6: The number of identified polymorphic loci per chromosome by June 1989 (HGM10).

Although the principle for linkage mapping is simple, it requires a great deal of work to both generate the data and to analyse it. A haploid genome contains about 3×10^9 nucleic acids. It has been estimated that in the human genome there are appoximately 50,000-100,000 genes. In a disease with a Mendelian pattern of inheritance, a single gene among the 100,000 genes will be defective. Where does one begin to search to localize the gene? To be able to locate any disease gene one needs to study families with 100-200 evenly-spaced genetic markers. DNA must be collected from hundreds of individuals, in dozens of large families and tested for the RFLPs characterizing each marker set. If one knows which chromosome to search, the number of markers that must be tested can be reduced from several hundreds to dozens. If, for example, a genetic disease shows an X-linked inheritance pattern, then finding the gene will only require that markers known to be carried on the X chromosome be tested. The "candidate gene" approach may also reduce the number of probes to be used. This approach is based on selecting the marker because of its position on the genetic map and its known function[9]. For example, by biochemical study, type IV Ehler's-Danlos syndrome was shown to have a deficiency of type III collagen, which is coded by a gene symbolized COL3A1. Absolute linkage of a COL3A1 RFLP and E-D IV indicates that at least in the families studied, the disorder is caused by a mutation in the structural gene for type III collagen.

For the analysis of linkage studies, the lod score method is used to quantify the degree of linkage. A lod score is the logarithm of the odds in favor of the linkage, calculated at a particular value of θ. To calculate the lod score at a particular value of θ, $\hat{\theta}$, it is necessary to calculate the likelihood of the pedigree with $\theta=\hat{\theta}$ and $\theta=0.5$. Then, the lod score at $\theta=\hat{\theta}$ is the logarithm, base 10 of the ration of two likelihoods:

$$\text{LOD} = \text{Log}_{10} = \frac{\text{likelihood of family given, 2 loci are linked with a recombination fraction, } \hat{\theta}}{\text{likelihood of family given, 2 loci are unlinked, } \theta = 0.5}$$

A positive lod score favours linkage and a negative lod score is evidence against linkage. The threshold for significance are +3 and −2. With a lod of 3, the odds in favor of linkage are 1000 to 1. A plot of the lod scores against recombination fractions is shown in Fig. 7. Curve 1 does not cross the +3 or −2 threshold and, therefore, is inconclusive. Curve 2 shows linkage, the peak is a lod score of 7 at zero, indicating an absence of recombination, suggesting that the marker localizes very close to the disease gene. Curve 3 crosses the −2 threshold at 0.1 recombination fraction, indicating that linkage closer than 10 cM can be excluded.

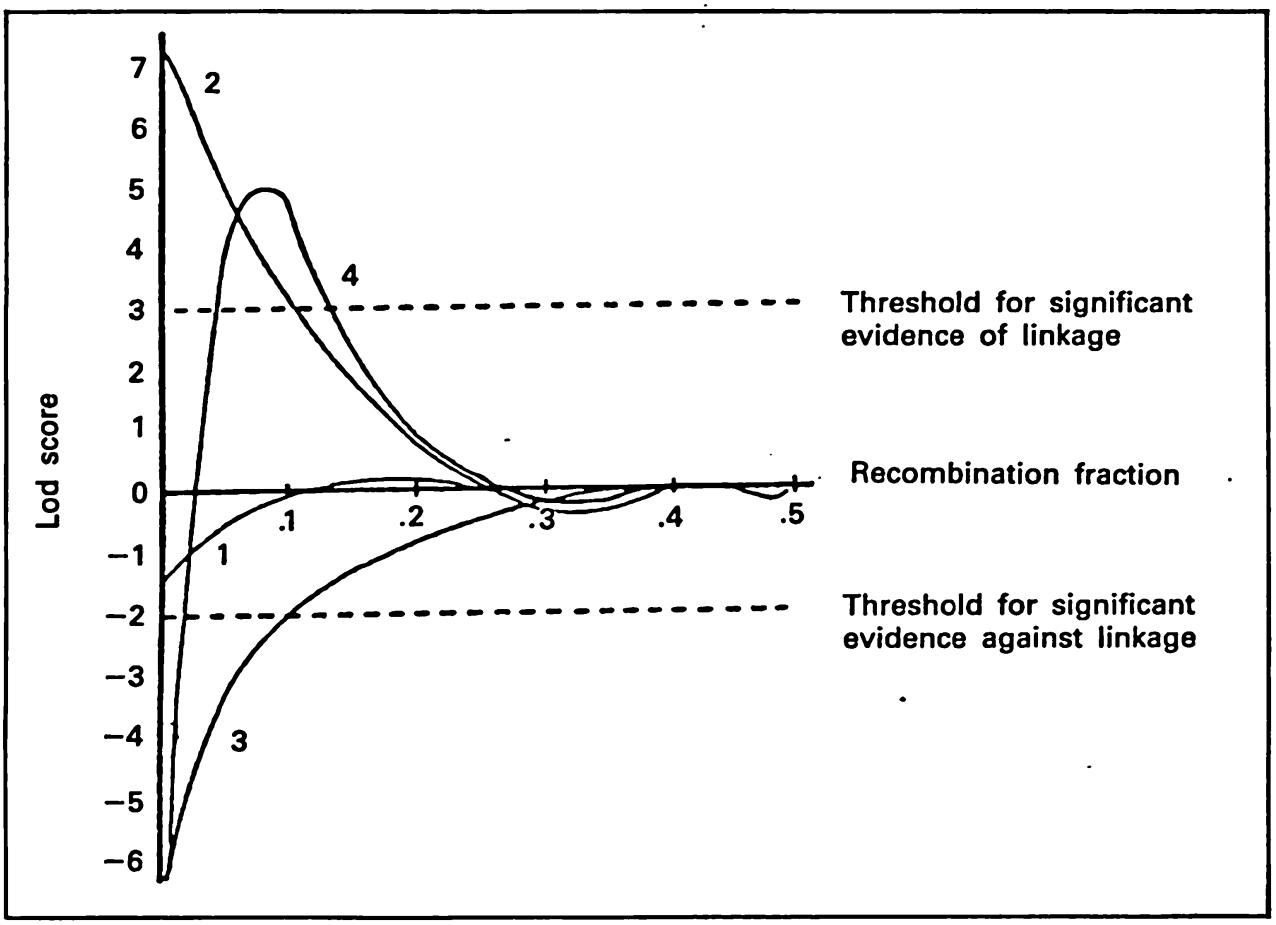

Fig. 7: Evaluation of the result of a linkage analysis (plotting of the lod scores against recombination fractions. Reprinted with the permission of Davies KE, Read AP. *Molecular Basis of Inherited Disease*, 1988 p. 19).

Curve 4 shows linkage, the peak lod score being around 5, at an estimated distance of 10 cM.

The lod score obtained from each pedigree are added together to obtain a cumulative lod score for the disease of interest and a particular marker. When several researchers are studyng the same disease, the lod scores obtained by each group can be added together provided that similar parameters are used in the calculations (e.g. allelic frequencies or disease frequency). This feature is very useful, particularly when working with a rare disease, where in each center only a few families can be studied. We have applied exactly this approach to the linkage analysis of a rare disease called "ataxia-telangiectasia"[1,3,10].

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SEROLOGICAL EVALUATION OF 52 CHILDREN IMMUNIZED WİTH THE COMBINED MEASLES, MUMPS AND RUBELLA VACCINE*

*Burhan Topal MD**, Güler Kanra MD***, Mehmet Ceyhan MD****

SUMMARY: Topal B, Kanra G, Ceyhan M. (Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Serological evaluation of 52 children immunized with combined measles, mumps and rubella vaccine. Turk J Pediatr 33: 13-18, 1991.

Fifty-two of 298 children vaccinated with the measles-mumps-rubella (MMR) vaccine at around the age of 16 months were evaluated for antibody titres against measles, mumps, and rubella. The seropositivity rates for measles, mumps, and rubella were 86%, 92%, and 98%, respectively. While the most prominent side effects were irritability (6.04%) and fever (4.69%), 83.55% of the vaccinated children showed no undesirable reaction to the vaccine. The MMR vaccine appeared to be immunogenic and nonreactogenic for the children in the study. *Key words: measles, mumps, rubella, vaccination.*

Following the development of combined vaccines against measles, mumps and rubella, it has been unequivocally demonstrated that these diseases can be eliminated by countries which carry out well-planned vaccination programs. Their successful use has resulted in a marked change of attitude towards these diseases all over the world. Whereas the lay public, medical profession and public health authorities had previously been forced to consider rubella, mumps and measles as unavoidable childhood diseases, the effective vaccination programs mounted during the last ten years have proven that these diseases can be eliminated.

Of the three said diseases, only measles is prevented by a routine national vaccination program in Turkey. The combined measles, mumps and rubella (MMR) vaccination is not routinely administered to healthy children in Turkey. Children whose parents can afford to purchase MMR vaccine from private pharmacies are vaccinated against these three diseases. The World Health Organization (WHO) recommends that the MMR vaccine be used because it is easier to administer and less troublesome when given to 15-month-old infants[1].

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Studies show that the percentage of immunity is about the same as the application of one or both of the three vaccines. In addition, the incidence of clinical signs and symptoms is approximately the same for all three vaccines[2-6].

The purpose of this study was to assess the rate of immunologic response to MMR vaccine, and the occurrence of clinical reactions in children who were vaccinated at the age of fifteen months in a private clinic.

Material and Methods

From May 1983 to September 1988, two hundred and ninety-eight healthy children were vaccinated with the MMR vaccine at our clinic. All of them had been brought to our clinic for monthly physical examinations. According to their past histories, they had never had any allergies to eggs, neomycin or kanamycin, had never received immunosuppressive drugs, had never had any symptoms or clinical signs of mumps, measles or rubella, and had never been innoculated with vaccines against mumps, measles or rubella.

The MMR combined vaccine used contained the Schwarz (measles), Urabe AM/9 (mumps) and the Wistar RA 27/3 (rubella) live attenuated virus strains. The vaccines were reconstituted immediately before use with 0.5 ml of diluent and administered into the right anterolateral aspect of the upper arm subcutaneously. Thirteen of the vaccines were produced by the Behring Institute, one by the Smith Kline Institute and 38 by Merieux.

The parents were informed of the nature and timing of any possible reactions. They made a notation if the child had fever, coryza, irritability, rash etc. and telephoned the doctor. The parents controlled the child's temperature by touch, and measured it if the child seemed feverish. Between the 7th and 10th day after injection, 30 mg/kg/day (b.i.d.) acetaminophen was given to all the children.

Measles and mumps antibody titres were determined by hemaggultinination-inhibition techniques. The initial dilution was 1:5. The ELISA (enzyme-linked immunosorbent assay) technique was used for rubella antibodies. The values below 2 IU/ml were considered seronegative. The serological results for each child were sent to the child's parents and re-immunization was recommended for those who were seronegative.

Results

Even though a total 298 children were vaccinated with MMR, only fifty-two had parental consent to be enrolled in this study, and came to our clinic for an examination in January 1989. Since the vaccination, none of the children contracted measles, mumps or rubella. The mean age at immunization was 16.4

months, and blood samples were obtained at a mean age of 38.3 months. The mean value time between vaccination and obtaining blood samples was 20.5 months (minimum 3.0; maximum 67.0 months). About ninety percent of the children were vaccinated approximately at 15 months of age, considered by WHO to be the ideal age for immunization[1,7] (Table I).

TABLE I: Age Distribution of Vaccinees

Age Group (mos.)	No. Patients (%)	Mean Vaccination Age (mos.)
All ages	52 (100.0 %)	16.4
13-18	47 (90.4 %)	14.6
19-24	3 (5.8 %)	21.0
25-48	1 (1.9 %)	26.0
49-96	1 (1.9 %)	80.0

The symptoms and clinical signs after vaccination are shown in Table II. Most of the vaccinated children were asymptomatic (83.6 percent) and did not have any clinical signs. While others were irritable and had a slight fever. Rash and parotitis were very rare.

TABLE II: Number of Children With Signs and Symptoms Three Weeks After Immunization

Symptoms and Signs	No. Patients (%)
Irritability	18 (6.04 %)
Maculopapular rash	5 (1.67 %)
Coryza	5 (1.67 %)
Fever	14 (4.69 %)
Conjunctivitis	2 (0.67 %)
Parotitis	2 (0.67 %)
Lymphadenopathy	1 (0.33 %)
Local skin reactions	2 (0.67 %)
Asymptomatic	249 (83.55 %)

In this study, the interval between vaccination and serological evaluation was approximately two years, which is shown in Table III. Out of the 52 children, the titres that were found negative of measles, mumps, and rubella were seven (13.5%), four (8%), and one (2%), respectively (Tables IV, V, VI.

TABLE III: Interval Between Vaccination and Serological Evaluation

Age Group (mos.)	Interval (mos.)
13-18	20.0
19-24	23.3
25-48	17.0
49-96	3.0

TABLE IV: Distribution of Measles Antibody Titres

Titres	No. Patients (%)
Less than 1/5	7 (13.5 %)
1/5	7 (13.5 %)
1/10	9 (17.3 %)
1/20	4 (7.7 %)
1/40	9 (17.3 %)
1/80	13 (25.0 %)
1/160	1 (1.9 %)
1/320	2 (3.8 %)

TABLE V: Distribution of Mumps Antibody Titres

Titres	No. Patients (%)
Less than 1/5	4 (7.7 %)
1/5	3 (5.8 %)
1/10	7 (13.5 %)
1/20	6 (11.5 %)
1/40	3 (5.8 %)
1/80	9 (17.3 %)
1/160	12 (23.0 %)
1/320	8 (15.4 %)

TABLE VI: Distribution of Rubella Antibody Titres

Titres	No. Patients (%)	Mean Titres
Less than 2	1 (2.0 %)	2.0
5-20	10 (19.2 %)	14.0
21-40	10 (19.2 %)	26.3
41-80	13 (25.0 %)	53.6
81-160	12 (23.1 %)	113.9
161-320	2 (3.8 %)	211.5
321-399	– –	–
More than 400	4 (7.7 %)	400

Discussion

MMR vaccine has been used for 15 years in the USA, and ten years in the Scandinavian countries[8,9]. On the other hand, the utilization of this vaccine in Turkey is very recent. Because of the cost of the vaccine, most of the children that we vaccinated came from families of a higher socio-economic level. Up until two years ago, families had purchased the vaccines from European countries. However, during the past two years, some companies have started importing large amounts of this vaccine.

Although infants are innoculated with the measles vaccine at nine months of age, in private clinics, the monovalent measles vaccine and MMR are given at fifteen months of age, which is the optimal age for obtaining the highest immunologic response.

According to our results, the antibody responses were as high as those reported in previous studies: 86.5% (measles) 92.3% (mumps) 98.0% (rubella)[2,8,9]. These results were obtained by using vaccines that were transported and stored under suitable cold-chain conditions.

The subjects in our study were from families of a high socio-economic level. None of the infants were malnourished. Although their antibody responses do not reflect the whole of Turkish society, we can draw certain conclusions from these findings. On the other hand, if we could have obtained prevaccination antibody titres, it might have been possible to speculate about the actual seroconversion of these diseases.

Robertson et al[2] and Vesikari et al[8] found many adverse reactions both after innoculation with MMR and the monovalent measles vaccine. Surprisingly, we found that the incidence of reactions from MMR vaccine was very low. Eighty-five

percent of the children had no symptoms or clinical signs. However, all the vaccinated children were given 30 mg/kg/day acetaminophen between the 7th and 10th day after injection as a routine procedure, which may account for this low incidence.

In this retrospective study, the results show high serum antibody levels against mumps, measles and rubella in children who were vaccinated with MMR vaccine at the age of 15 months. We suggest that all children should be vaccinated with MMR at about 15 months of age, even if they had been innoculated with the measles vaccine at 9 months of age.

We plan to conduct a prospective study to compare the immunologic response in Turkish children innoculated at nine months of age with the MMR vaccine to those innoculated at 15 months of age.

Acknowledgement

We would like to thank Dr. H. Bogaerts, Clinical Research Manager of Smith Kline Biologicals for his assistance.

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LIPIDS AND LIPOPROTEINS IN THE SEXUAL MATURATION STAGES OF MALE ADOLESCENTS*

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SUMMARY: Büyükgebiz A, Ciliv G, Kınık E. (Departments of Pediatrics and Biochemistry, Hacettepe University Faculty of Medicine, Ankara, Turkey). Lipids and lipoproteins in the sexual maturation stages of male adolescents. Turk J Pediatr 33: 19-25, 1991.

The study population consisted of 144 healthy, non-obese male adolescents, aged between 11-18 years, who were in different stages of sexual maturation as described by Tanner. The fasting plasma cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (C-HDL), low density lipoprotein cholesterol (C-LDL), and very low density lipoprotein cholesterol (C-VLDL) levels were calculated for each subject.

There were significant differences observed in the following: mean TC levels between G1 and G2; mean C-HDL levels between G2 and G3 and between G3 and G4; mean TG levels between G1 and G2 and between G2 and G3; mean C-LDL levels between G1 and G2, and mean C-VLDL levels between G1 and G2 and between G2 and G3. There were no significant differences for lipids and lipoproteins between the prepubertal (G1) and postpubertal (G5) stages.

It is generally believed that testosterone may play a role in mediating lipid and lipoprotein levels in the pubertal phase, but, since we found no significant differences in the levels of lipids and lipoproteins between G1 and G5, and also because these levels fluctuated from G1 to G5, it strongly suggests that the effect of testosterone on lipids and lipoproteins is dependent on other factors such as hormones, dietary habits, age, race, etc. *Key words: lipids, lipoproteins, male adolescents, Tanner sexual maturation stages.*

The association of total serum cholesterol (TC) and low density lipoprotein cholesterol (C-LDL) levels with the development of atherosclerosis has been well established[1-3]. However, the high density lipoprotein cholesterol (C-HDL) concentration is inversely related to the incidence of coronory artery disease[4-5].

Age and gender have been demonstrated to affect the C-HDL level[6]. Women tend to have higher C-HDL levels than men. Plasma C-HDL level are similar in both sexes during childhood and adolescence, and by the end of sexual maturation, changes in lipids and lipoproteins occur, which result in "adult" male-female lipoprotein differences[7].

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Most, but not all, cross-sectional and longitudinal studies have reported reductions in plasma cholesterol during adolescence[7-10]. The fall in total plasma cholesterol in males during adolescence is thought to be primarily accounted for by reductions in C-HDL and increases in C-LDL in late adolescence[7]. Subsequently, males maintain lower C-HDL levels than females throughout adult life.

This study was designed to assess cross-sectional changes in lipids, lipoproteins and stages of sexual maturation in male adolescents.

Material and Methods

The study population consisted of one hundred and forty-four healthy, non-obese male adolescents, aged between 11-18 years. The genitalia of each adolescent were classified, by the same observer, according to the stages of development described by Tanner[11], which are as follows: (G1) Prepubertal stage (G2) marked by enlargement of the scrotum and testes and reddening of the scrotal skin. (G3) Further growth of the scrotum and testes and an increase in the size of the penis, mainly in length. (G4) Still further growth of the scrotum and testes and an increase in the size of the penis, mainly in breadth. (G5) Adult developmental stage. Fasting plasma cholesterol, triglyceride (TG), C-LDL, C-HDL and very low density lipoprotein cholesterol (C-VLDL) levels were calculated for each adolescent.

TC was determined by the iron chloride-sulphuric acid method and the C-HDL level by the phosphotungstate-magnesium chloride precipitation technique[12-14]. The TG level was measured colorimetrically[15]. C-LDL and C-VLDL levels were calculated using the following formula: C-LDL (mg/dl):TC-(C-HDL + TG/5); the TG/5 value corresponds to the C-VLDL value[16].

Results

Table I gives a cross-sectional distribution of lipids and lipoproteins according to the Tanner stages of sexual maturation.

There were statistically significant differences observed in the following: mean TC levels between G1 and G2 ($p < 0.05$); mean C-HDL levels between G2 and G3 ($p < 0.001$) and between G3 and G4 ($p < 0.05$); mean TG levels between G1 and G2 ($p < 0.001$) and between G2 and G3 ($p < 0.001$); mean C-LDL levels between G1 and G2 ($p < 0.001$), and mean C-VLDL levels between G1 and G2 ($p < 0.001$) and between G2 and G3 ($p < 0.001$). There were no other statistically significant differences noted between the other stages of Tanner's sexual maturation classification as regards lipids and lipoproteins ($p > 0.05$). In addition, there were no statistically significant differences found in the values for lipids and lipoproteins when comparing the prepubertal (G1) stage with the postpubertal (G5) stage ($p > 0.05$) (Fig. 1).

TABLE I: Distribution of Serum Lipids* and Lipoproteins* According to the Tanner Stages of Genital Development (mean±SD)

Genital Stage	Mean chronological age and range (Yrs)	Number of Adolescents	TC	C-HDL	TG	C-LDL	C-VLDL
G 1	11.3 (11.0–12.2)	26	141.5±27.3	48.6±13.0	100.6±50.4	72.7±22.9	20.2±10.2
G 2	12.0 (11.2–13.4)	25	155.4±11.9	53.0±7.7	48.0±23.6	92.8±17.1	9.6±4.7
G 3	12.9 (11.8–15.1)	30	146.3±29.8	42.9±8.0	105.5±61.5	82.1±28.7	21.2±12.5
G 4	13.8 (12.4–16.4)	32	139.0±15.1	48.4±10.9	82.0±53.5	71.0±10.7	19.5±12.5
G 5	16.2 (14.8–18.0)	31	141.1±25.8	51.4±12.4	110.2±62.0	68.0±27.7	22.0±12.3
			G1vsG2 $p < 0.05$	G1vsG2 $p > 0.05$	G1vsG2 $p < 0.001$	G1vsG2 $p < 0.001$	G1vsG2 $p < 0.001$
			G2vsG3 $p > 0.05$	G2vsG3 $p < 0.001$	G2vsG3 $p < 0.001$	G2vsG3 $p > 0.05$	G2vsG3 $p < 0.001$
			G3vsG4 $p > 0.05$	G3vsG4 $p < 0.05$	G3vsG4 $p > 0.05$	G3vsG4 $p > 0.05$	G3vsG4 $p > 0.05$
			G4vsG5 $p > 0.05$	G4vsG5 $p > 0.05$	G4vsG5 $p > 0.05$	G4vsG5 $p > 0.05$	G4vsG5 $p > 0.05$
			G1vsG5 $p > 0.05$	G1vsG5 $p > 0.05$	G1vsG5 $p > 0.05$	G1vsG5 $p > 0.05$	G1vsG5 $p > 0.05$

* mg/dl

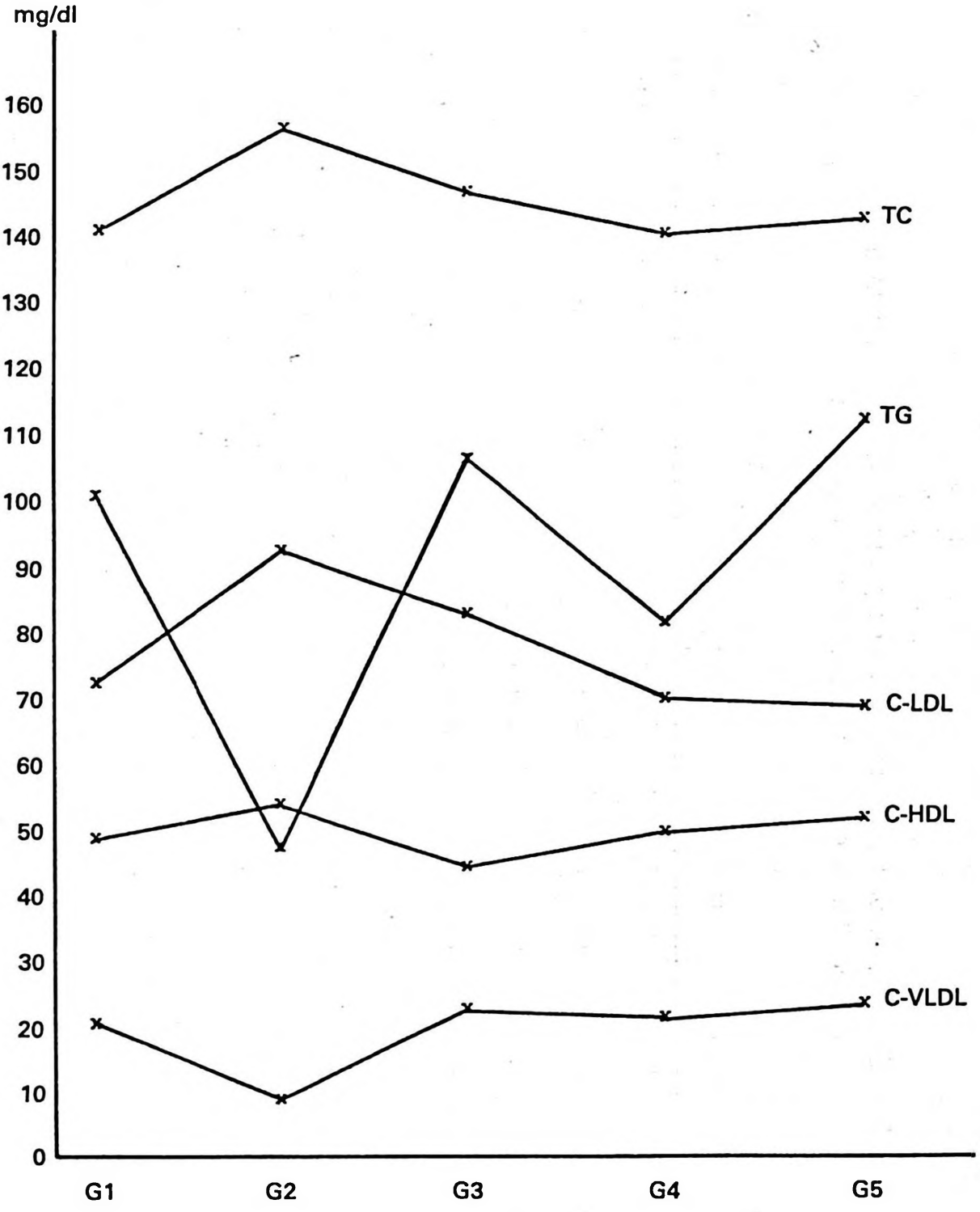

Fig. 1: Mean total cholesterol (TC), tryglyceride (TG), low density lipoprotein cholesterol (C-LDL), high density lipoprotein cholesterol (C-HDL) and very low density lipoprotein cholesterol (C-VLDL) in male adolescents at different Tanner stages.

Discussion

Adolescence is characterized by rapid alterations in physical growth and sexual maturation with a broad distribution of sexual maturation by calendar age[11-17]. Although adolescents follow the same sequence of changes (unless there is an intervening physical or hormonal abnormality), they enter, pass through and complete puberty at different ages.

Appreciable hormonal changes, primarily increased testosterone production in males, accompany the manifestations of adolescence[18-20]. Since the stage of sexual maturation (Tanner Classification), and not the age, coincides with an increase in the testosterone level, the adolescents in our study were classified according to the sexual stages described by Tanner[11,21,22].

Morrison et al[21] speculated that a decrease in C-HDL and a late increase in C-LDL, as sexual maturation progresses, are associated with increased testosterone production. In two studies, one by Barr[23], and the other by Nikkila[24], it was demonstrated that the administration of methyltestosterone in adult males produced a decrease in C-HDL and an increase in C-LDL. However, in 1987, Kirkland et al[22] reported just the contrary, as regards the relationship of testosterone to -HDL, and emphasized that testosterone should be considered a significant determinant of plasma C-HDL levels during pubertal development. Although in our study there was a decline in C-HDL levels in the G3, G4 and G5 stages with respect to G2, those values were statistically insignificant. We found a sharp increase in C-LDL in the early pubertal stage (G2), and not in the late pubertal stages, as Morrison had mentioned[21]. Even though it is known that in adolescence plasma testosterone increases, the values of C-HDL and G-LDL in the various Tanner Stages might be the result of the effects of testosterone on these two lipoproteins. Although Bradley[25] mentioned that an inverse relationship exists between TG and C-HDL, the increase in TG during sexual maturation which accompanies the decrease in C-HDL is expected. Since we obtained significantly higher TG levels in G3 with respect to G2, the high levels in G3, G4 and G5 were not significantly different from each other.

Since there is a relationship between C-VLDL and TG, we found a significant decline in G2 with respect to G1, and a significant increment in G3 with respect to G2, which are similar to TG results. Whether the initiating step in the sequential changes in C-HDL and TG during sexual maturation in males is a testosterone-mediated effect on high density lipoproteins, with a secondary reduction in C-VLDL removal or vice versa, remains to be determined by kinetic studies[23-25].

In conclusion, we believe that testosterone may play a role in mediating the levels of lipoproteins and lipids in the pubertal phase but the presence of statistically insignificant differences between prepubertal (G1) and postpubertal (G5) lipid and

lipoprotein levels and the fact that these levels fluctuate in the pubertal stages from G1 to G5, support the view that the effect of testosterone on lipids and lipoproteins is mediated by a combination of other factors (hormones, dietary, habits, age, race, etc) during puberty.

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SURGICAL TREATMENT OF RENOVASCULAR HYPERTENSION IN CHILDREN*

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SUMMARY: Paşaoğlu İ, Böke E, Doğan R, Bozer AY. (Department of Thoracic and Cardiovascular Surgery, Hacettepe University Faculty of Medicine, Ankara, Turkey). Surgical treatment of renovascular hypertension in children. Turk J Pediatr 33:. 27-34, 1991.

Hypertension of renovascular origin in pediatric patients is frequently encountered. Herein, we review our experience, as well as that of others, with this type of patient, and discuss the characteristic features of renovascular hypertension and the favourable response to reconstructive vascular surgery. *Key words: renovascular hypertension, renal artery stenosis, arterial hypertension.*

Hypertension is being increasingly recognized in pediatric patients. Although essential or primary hypertension occurs in children, in 70-80 percent of the cases of hypertension found in this age group, a secondary cause is involved[1]. Renovascular hypertension is the second most frequent secondary cause of arterial hypertension reported in children after thoracic aortic coarctation, which is also surgically correctable[1-3]. Recent improvement in diagnostic modalities and operative techniques have markedly enhanced the recognition and management of this entity. In this report, we present four children with renovascular hypertension treated surgically at our clinic.

Case Reports

Case 1

A six-year-old boy who had been diagnosed as having hypertensive encephalopathy was referred to Hacettepe University Children's Hospital on March 30, 1985. He had had a cerebrovascular accident. It was learned that he had been admitted to another university hospital in February 1985, for evaluation of fever, headache, vomiting and irritability. Physical examination on admission revealed a blood pressure of 230/170 mm Hg, left peripheral facial paralysis and hemiparesis

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on the left extremities. On auscultation, the second heart sound was accentuated and a grade II/6 systolic ejection murmur was heard along the left sternal border. Blood pressure readings ranged from 170/120 to 230/170 mm Hg, despite the administration of antihypertensive therapy. The ECG showed severe left ventricular strain. Serum creatinine and blood urea nitrogen levels were within normal limits.

On the intravenous rapid sequence urogram the left kidney appeared hypoplastic and pyelographic density on the left side was delayed. Digital subtraction angiography showed severe stenosis of the right renal artery, diagnosed as fibromuscular hyperplasia. The captopril test was positive. Selective renal vein catheterization showed increased serum renin levels in the right renal vein. The medical treatment administered during a two-month period proved to be only moderately effective, and the reduction in hypertension achieved could not be maintained.

On May 2, 1985, a polytetrafluroethylene graft (Gore-tex), 6 mm in diameter, was inserted between the infrarenal aorta and the distal right renal artery where an end-to-side anastomosis was made.

The post-operative course was uneventful, and the blood pressure was slightly decreased. The arterial hypertension was easily controlled and the medication was reduced. Control arteriography performed five years after the aorto-renal bypass revealed that the graft and distal vessels were patent (Fig. 1).

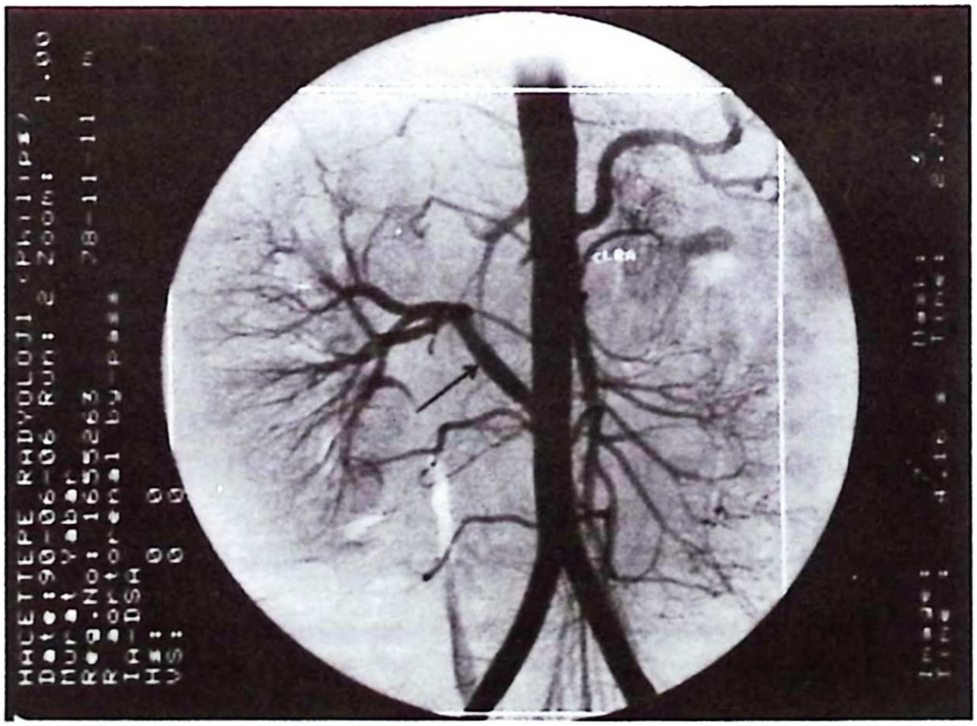

Fig. 1: Postoperative aortogram showing patent Gore-tex interposition graft (arrow) with excellent anatomic results.

Case 2

A nine year-old-boy was first seen at Hacettepe University Children's Hospital on December 16, 1982, with the main complaints of occipital headache, vomiting, and abdominal pain of one year's duration. Physical examination on admission revealed a blood pressure of 160/120 mm Hg. On auscultation there was a grade I/6 systolic ejection murmur, best heard along the left sternal border and apex, and the first heart sound was accentuated. The ECG showed a left ventricular systolic strain pattern. Serum creatinine, blood urea nitrogen, and electrolyte levels were found to be within normal limits. Funduscopy disclosed grades I-II alteration. He was placed on antihypertensive medication. However, the blood pressure readings ranged from 170/120-130/90 during a five-year follow-up.

The intravenous rapid sequence urogram showed the left kidney to be 1.5 cm smaller than the right, and there was a delay in washout of contrast medium. Selective renal arteriography revealed segmental abdominal aortic hypoplasia, severe ostial stenosis of the left renal artery and poststenotic dilatation. Selective renal vein catheterization revealed increased serum renin levels on the left side.

On November 23, 1987, the patient underwent surgery. A polytetrafluroethylene graft (Gore-tex), 5 mm in diameter, was used as an interposition graft between the abdominal aorta (end-to-side) and the main left renal artery distal to the stenosis (end-to-side). The post-operative course was uneventful, and the patient has been normotensive for two years. Aortograms taken two years postoperatively showed a patent interposition graft (Fig. 2).

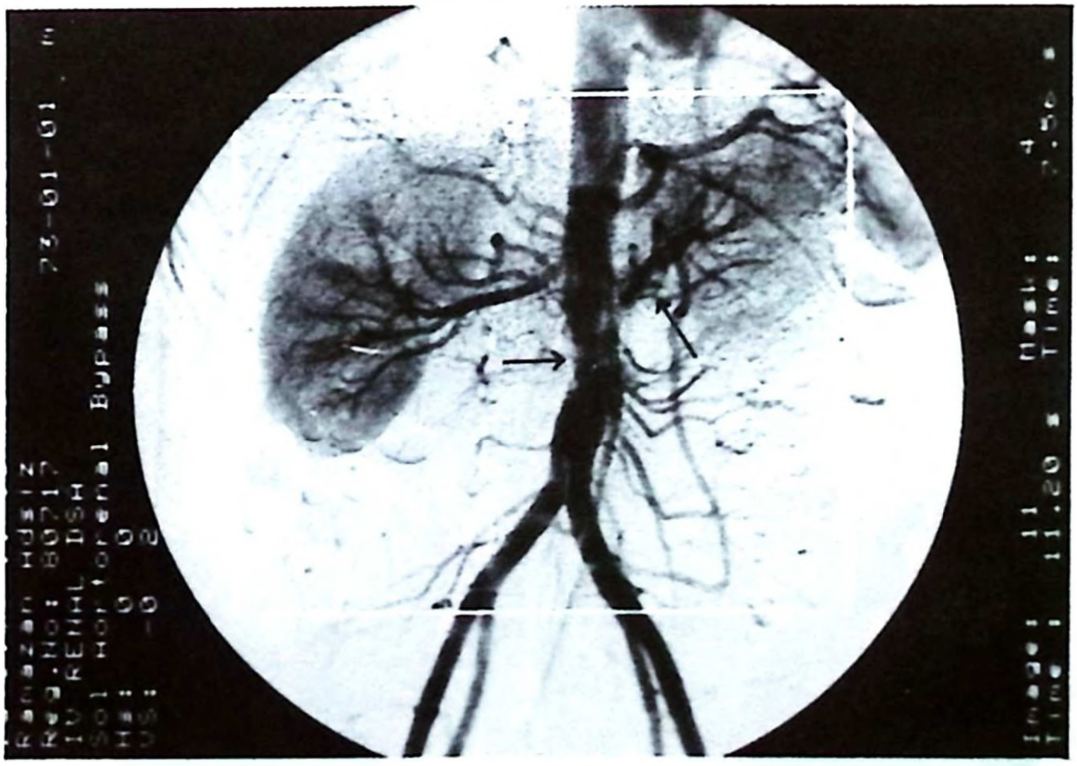

Fig. 2: Postoperative aortogram showing segmenter hypoplasia of the abdominal aorta and patent Gore-tex interposition graft (arrow).

Case 3

A seven-year-old-girl was admitted to Hacettepe University Children's Hospital on January 14, 1990, with a two-day history of vomiting, weakness, headache and convulsions. Physical examination revealed a stiff neck. The Brudzinski, Kernig, and Babinski signs were positive bilaterally. A lumbar puncture was performed and yielded cerebrospinal fluid, diagnostic of meningitis. The patient was then hospitalized. On auscultation, a grade I-II/6 ejection murmur was heard over the precordium. The blood pressure was 170/110 mm Hg, and funduscopy disclosed grade I-II alterations. After the initiation of an antibiotic regimen, the patient's clinical course rapidly returned to normal, but she was still being treated for the arterial hypertension with captopril, a beta-blockade agent and prazosin.

Normal serum creatinine and blood urea nitrogen levels and urinalysis were within normal limits which excluded the possibility of renal parenchymal disease. Intravenous rapid sequence urography showed calyceal clubbing on the right kidney. The right kidney appeared to be one cm smaller than the left, with a delayed and increased pyelographic density on the right side. Renal arteriography showed right-sided, severe, renal artery stenosis with poststenotic dilatation (Fig. 3a).

On February 2, 1990, the patient underwent aorto-renal bypass surgery in which the saphenous vein was grafted. The patient's postoperative course was uneventful, and the blood pressure returned to normal levels within a few days. One month post-operatively, a control arteriography showed a well-functioning right kidney (Fig. 3b).

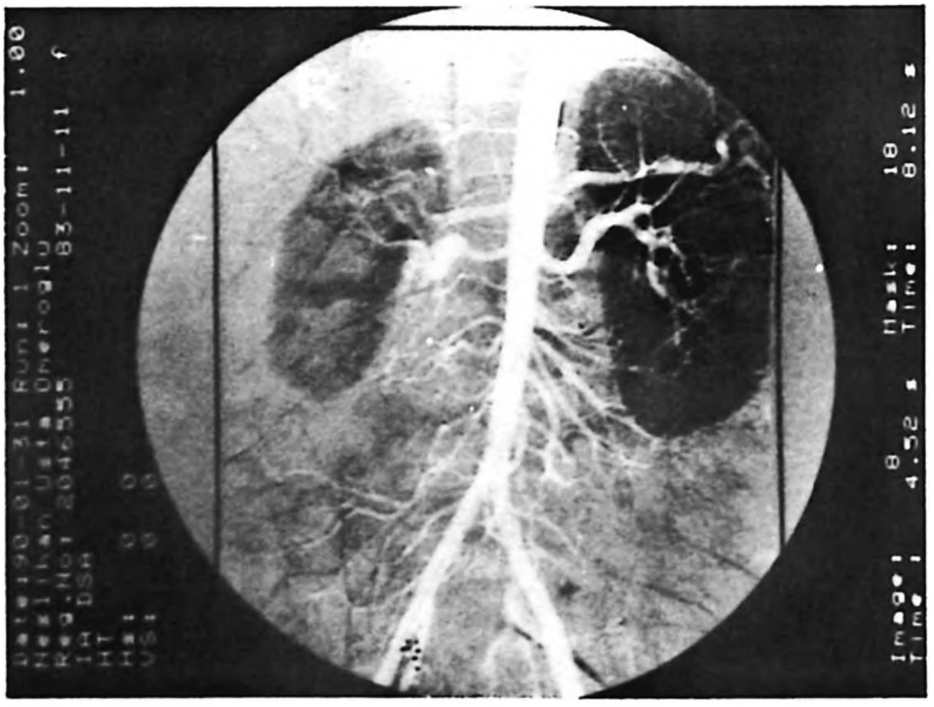

Fig. 3a: Preoperative aortogram shows fibromuscular disease of the right renal artery with poststenotic dilatation.

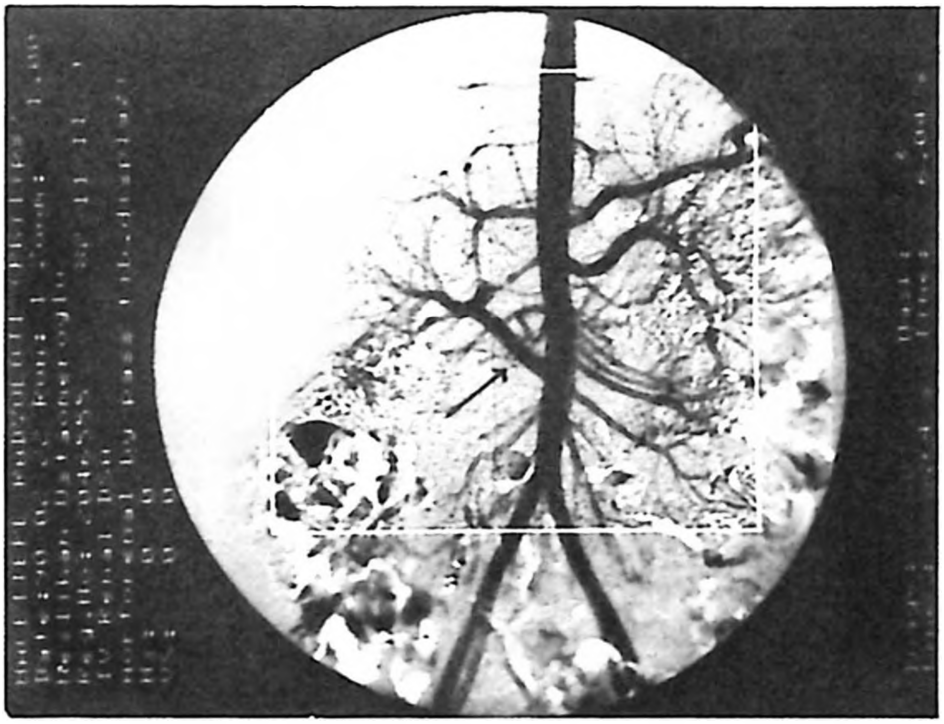

Fig. 3b: Postoperative arteriogram shows patent autogenous saphenous vein graft (arrow).

Case 4

A nine-year-old-boy was admitted to Hacettepe University Children's Hospital in April 1990, with a two-year history of headache and hypertension which could not be controlled by medical treatment. Physical examination revealed a blood pressure of 200/150 mm Hg, with grade I alterations at funduscopy. The ECG showed left ventricular hypertrophy and a strain pattern. Serum creatinine and blood urea nitrogen levels were elevated and the rate of glomerular filtration was found to be decreased.

The intravenous urogram showed the right kidney to be slightly smaller than the left, with a delayed and increased pyelographic density on the affected side. Selective intraarterial digital subtraction angiography showed that the right kidney had two separate renal arteries with severe proximal stenosis (Fig. 4a), and an aortogram revealed localized narrowing of the abdominal aorta.

On May 15, 1990, the patient underwent surgery in which both renal arteries were repaired by two separate aorto-renal bypasses employing saphenous vein grafts. After the operation, the blood pressure decreased slightly. The blood pressure reached normal levels as a result of treatment with lower dosages of prazosin and captopril compared to the doses used preoperatively. Control arteriography showed good revascularization with some dilatation of the vein graft (Fig. 4b).

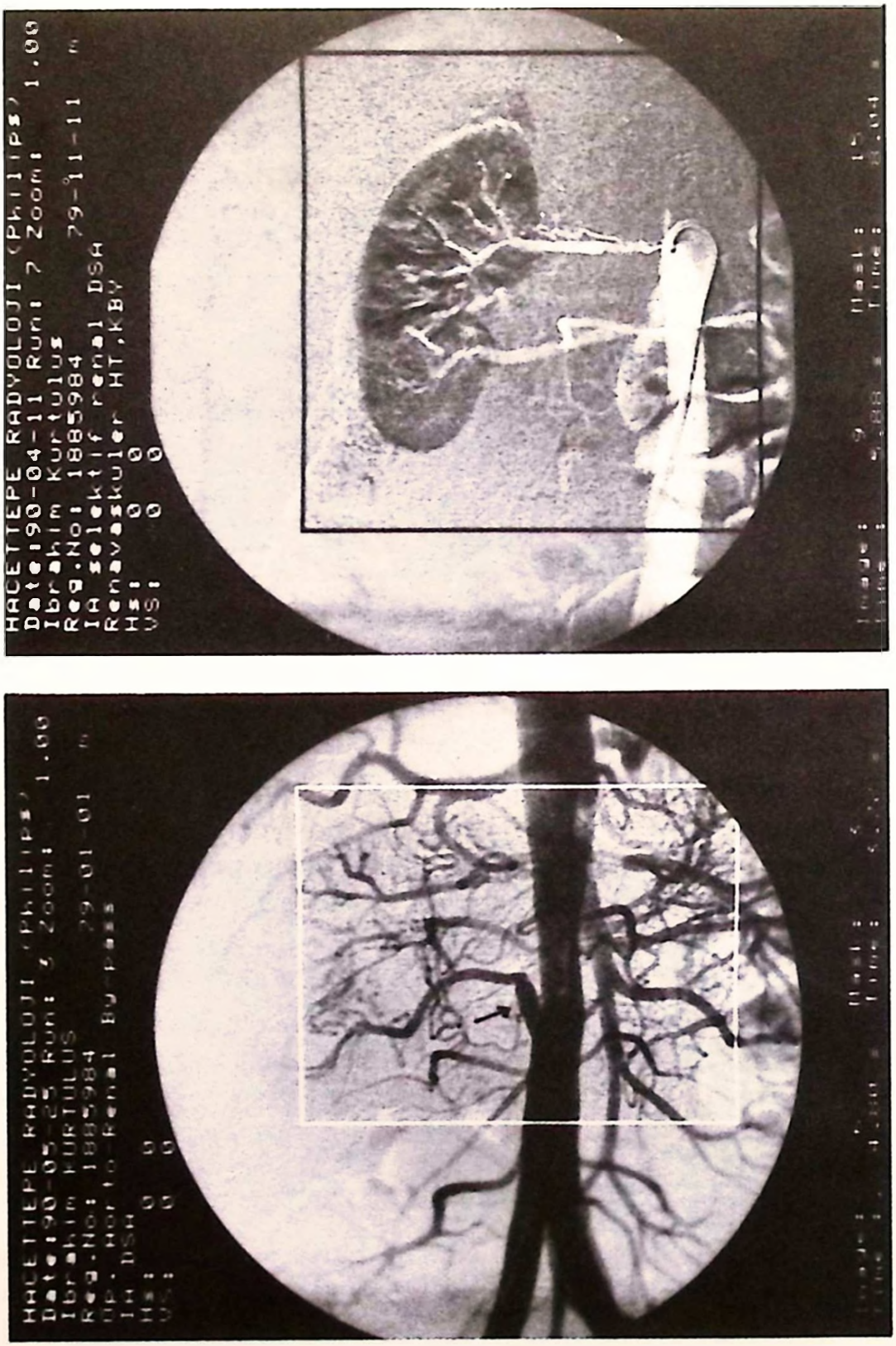

Fig. 4a: Preoperative selective right renal arteriography shows proximal stenosis of both upper and lower artery branches. b.- After aortorenal bypass, aortogram shows saphenous vein graft dilatation (arrow), and segmenter narrowing of the abdominal aorta is also present preoperatively.

Discussion

Approximately 1-2 percent of children have hypertension, and 15-20% of this group will have renovascular pathology[4,5]. Intimal and medial-paramedial fibrodysplasias are the most common histologic forms of renal artery disease in pediatric renovascular hypertension, affecting 95 percent of patients[3].

The clinical presentation of pediatric renovascular hypertension is often deceiving. Although most of the children with this disease are asymptomatic, the most common complaints are hyperexcitability, occipital headache, fatigability, and failure-to-thrive, which are not specific. Less than half of patients have hypertension diagnosed during a routine physical examination. Several patients seek medical attention only after developing convulsions. Hypertensive encephalopathy and irreversible deterioration of cerebral function secondary to uncontrolled hypertension generally carry a poor prognosis[6].

Although intravenous rapid sequence urography has been widely used in the past, it has been documented that urograms have a limited diagnostic value, and that they can be very misleading when employed to diagnose pediatric hypertensive patients. In three separate series, the incidences of renovascular hypertension in children have been reported as 52 percent[7,8], 54 percent[9], and as low as 24 percent[10]. In our limited series, all the patients showed lateralization.

Excessive production of renin in pediatric hypertension often reflects underlying renal vascular disease. This may be evident either in high peripheral or renal venous renin activity[7,11,12]. Elevation of plasma renin activity in the renal vein has been used to identify patients with unilateral renal disease causing hypertension, and to predict surgical curability[13,14]. Renal vein renin ratios which compare the effluent activity of each kidney have been suggestive of functionally important renovascular disease when greater than 1.5. Lateralization has been found in 82-93 percent of cases[7,10,12]. Although there are many useful screening tests, the only accurate method of diagnosis is the arteriogram.

The choice of surgical therapy depends on the morphology of the lesion, the natural history of the disease, and the surgeon's experience. The ideal surgical treatment is revascularization. Continued improvement in macro-and microvascular techniques has lessened the incidence of primary nephrectomy and has increased the success rate of renovascular reconstructive surgery. Although the autogenous saphenous vein is the most preferred graft material, in recent years the hypogastric artery has been accepted to be an excellent prosthesis for children[8,15,16,17].

In conclusion, we are convinced that the results of surgery for treating renovascular hypertension are quite favorable. Long-term use of medication to treat hypertension for the purpose of facilitating surgical therapy by dilating the

arteries might be dangerous, and therefore, may reduce the possiblity of a cure. Therefore, patients with renal occlusive disease should undergo surgery as early as possible.

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PULMONARY HYPERTENSION DUE TO CHRONIC UPPER AIRWAY OBSTRUCTION: A CLINICAL REVIEW AND REPORT OF FOUR CASES*

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SUMMARY: Aji DY, Sarıoğlu A, Sever L, Arısoy N. (Department of Pediatrics, Cerrahpaşa Faculty of Medicine, and Institute of Cardiology, İstanbul University, İstanbul, Turkey). Pulmonary hypertension due to chronic upper airway obstruction: clinical review and report of four cases. Turk J Pediatr 33: 35-41, 1991.

Partial airway obstruction due to the enlargement of the tonsils and adenoids is a well recognized clinical entity, but cardiorespiratory changes due to chronic obstruction have infrequently been reported. Four children with severe nasopharyngeal obstruction due to tonsil and adenoid hypertrophy, who developed pulmonary hypertension and cardiac failure, were studied. Relief of upper airway obstruction by adenotonsillectomy resulted in a regression of the presenting signs and symptoms.
Key words: adenoid hypertrophy, tonsil hypertrophy, pulmonary hypertension, adenotonsillectomy.

Hypoventilation is listed as one of the causes of pulmonary hypertension. Obstructive respiratory tract disease with hypoxia, hypercapnia and acidosis is extremely rare in childhood, except in patients with chronic asthma and cystic fibrosis[1]. Pulmonary hypertension resulting from upper airway obstruction has recently been reported in children[2-7]. The present report describes the clinical course of four children with tonsil and adenoid hypertrophy.

Case Reports

Case 1

A 3-year-old boy was admitted to our hospital in January 1987, with complaints of frequent upper respiratory tract infection, sleep associated stertorous breathing and shortness of breath since infancy.

On examination, while awake, the child appeared dull. The mouth was held open and there was an audible snoring sound with respiration. Adenoid facies, perioral cyanosis and pretibial edema were present. He was 89 cm in height and weighed 14.3 kg. The heart rate was 140/min, and respiration rate, 38/min. The blood

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pressure was 110/60 mmHg, and axillary temperature, 37°C. During sleep the child was cyanotic and diaphoretic, and exhibited supraclavicular and intercostal retractions which disappeared while awake. The tonsils and adenoids were almost occluding the oropharynx.

On auscultation, the pulmonary valve closure sound was moderately accentuated, and a short grade II systolic murmur was heard over the pulmonary area. Crepitations were present on both lung fields. The firm liver edge was palpable four cm below the right costal margin.

Laboratory data revealed a hemoglobin level of 8 g/dl, hematocrit 42% and white blood cell count 11,200/mm^3. The urine analysis was normal.

The chest X-ray showed a cardiothoracic ratio of 0.66, with pulmonary congestion. The electrocardiogram (ECG) revealed right axis deviation, peaked p waves of right atrial hypertrophy and right ventricular hypertrophy (Fig. 1). Two-dimensional echocardiography revealed no intracardiac pathology, except for right atrial and ventricular enlargement. M-mode tracings showed horizontal positioning of the pulmonary valve and disappearance of the "a" wave, leading to a diagnosis of pulmonary hypertension.

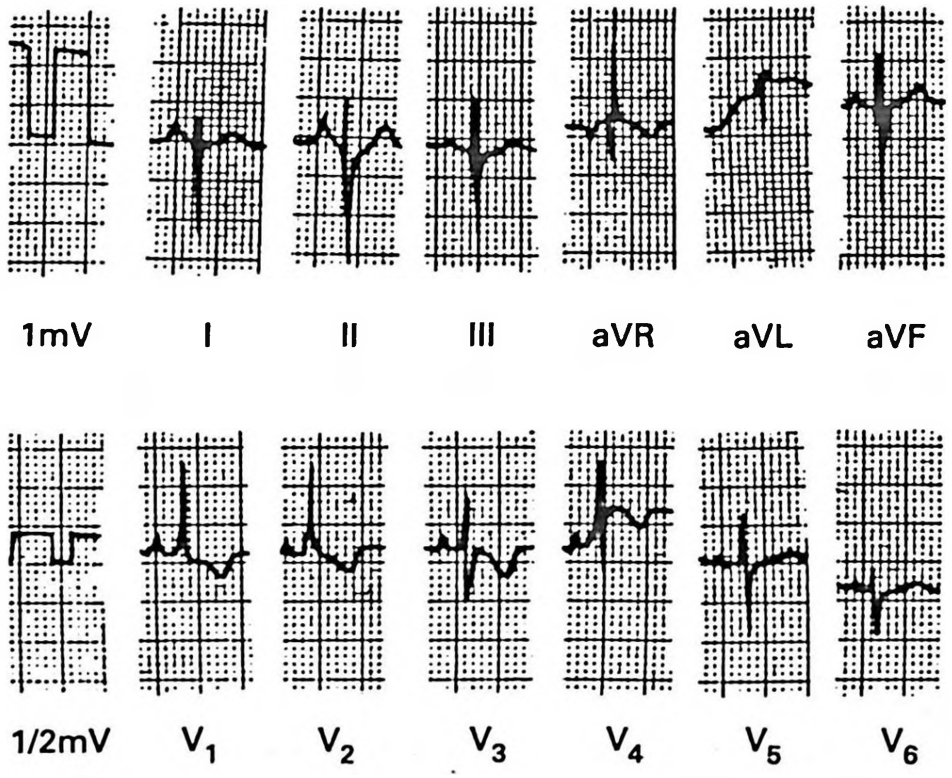

Fig. 1: Electrocardiogram of Case 1.

A diagnosis of pulmonary hypertension and congestive heart failure secondary to upper airway obstruction was made, and the patient was treated with digoxin and diuretics. On the seventh day of admission, adenotonsillectomy was performed which was followed by rapid improvement. The medical treatment was discontinued. One year later, the clinical and laboratory findings were completely normal (Fig. 2).

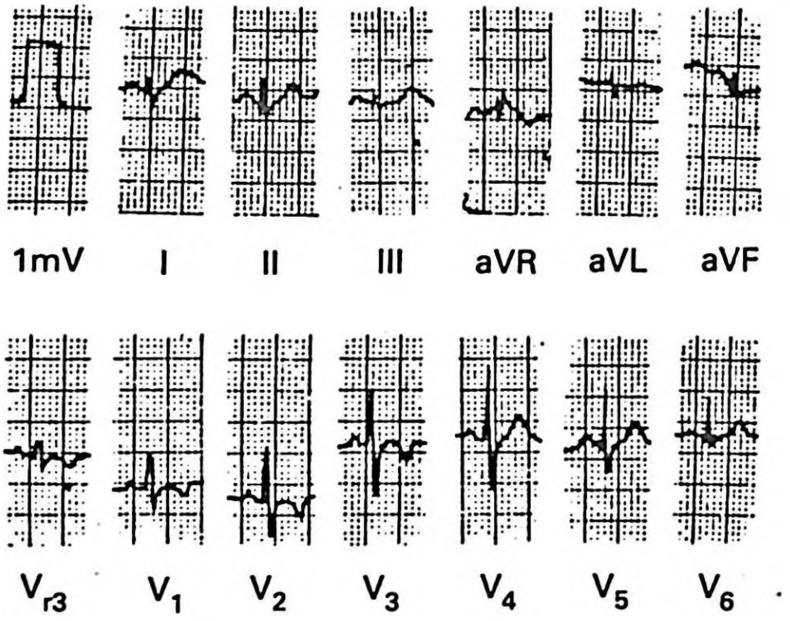

Fig. 2: Electrocardiogram of Case 1 following medical treatment.

Case 2

A 2 1/2-year-old boy was admitted to our hospital in March 1988, with complaints of shortness of breath and difficulty in breathing, especially at night, of two months' duration. He had been referred from Trabzon Community Hospital (a mountainous city on Turkey's Black Sea Coast) for cardiologic evaluation.

Physical examination revealed a boy who was 86 cm in height and weighed 14 kg. He had adenoid facies and a plethoric appearance. During sleep he snored, and apnea and cyanosis developed which awakened the child.

The heart rate was 120/min, and respiration rate 42/min. The blood pressure was 110/80 mmHg, and axillary temperature 38°C. The adenoids and tonsils were extremely enlarged, and acute tonsillitis was present. The pulmonary valve closure sound was accentuated but there were no heart murmurs. Coarse rales were detected over the lungs, especially at the bases. The liver was palpable two cm below the right costal margin.

The hemoglobin was 14 g/dl, hematocrit 55% and white blood cell count 7000/mm^3. The chest X-ray revealed increased interstitial markings and a cardiothoracic ratio of 0.61. ECG showed right axis deviation and peaked p waves.

The two-dimensional echocardiogram revealed no intracardiac pathology other than right ventricular enlargement. M-mode tracings showed pulmonary hypertension with horizontal positioning of the pulmonary valve in diastole and disappearance of the "a" wave.

The patient was treated with antibiotics for the tonsillitis. On the sixth day of admission, adenotonsillectomy was performed, followed by dramatic clinical improvement, a decrease in heart size on X-ray, and a regression of electrocardiographic findings.

Case 3

A 22-month-old boy was admitted to our hospital in November 1988, with complaints of shortness of breath, orthopnea and stertorous sleep of over one year's duration. Swelling of the face, neck and legs had developed one week before his admission to a local hospital. A diagnosis of congestive heart failure was made, and he was treated with digoxin, prednisolone and antibiotics, with no clinical improvement noted. He was then referred to our hospital for cardiologic evaluation.

Physical examination revealed an underdeveloped boy who was 74 cm in height and 8 kg in weight. He was lethargic, and cyanosis and edema on the face and legs were present. The respiration rate was 40/min and irregular. The pulse rate was 100/min, and a grade II systolic murmur was heard over the pulmonary area. The pulmonary valve closure sound was accentuated. The liver was palpable six cm below the right costal margin. The tonsils and adenoids were enormous, and postnasal purulent dripping was present.

Laboratory data showed a hemoglobin of 10 g/dl, hematocrit 38%, and white blood cells 9400/mm^3.

Arterialized blood showed a normal pH, PCO_2 of 85.7 mmHg, PO_2 61.4 mmHg and HCO_3, 58 mmol/1.

ECG showed right axis deviation, p pulmonale, right ventricular hypertrophy and negative T waves in V_5 and V_6. The chest X-ray showed an enlarged heart with a cardiothoracic ratio of 0.59. Pulmonary congestion was present.

Right ventricular and right atrial enlargement were the only intracardiac pathological features which appeared in two-dimensional echocardiography. M-mode tracings of the pulmonary valve illustrated a horizontal "e-f" slope in diastole and absence of the "a" wave, evidence of pulmonary hypertension.

A diagnosis of pulmonary hypertension and congestive hert failure secondary to upper airway obstruction was made. The patient was treated with antibotics, digoxin and diuretics, and was maintained in an upright position. On the ninth day of admission, he underwent adenotonsillectomy, followed by improvement in his clinical status, chest X-ray and electrocardiogram.

Case 4

A 6-year-old girl was admitted to our hospital in May 1989, with complaints of shortness of breath, chest pain and swelling of the face and feet. Frequent upper respiratory infections, stertorous breathing and a disturbed sleep pattern were described.

Physical examination revealed a girl who was 100 cm in height and 22 kg in weight. Dyspnea, perioral cyanosis, increasing during sleep, edema on the face and legs and ascites were present. The tonsils and adenoids were extremely enlarged. The respiration rate was 52/min and the heart rate, 124/min. The pulmonary valve closure sound was accentuated but there were no heart murmurs. The blood pressure was 110/70 mmHg. Crepitations were present on both lung fields. The liver was enlarged five cm below the right costal margin.

Laboratory data showed a hemoglobin level of 11.6 g/dl, hematocrit 37% and white blood cell count 7800/mm^3. Urine analysis was within normal limits.

The chest X-ray showed a cardiothoracic ratio of 0.62, with pulmonary congestion. ECG revealed right axis deviation, peaked p waves and right ventricular hypertrophy.

The cross-sectional echocardiogram showed right atrial and ventricular enlargement and leftward bulging of the atrial septum. In M-mode echocardiograms of the pulmonary valve, the "a" wave was missing, the "b-c" slope appeared more vertical and the "e-f" slope more horizontal than normal which suggest a diagnosis of pulmonary hypertension.

The child was treated with digoxin and diuretics for heart failure. The dyspnea and edema disappeared on the fourth day of treatment, and adenotonsillectomy was performed on the tenth day of admission, followed by rapid improvement. The patient is now leading a normal life, and does not use any medication.

Discussion

Partial upper airway obstruction due to tonsil and adenoid hypertrophy is frequently encountered in children between two and five years of age[6]. Infection and allergy effect its severity.

Cor pulmonale due to chronic upper airway obstruction in children was first reported by Menashe et al[7] in 1965. However, children with enlarged tonsils and adenoids do not all develop pulmonary hypertension. Talsat et al[8] reported only two cases of cor pulmonale among thirty such cases.

Wilkinson et al[9] have examined 92 patients with tonsil and adenoid hypertrophy and diagnosed pulmonary hypertension in only 3.3 percent of them. Macartney et al[10] have suggested that pulmonary vasculature is hyperreactive towards hypoxemia in some children, as seen in 20% of people who live at high altitudes.

Other factors, such as race and central nervous system pathology leading to abnormal respiration control have also been suggested[3].

Figure 3 shows the mechanism involved in upper airway obstruction which leads to pulmonary hypertension and heart failure.

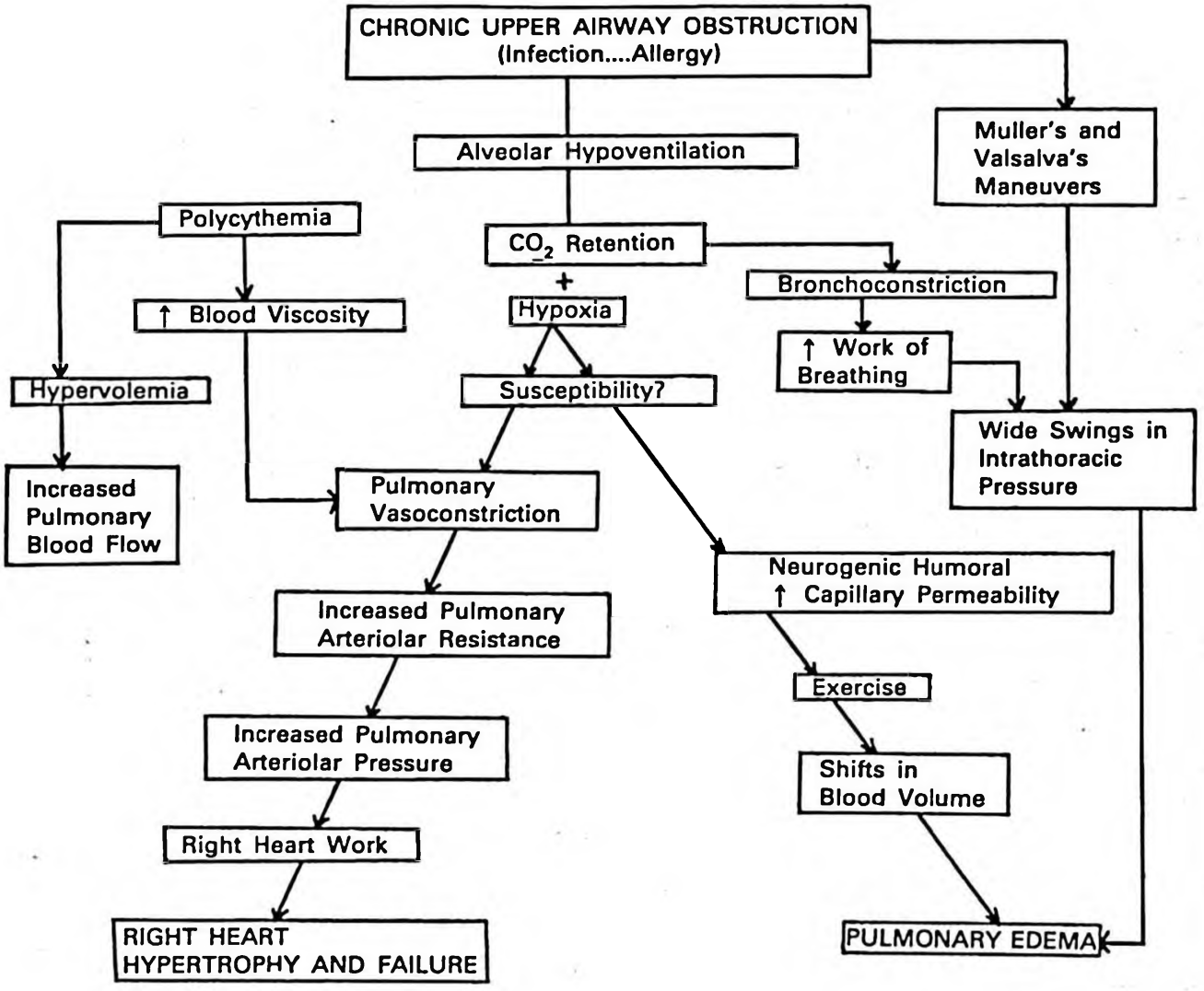

Fig. 3: Flow chart showing the mechanism of pulmonary hypertension and heart failure in upper airway obstruction.

Patients with tonsil and adenoid hypertrophy who develop pulmonary hypertension present with noisy mouth breathing, dangerous nocturnal disturbance of sleep leading sometimes to sleep-associated apnea, lethargy, rhinitis, cyanosis, clubbing, respiratory distress, cardiomegaly, right axis deviation, congestive heart failure, pulmonary accentuated valve closure, hypoxemia and hypercapnia, as demonstrated in our four cases.

It is well known that polycythemia which results from residing at high altitude causes pulmonary hypertension[11,12]. Therefore, polycythemia may well have played a role in the development of pulmonary hypertension in our second case,

who lived in the mountainous region of the Black Sea Coast, in addition to hypoxemia, due to chronic upper airway obstruction.

Cor pulmonale due to tonsil and adenoid hypertrophy is reversible. After adenotonsillectomy, clinical and laboratory findings rapidly improve, as was observed in our four cases. The only risk factor reported during the operation is sudden death caused by the anesthesia[9].

On clinical grounds, the relation between tonsil and adenoid hypertrophy and cardiorespiratory pathology can easily be overlooked. Assessing these children as primary heart patients and postponing adenotonsillectomy for thorough cardiologic evaluation could lead to loss of time, and is important in prognosis.

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The Turkish Journal of Pediatrics 33:43-47, 1991

GASTRIC INVOLVEMENT IN CHILDHOOD NON-HODGKIN'S LYMPHOMA: A CASE REPORT*

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*Tahsin Teziç MD*****, Yavuz Özoran MD******

SUMMARY: Bakır T, Gümüştekin E, Bozalioğlu H, Teziç T, Özoran Y. (Department of Gastroenterology, Karadeniz Technical University Faculty of Medicine, Trabzon). Gastric involvement in childhood non-Hodgkin's lymphoma: a case report. Turk J Pediatr 33: 43-47, 1991.

A 14-year-old girl with non-Hodgkin's lymphoma involving the stomach is presented because of the rarity of the case, and the literature is reviewed in order to evaluate the management of these patients. *Key words: gastric involvement, non-Hodgkin's lymphoma, childhood tumors.*

Non-Hodgkin's lymphoma of the gastrointestinal tract in childhood mainly involves the ileocecal region of the bowel. Involvement of the stomach rarely occurs in children[1-5]. In this report, a case of non-Hodgkin's lymphoma involving the stomach is described, and suggestions are made regarding the management of non-Hodgkin's lymphomas of the stomach in children.

Case Report

A fourteen-year-old girl had a history of epigastric pain and weight loss two weeks prior to presentation at the hospital. She also complained of nausea, vomiting and general malaise.

Physical examination revealed a pale, weak patient. The abdomen was slightly distended. Hepatosplenomegaly and lymphadenopathy were not detected. A movable mass, measuring 10 cm in diameter, was palpable in the epigastrium.

Laboratory examination revealed a hemoglobin of 8.9 g/dl, white blood cell count 11,200/mm^3 with normal peripheral blood smear findings, and an erythrocyte sedimentation rate of 72 mm/h. Routine liver and renal function tests and bone marrow examination were normal. Lumbar puncture was not performed because there was no sign of central nervous system manifestation.

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Posterior-anterior and lateral roentgenograms of the chest were normal. Abdominal ultrasonography revealed a dilated stomach filled with fluid. The liver and spleen were not enlarged, and ascites were not detected.

Barium examination of the stomach showed a large filling defect in the antrum (Fig. 1). Gastroscopy revealed a polypoid tumor with central ulceration involving the antrum and the corpus.

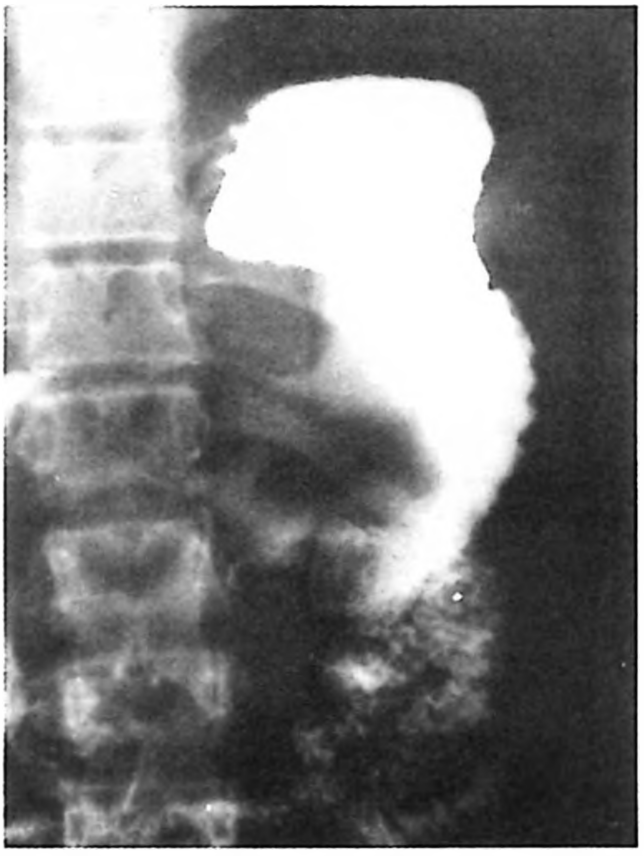

Fig. 1: Gastrointestinal roentgenogram shows a large-filling defect in the antrum of the stomach.

At laparotomy an infiltrative tumor arising from the posterior wall of the antrum and corpus of the stomach was detected. The tumor was firm, irregular and fixed to the pancreas and omentum majus. There were several metastatic nodules on the omentum. The liver and spleen were normal.

Extensive involvement of the stomach suggested that the disease started in this organ and had spread to adjacent organs. A palliative gastrojejunostomy was performed. Microscopic examination of the tumor showed diffuse lymphocytic lymphoma (Figs. 2a, 2b).

The LSA_2-L_2 protocol[6] was contemplated in the immediate postoperative period, but the patient's general condition rapidly deteriorated, and she died of massive upper gastrointestinal bleeding and cardiac arrest on the fifteenth postoperative day. Permission for postmortem examination was denied.

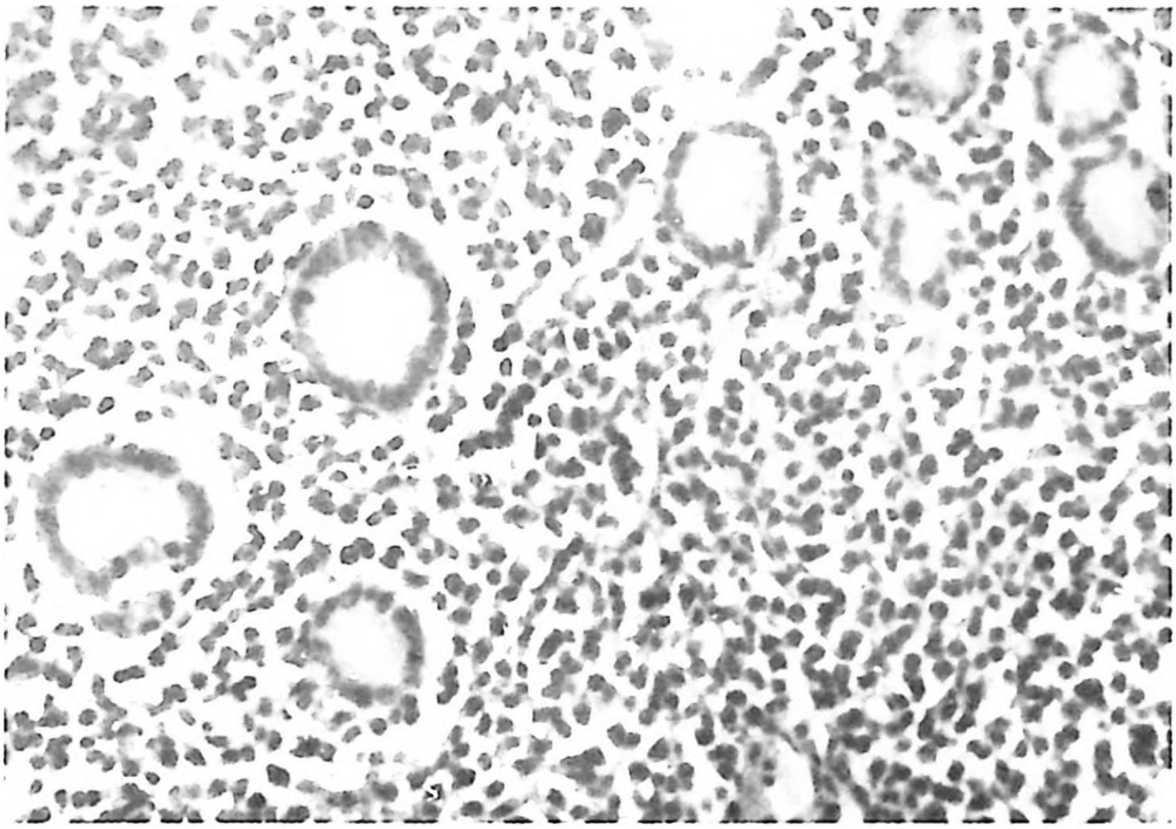

Fig. 2 a: Malignant lymphocytic cell infiltration producing atrophy and deformity in the mucosal glands. (H.E × 25).

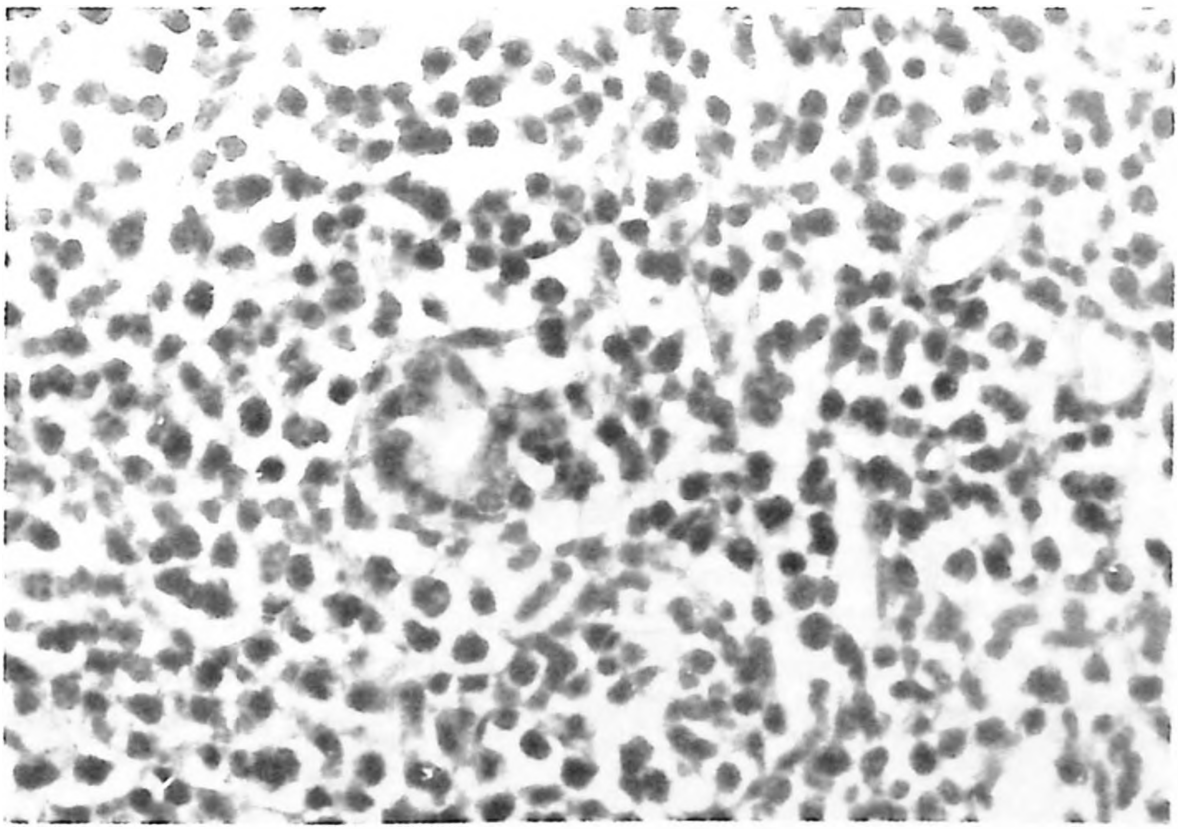

Fig. 2 b: Intensive lymphocytic lymphoma infiltration and atrophic mucosal glands. (H.E × 40).

Discussion

Malignant neoplasms of the stomach rarely occur in children. The majority of these tumors are malignant lymphomas or sarcomas. Lymphomas arise from the lymphoid tissue of the lamina propria and spread into the deep layer of the mucosa and submucosa. Gastric lymphomas are usually of the non-Hodgkin's type. Hodgkin's disease and true histiocytic lymphoma of the stomach are rarely seen in children. Virtually all childhood non-Hodgkin's lymphomas have a diffuse pattern, as nodular lymphomas are extremely rare in this age-group[2-4,7-13].

Grossly, these tumors have an appearance similar to stomach carcinoma. They may be polypoid, fungating or diffuse in type. Some are multicentric or simulate benign hypertrophic gastropathy with pronounced ridges and folds. Ulcers are often present and frequently multiple[10-12].

Clinically, patients with gastric lymphoma have late-onset, non-specific symptoms such as epigastric pain, nausea, vomiting and weight loss, which cannot be distinguished from those caused by other gastric neoplasias or peptic ulcer disease[4,9,13].

Barium study of the stomach reveals the gastric lesion. Endoscopic examination combined with biopsy and cytology is the best diagnostic method. Ultrasonography, computed tomography and endoscopic ultrasonography are recommended as adjunctive procedures in the evaluation of gastric lymphoma[7,14-17].

Despite total resection of the tumor, surgery is insufficient therapy in children with non-Hodgkin's lymphomas because they are systemic tumors with a potential for rapid dissemination from localized sites of disease. Therefore, systemic chemotherapy with or without radiation therapy should always be given. Several multi-agent drug programs have been used for systemic chemotherapy of non-Hodgkin's lymphoma in children[4,7,9,18-20].

The overall five-year survival rate for non-Hodgkin's lymphoma is better than that for gastric carcinomas. Penetration beyond the serosa is associated with significantly decreased survival, as is the presence of regional lymphadenopathy. The prognosis of nodular type and lymphocytic lymphomas are more favourable than the diffuse type and histiocytic lymphomas[4,5,7,10,17].

Ultimately, non-Hodgkin's lymphoma of the stomach should be considered a possibility in any child with symptoms of epigastric pain, vomiting, gastrointestinal bleeding, weight loss or epigastric mass. The same detailed diagnostic evaluation and appropriate treatment should be given to pediatric as well as adult patients.

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ACUTE HEMORRHAGIC LEUKOENCEPHALITIS*

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SUMMARY: Göğüş S, Yalaz K, Koçak N. (Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Acute hemorrhagic leukoencephalitis. Turk J Pediatr 33: 51-56, 1991.

The clinical and pathological findings of a ten-year-old girl, diagnosed as having acute hemorrhagic leukoencephalitis at postmortem examination, are presented.

The diagnosis of this disease is usually established at autopsy. In this paper, emphasis is given to the diagnosis of acute hemorrhagic leukoencephalitis, and the possibility of its clinical recognition is discussed. *Key words: acute necrotizing hemorrhagic leukoencephalitis, acute necrotizing hemorrhagic leukoencephalopathy.*

Acute hemorrhagic leukoencephalitis (AHL) is a rare hyperacute, inflammatory and demyelinating disease of the white matter with an abrupt onset and catastrophic course[1-6]. These characteristics make diagnosis difficult during life but diagnosis and early institution of therapy may be life-saving. Computed tomography (CT) contributes to the rapid diagnosis of AHL, nevertheless cerebral biopsy may be the only way of clarifying the diagnosis[3,5-11].

In the past twenty years, we have had only one autopsy-proven case of AHL at the Hacettepe University Children's Hospital. The clinical and pathological findings of this case are described below.

Case Report

A ten-year-old girl was admitted to the Hacettepe University Children's Hospital because of paralysis on the right side and loss of consciousness, which occurred on the way to the hospital. Past history revealed that five days prior to admission the patient had developed a nasal discharge and intermittent fever but, otherwise, she had been in good health. Twenty-four hours prior to admission, the child vomited twice and progressive weakness of the right arm and leg were observed during the next 12 hours.

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Physical examination revealed a comatose girl. The temperature was 36 C, pulse 86/min, respiration rate 28/min and blood pressure 120/70 mmHg. She responded to painful stimuli by moving her left extremities. Her pupils were of equal size, slightly dilated and reacted poorly to light. The margin of the left optic disc was blurred and the veins were engorged bilaterally. There was right central facial paralysis. Deep tendon and abdominal reflexes were absent on the right side but Babinski's sign was noted.

Laboratory findings revealed a white blood cell count of 7000/mm^3 with 79% neutrophils and 21% lymphocytes. Hemoglobin, erythrocyte sedimentation rate, serum glucose, nonprotein nitrogen and electrolytes were all within the normal range. There was 1+ protein in the urine.

An EEG on admission showed irregular background activity on the left side and epileptic discharges initiating from the left parieto-occipital region. CT findings suggested an ischemic process centrally located in the left hemisphere. Skull X-rays were normal.

Dexamethasone and diphenylhydantoin were given for a prospective diagnosis of an acute cerebrovascular accident or an intracranial lesion. After the first 18 hours, the patient was able to respond to verbal stimuli by opening her eyes. Alternating spasticity developed in her arms and legs. Her vital signs deteriorated and she died 73 hours after admission. The cerebrospinal fluid obtained after death contained 60 red blood cells/mm^3, sugar 90 mg/dl and protein 540 mg/dl. Smears and cultures were negative.

Post-mortem examination was restricted to the head. The brain was swollen and weighed 1400 g (expected weight, 1226 g). There was bilateral cerebellar herniation. Coronal sections showed numerous petechial hemorrhages and reddish-brown discoloration in the white matter of the cerebrum. There was a large hemorrhagic necrotic area near the left lateral ventricle which mainly occupied the internal capsule but also spread into surrounding tissue (Fig. 1). Brain involvement was asymmetrical, with strong predilection for the white matter. On microscopic examination there was damage to many vessel walls. Perivascular necrosis, edema, hemorrhages, focal demyelination and intense neutrophilic exudation were noted around the vessels which were spreading throughout the tissue (Fig. 2, 3, 4).

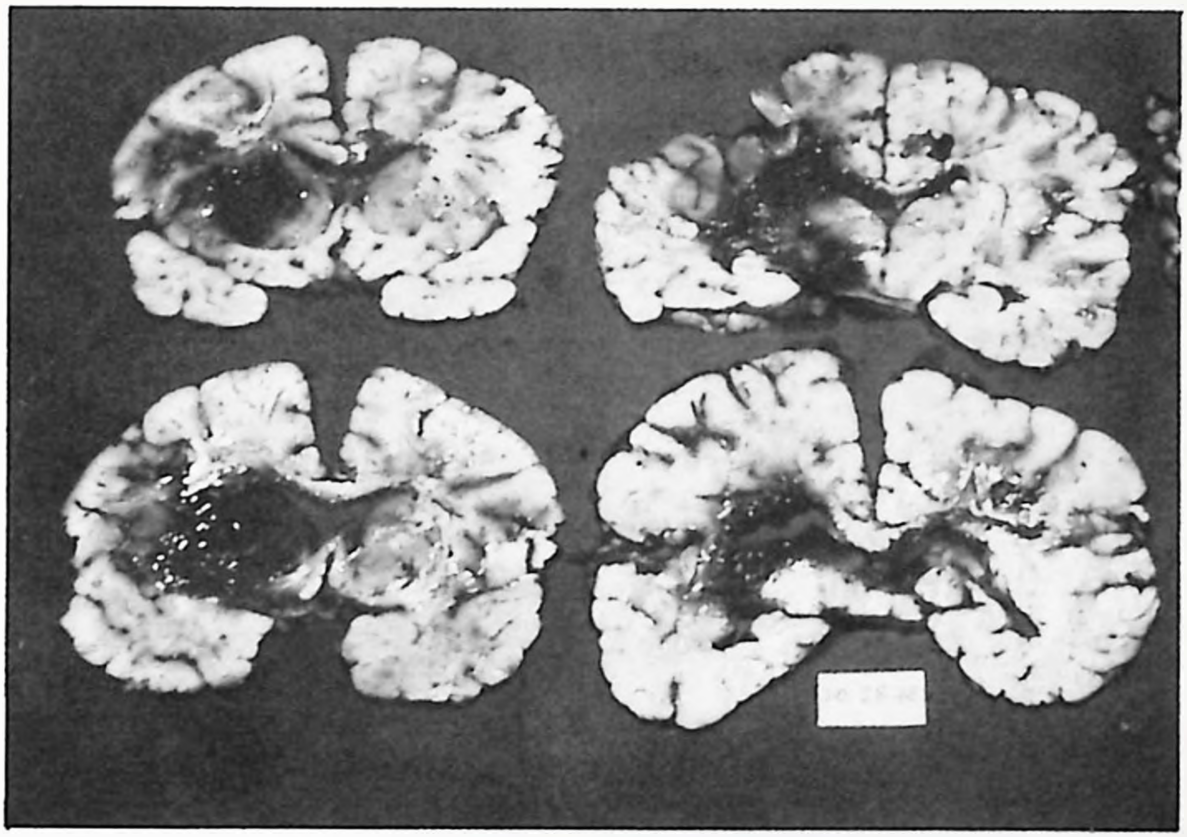

Fig. 1: Macroscopic appearance of the lesions.

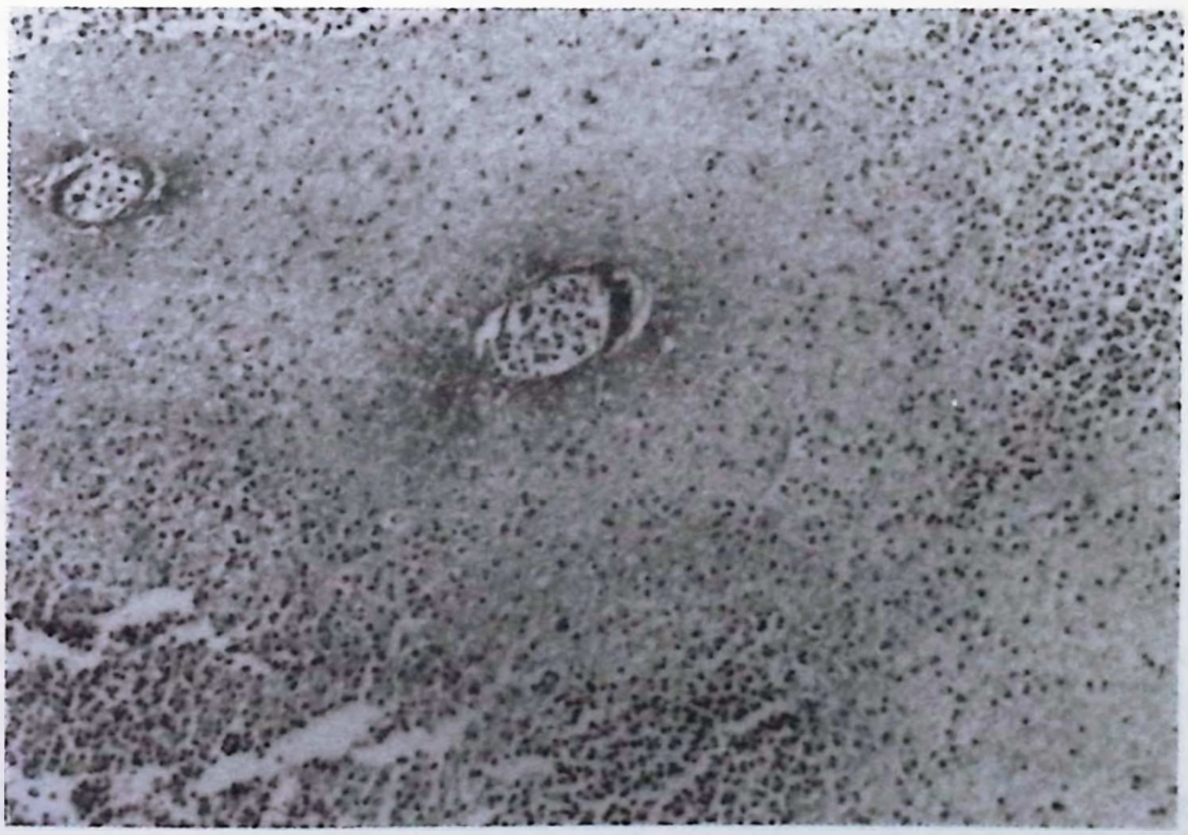

Fig. 2: Necrosis in the vessel walls and inflammatory cells in the tissue PAS × 115.

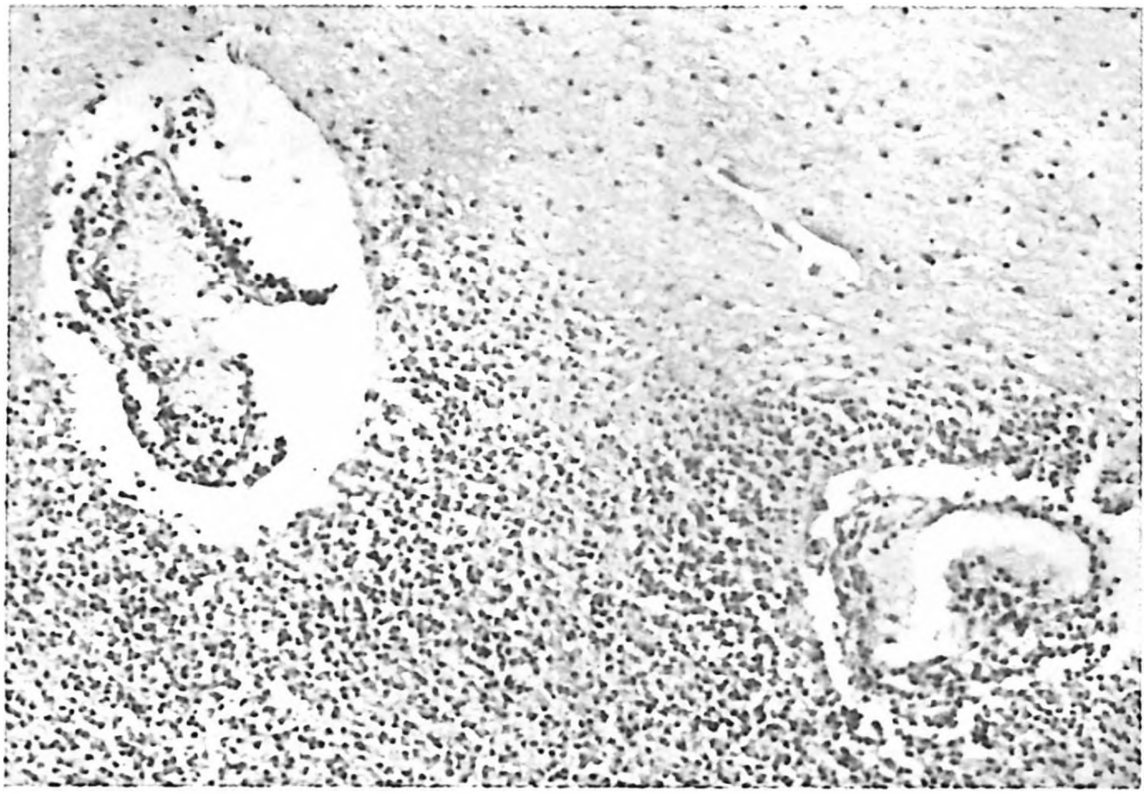

Fig. 3: Infiltration of inflammatory cells, mainly neutrophils and hemorrhage in the tissue H+E × 230.

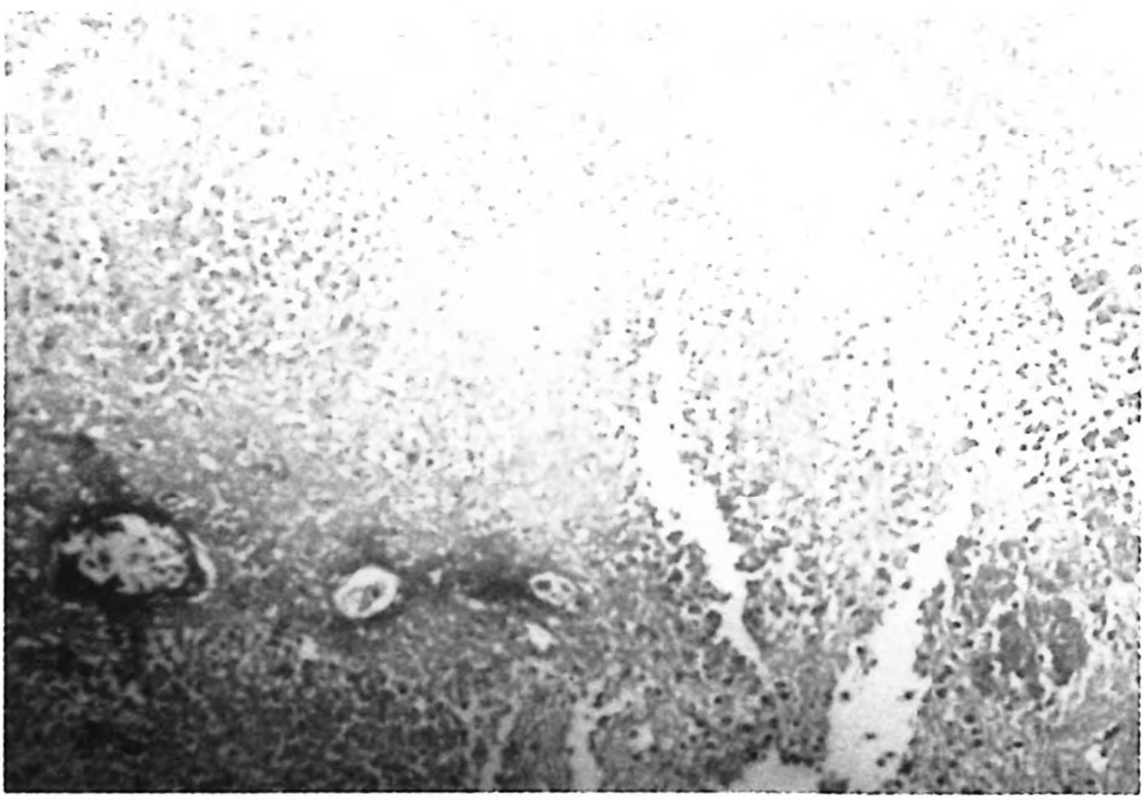

Fig. 4: Extravasation of neutrophils from the affected vessels spreading throughout the tissue. H+E × 115.

Discussion

Acute necrotizing hemorrhagic leukoencephalitis is a rare disease which is usually diagnosed at autopsy and rarely suspected during life[1-6]. However, there have been a few reported cases with recovery, in which diagnosis was made by cerebral biopsy[3]. Cases of relapse have also been reported[3,11].

This disease usually affects young males but may also be seen in childhood. An upper respiratory infection is the most common antecedent illness. Presenting neurologic abnormalities are hemiplegia, confusion, aphasia, and seizures progressing to coma. Etiologic speculation has included infections, toxic substances and an immunopathologic mechanism[4,5]. Laboratory findings usually include urine, peripheral blood and cerebrospinal fluid abnormalities. In reports in which the results of urinalysis have been given, proteinuria has been noted. Leukocytosis appears early and is predominantly neutrophilic. Most cerebrospinal fluid specimens have a high white blood cell count composed mainly of neutrophils. Red blood cells may be present and protein is usually elevated[4,5].

Our patient had a previous undetermined illness five days prior to admission and had many of the usual clinical and laboratory findings for the diagnosis of AHL.

The pathology of AHL is striking[1-8,10,11]. There is necrotizing angiitis of the white matter. The vessel walls are necrotic with fibrinous exudate into the walls and surrounding tissue. Early in the course of the disease, there is extravasation of neutrophils found in the vessel walls and neighbouring parenchymal tissue, which is later replaced by lymphocytes. Diapedesis of red cells occurs especially around the affected vessels, forming ball and ring hemorrhages. These often become large and confluent. Demyelination within the cellular cuffs is also detected. Edema involves areas around the affected vessels which becomes diffuse. Meningeal involvement can also be seen.

Our patient had typical histopathological findings of AHL. The lesion on the left internal capsule was very severe and spread towards the basal ganglia and ventricle. Although the cortical gray matter is usually spared, basal ganglia involvement and brainstem, cerebellum and cord lesions can be detected[5].

Confirmation of diagnosis by cerebral biopsy is academically important in the evaluation of treatment, and it should be performed early in the course of the illness.

Recently, many authors have accepted the use of CT as an aid in diagnosing AHL. They claim that it would be possible to make the diagnosis of AHL during life-time on the basis of characteristic clinical and CT findings[7-10].

Corticosteroids are recommended for treatment[4,5] therapeutically of this condition. However surgical decompression has also been reported to be beneficial[3,11].

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INTRAUTERINE INTUSSUSCEPTION: A RARE CAUSE OF ILEAL ATRESIA WHICH CAN LEAD TO CONFUSION IN DIAGNOSIS*

*Feza M. Akgür MD***, F. Cahit Tanyel MD***, Haşmet Üner MD****
*Nebil Büyükpamukçu MD*****, Akgün Hiçsönmez MD*****

SUMMARY: Akgür FM, Tanyel FC, Üner H, Büyükpamukçu N, Hiçsönmez A. (Departments of Pediatric Surgery and Pediatric Pathology, Hacettepe University Faculty of Medicine, Ankara, Turkey). Intrauterine intussusception: a rare cause of ileal atresia which can lead to confusion in diagnosis. Turk J Pediatr 33: 55-58 1991.

A case of ileal atresia resulting from intrauterine intussusception is presented to stress the confusing differences between this condition and typical ileal atresias. *Key words: ileal atresia, intrauterine intussusception, neonatal intestinal obstruction.*

Ileal atresia is a significant cause of intestinal obstruction encountered in the neonatal period. Its incidence varies from one in 330 to one in 1500 live births[1,2].

Intrauterine compromise of the vascular supply to the ileum is suggested to be the most common cause of ileal atresia. Volvulus, congenital bands, internal herniation and intussusception lead to vascular compromise and, thus, to atresia. The typical case of ileal atresia presents with bilious vomiting, inability to pass meconium, and air-fluid levels on plain erect abdominal radiographs. Diagnosis is easily established with the appearance of a microcolon on barium enema examination[1].

Intrauterine intussusception is an infrequently reported cause of ileal atresia. Fifty such cases have been reported in the literature. Ileal atresia, resulting from intrauterine intussusception, presents with different clinical and radiological signs[3-13]. A case of ileal atresia, resulting from intrauterine intussusception, is presented to stress the confusing differences between this condition and typical ileal atresias.

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Case Report

A full-term female weighing 3500 g was referred to the Hacettepe University Children's Hospital at 24 hours of age with a history of bilious vomiting and abdominal distension. Past history of the passage of meconium was not obtained. Physical examination was normal except for abdominal distension. A plain erect abdominal radiograph revealed multiple, wide-based air-fluid levels, suggesting low intestinal obstruction (Fig. 1). A barium enema examination revealed a colon of normal caliber (Fig. 2). Later, the patient passed a dark green, somewhat dry stool measuring from 5-10 Cm^3. At laparotomy, a fibrous cord type of ileal atresia (Grosfeld Classification-Type II) was detected about 20 cm proximal to the ileocecal valve (Fig. 3). Upon entering the post-atretic segment, a polypoid mass was discovered (Fig. 4). Resection and an end-to-end anastomosis were performed.

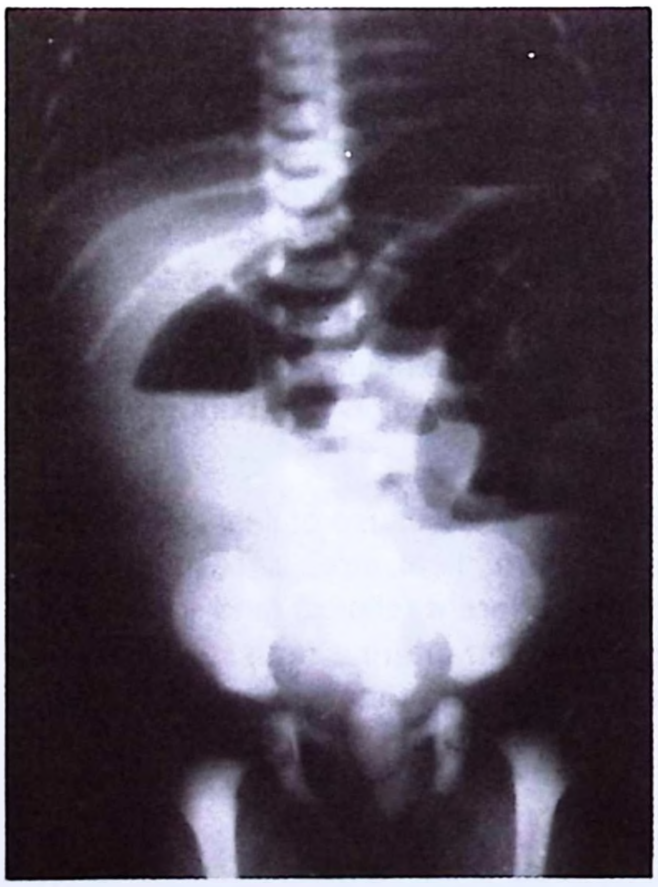

Fig. 1: Plain erect abdominal radiograph at admission revealing multiple wide-based air-fluid levels.

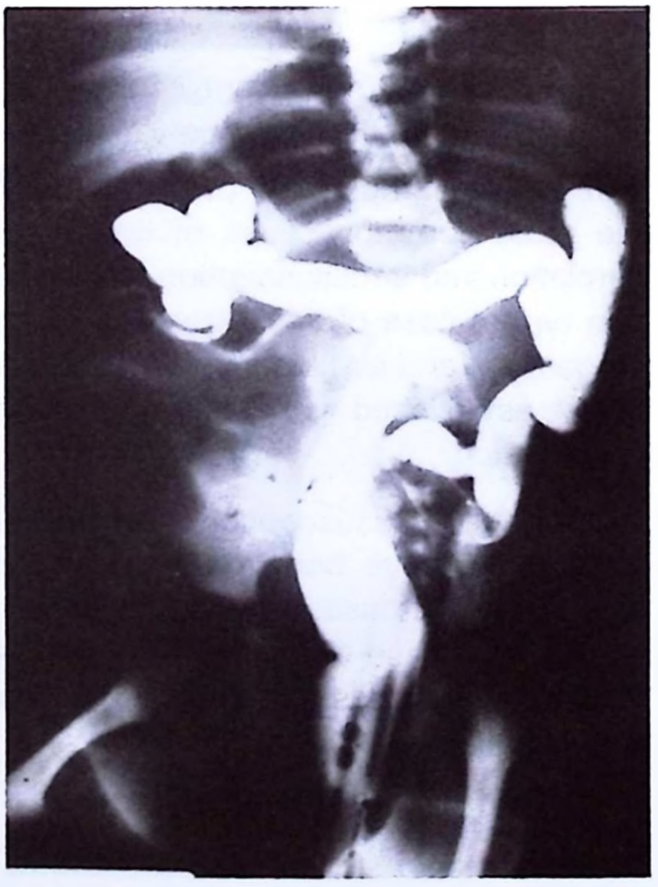

Fig. 2: Barium enema examination revealing colon of normal caliber.

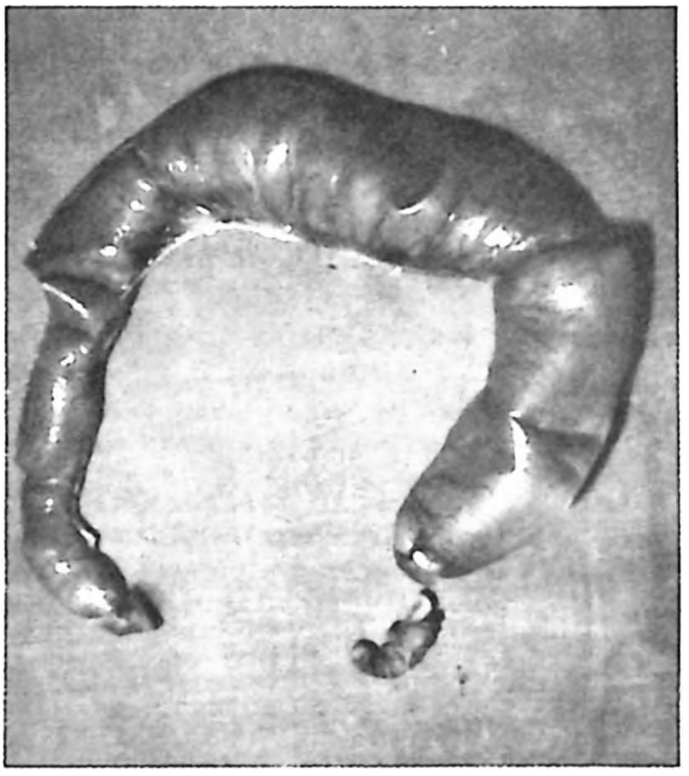

Fig. 3: Specimen of the atretic bowel segment with proximal dilatation.

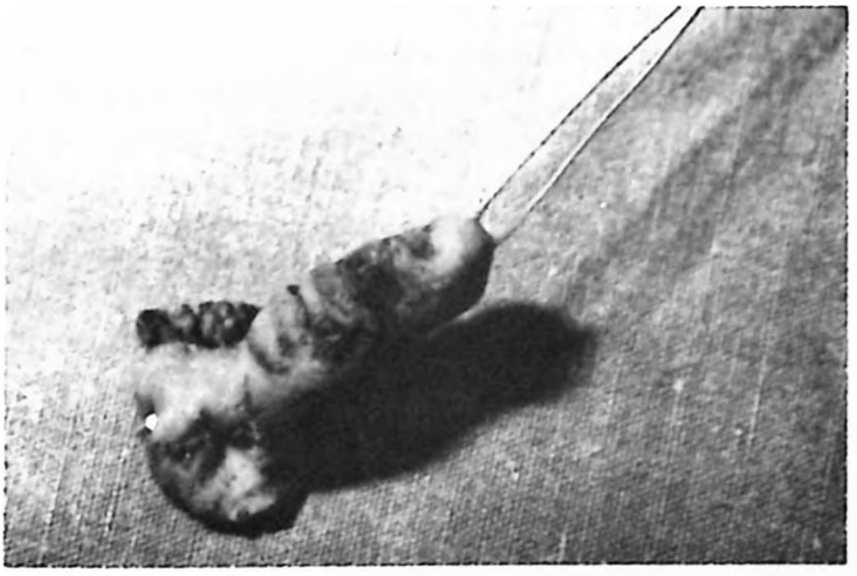

Fig. 4: Polypoid mass in the post-atretic segment.

Microscopically, the lumen and epithelium were not present in the cord, as in the atretic segment. However, the muscular layer was present, and there were focal calcifications in the serosa. The intestinal wall was recognized in the polypoid mass in the post-atretic segment. Ganglion cells were seen in the myenteric plexus of the pre-and post-atretic segments.

The postoperative course was uneventful. The patient was followed for one year, and she showed neither symptoms nor pathologic findings.

Discussion

Of the 50 reported cases of ileal atresia resulting from intrauterine intussusception, data is available for 35[3-13], and of these, 85 percent are mature babies as in our case. The passage of bile-stained meconium, despite surgically proven atresia, implies that atresia occurred after the passage of meconium to the colon, and most probably late in fetal life. Such atresias may occur as a result of intrauterine intussusception[3-13]. Another characteristic finding in these atresias is the presence of a polypoid mass in the distal atretic segment[3-13]. In view of the foregoing, a diagnosis of ileal atresia caused by intrauterine intussusception was made in our patient.

Since the colon functions before intrauterine intussusception occurs, contrary to atresias resulting from other causes, barium enema reveals a colon of normal caliber, and meconium is found in the distal segment.

The passage of bile-stained meconium and the presence of a normal caliber colon on barium enema examination should not exclude the possibility of ileal atresia caused by intrauterine intussusception.

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FUSED PELVIC KIDNEY DRAINED BY A SINGLE URETER*

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SUMMARY: Tekant G, Bulut M, Akansel G, Yılmaz N. (Department of Pediatric Surgery, Şişli Children's Hospital, İstanbul, Turkey). Fused pelvic kidney drained by a single ureter. Turk J Pediatr 33: 59-63, 1991.

A case of fused pelvic (discoid) kidney drained by a superiorly inserted single ureter is presented. This is the twentieth case of fused pelvic kidney, and the fifth case in which drainage was carried out by a single ureter, to be reported in the English literature. The diagnosis and treatment of this condition is discussed and the relevant literature is reviewed. *Key words: kidney, fused pelvic kidney, discoid.*

Fused pelvic kidney (discoid) is considered to be an extremely rare genitourinary anomaly[1-13]. Goren and Eidelman[13] have recently reported the nineteenth such case. Fused pelvic kidney drained by a single ureter has been reported in four of the documented cases. In this paper, we describe a case of fused pelvic kidney with a superiorly inserted single ureter and review the pertinent literature.

Case Report

A two-year-old boy was admitted to the Pediatric Surgery Clinic of the Şişli Children's Hospital with the chief complaints of abdominal swelling, right lower quadrant pain, and vomiting.

The patient's history was noncontributory. Physical examination revealed a solid, immobile mass in the right lower abdominal cavity which measured 5 × 5 cm in diameter. The blood pressure was 110/70 mmHg. In order to determine the origin of the mass, an emergency abdominal ultrasonography was performed which revealed a cystic hydronephrotic kidney located in the right iliac fossa. The left kidney could not be visualized in its normal anatomical position. The patient was hospitalized for further investigation.

Laboratory studies revealed that the blood urea was 106 mg/dl, creatinine, 2 mg/dl, and blood cell counts and urinalysis were within normal limits. The urine culture remained sterile.

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Plain abdominal radiography showed no significant findings. A voiding cystourethrography (VCUG) demonstrated trabeculation on the right upper portion of the bladder but no vesicoureteral reflux was observed (Fig. 1). Renal isotope scans (Tc 99m-DTPA) demonstrated an ectopic kidney with a single ureter located in the right iliac fossa.

The mass in the right lower quadrant disappeared on the second day of hospitalization, and the blood urea level dropped to 38 mg/dl. A presumptive diagnosis of single ectopic kidney with ureteropelvic junction obstruction was established.

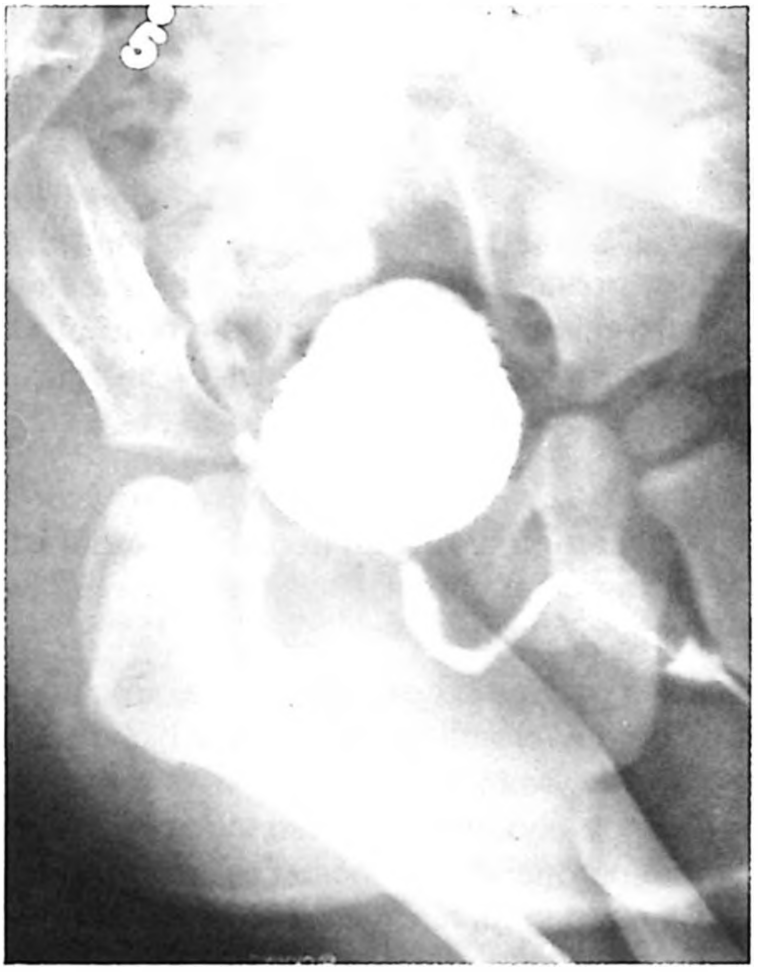

Fig. 1: VCUG demonstrating trabeculation on the right upper portion of the bladder.

To further determine the nature of this urinary abnormality, the abdomen was exposed with a long midline incision extending above and below the umbilicus. The mass was identified as a fused pelvic kidney with a superiorly inserted single ureter (Fig. 2). The renal artery and vein were seen entering the superior pole of the kidney. A dismembered pyeloplasty was performed to correct the ureteropelvic junction obstruction. Further dissection was considered to be hazardous to the

vascular supply of the kidney. The abdomen was closed with a pensore drain placed in the upper angle of the vesical space.

Renal biopsy demonstrated congestion of the glomeruli and tubular changes consisting of cloudy swelling of the tubulus epithelium.

The patient received systemic antibiotics, and had no problem in the postoperative course except for a urine discharge from the drain which was removed on the 13th day. Urinalysis showed no signs of infection, urine cultures remained sterile. Postoperative intravenous pyelography (IVP) demonstrated filtration of contrast material at five minutes and a pelvic fused kidney drained by a single tortous ureter. The patient was discharged on the 15th postoperative day.

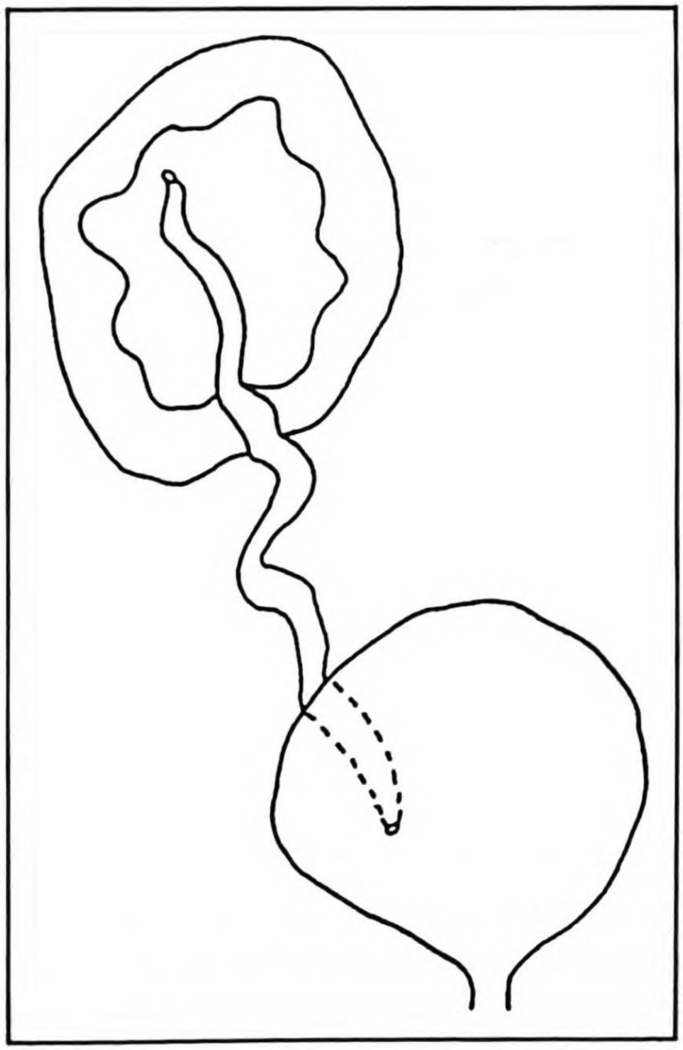

Fig. 2: Schematic drawing of the fused pelvic kidney with a superiorly inserted single ureter.

Discussion

Fused pelvic kidney is a rare congenital urologic abnormality which may be diagnosed in infancy and up until the eighth decade[1-13]. Because of its appearance and shape, this anomaly has been referred to as "cake", "discoid", "shield", "doughnut" or "lump" kidney[4,5,11]. The final shape of the fused kidney is dependent on the time and extent of fusion and on the degree of renal rotation that has occurred. In the lump or cake kidney, extensive joining has taken over a wide margin of renal anlage, so that the total mass is lobulated and both renal pelves drain separate renal areas anteriorly. On the other hand, in the discoid, shield or doughnut kidney, there is more extensive fusion along the entire medial aspect of each kidney, thus providing a better preserved reniform shape with anterior draining uncrossed ureters[11].

Embriologically, two buds of metanephrogenic tissue originate in the 5 mm human embryo in front of the second sacral segment. The kidneys migrate upward to their final lumbar position following movements of ascent, lateral migration, axial deflection and internal rotation. During their ascent in the 30 day nine mm embryo, the umbilical arteries squeeze the nephrogenic blastemas which may lead to fusion. Completely fused kidneys are prevented from ascending and remain ectopic in the pelvis. The weight of the fused kidney is almost equal to that of two separate kidneys. The single ureter draining the fused kidney may be due to regression of the second ureteral bud after fusion of the metanephric blastemas at the ten mm stage. The etiology of the lack of migration and fusion of renal structures is not known[1,3,7,9,11-13].

Vascular supply of the pelvic fused kidney is consistent with its arrested migration. The arterial blood supply is from the aorta near the bifurcation or from the common iliac vessels. Venous drainage is usually into the interior vena cava or into one of the common iliac veins[12,13]. This anomalous blood supply leads to an increased risk of vascular compromise caused by pelvic trauma, vascular disease or pregnancy[7]. In our case, the arterial supply was mainly from the aorta and venous drainage into the inferior vena cava.

It is important to stress that anomalies of the cardiovascular system (tetralogy of Fallot, ventricular septal defect, aortic coarctation), genitourinary tract (testicular maldescent, vaginal agenesis) or gastrointestinal tract (caudal regression, anal anomalies)[1-3,8-12] occur in association with this disorder and that the prognosis depends on these factors. No additional anomalies were found in our case.

Since fused pelvic kidney may be found in all age groups, it may be present with a variety of symptoms such as urine stasis, infection, stone formation, and vascular compromise[1-13]. Fused pelvic kidney does not carry a poor prognosis, however, accompanying complications may result in an unfavorable one. Thus, after the

diagnosis is established, patients should be closely followed for prompt detection of any complications. In our patient the only significant finding was the detection of an abdominal mass, resulting from urinary stasis, which necessitated surgical intervention.

A surgical approach and drainage of the fused pelvic kidney are not recommended because of the variable blood supply[1-13]. However, in our case, surgical intervention was mandatory because of uretero-pelvic junction obstruction of the single ureter. No further exploration or dissection has been performed.

This patient is the twentieth case of fused pelvic kidney, and the fifth case in which drainage was carried out by a single ureter, to be reported in the English literature. During the eight month follow-up, the patient remained clinically healthy, and laboratory and radiologic studies for renal functions were within normal limits.

In conclusion, the fused pelvic kidney with its presentation, diagnosis and prognosis remains a challange to the physician.

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