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THUMBSUCKING AND FALLING ASLEEP*

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A review of the studies on the etiology of habitual thumbsucking reveals either contradictory or inconclusive results. In this study carried out in Turkey, 50 thumbsuckers, 50 non-thumbsuckers, 250 school children and 312 'problem' children were investigated through interviews, questionnaires and other clinical techniques with their mothers. Among variables studied, were aspects of feeding, onset and incidence of thumbsucking, strength of the sucking drive, sex distribution, educational level and occupation of mothers, parental attitudes toward physical contact with children, mother-child relationships, and particular forms of falling asleep. It was found that thumbsucking was etiologically more related to ways of falling asleep than to other factors. An attempt was made to explain the social, psychological and physiological basis of the etiological significance of the falling asleep stage in habitual thumbsucking.

These findings now permit predictive longitudinal investigations to test this accuracy. *Key words: thumbsucking, sleeping.*

Habitual thumbsucking in children has been a subject of interest to pediatricians, dentists, psychoanalysts, psychiatrists and child psychologists. The interest of pediatricians and dentists has gradually diminished because of the general agreement that habitual thumbsucking is not necessarily a source of infection, and that it is not a serious cause of malocclusions[1-7]. In psychiatric and psychoanalytic circles, however, it is still regarded as an autoerotic activity of the child, possibly caused by deprivation of infantile needs. Some investigators believe that it is an entirely normal activity, while others regard it as a manifestation of emotional deprivation and a sign of neurotic predisposition. As

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This paper, previously published in the British Journal of Medical Psychology (50: 95, 1977), is included in this volume of our Journal in memory of the late Dr. Mualla Öztürk.

Milton Senn[8] has stated: 'Pediatricians and psychiatrists are prejudiced and subjective regarding this activity .

Habitual thumbsucking does not seem to be considered a problem in lower socioeconomic levels or in developing countries. But in societies where there is considerable pediatric and psychiatric practice, it draws the interest not only of professional people but also of families. Parents are often concerned, and they experience guilt or anxiety when they have thumbsucking children, wondering what they have done wrong to cause this.

It is beyond the scope of this paper to discuss, in detail, studies on thumbsucking, but a brief survey is indicated. Since Freud's[9] writings on infantile sexuality, thumbsucking has been viewed by psychoanalysts as an autoerotic activity and as indisputable evidence of oral sexuality. The first important study on its etiology was made by David Levy[10], who concluded that an insufficient sucking experience during infancy as a result of spontaneous withdrawal from sucking, a too rapidly flowing breast or bottle, forced withdrawal after a set short period of time, or diminished feeding time was etiologically responsible. Levy[11,12] was able to find experimental support using dogs and chicks. Childers and Hamil[13], Simsarian[14], Fredeen[15], Sears and Wise[16] and Sewell and Mussen[17] gave evidence contradicting or failing to support these findings, whereas Davis[18], Roberts[19] and Klackenberg[4] supported Levy's theory of an insufficient sucking experience in infancy. Halverson[20] pointed out the existence of natural suitable media to reinforce the necessary conditions favouring a conditioned pattern of non-nutritive sucking, but he gave no specific etiological explanation. Similarly, Palermo's[6] interesting paper can assist in understanding the mechanism of the learning process in habitual thumbsucking, but not in explaining its etiology. Deprivation of breast feeding was stressed by Mead[21,22] and Ribble[23,24], but found little or no support from other investigators such as Levy, Davis, Sears and Fredeen. Ribble also pointed out that inadequate mothering may be a factor in thumbsucking. Many psychiatrists and psychoanalysts tend to accept this view in varying degrees, and some highly esteemed textbooks consider it a neurotic manifestation caused by emotional deprivation[25,26]. Kunst[27] suggested that an increased hunger drive may stimulate non-nutritive sucking, and that emotional deprivation, as hunger would, could induce thumbsucking. On the other hand, Childers and Hamil[13] studied problem children and found no relation between thumbsucking and emotional deprivation or neurotic tendencies. Gesell[28] wrote that thumbsucking had nothing to do with sexuality, and he also thought that Levy's findings were unconvincing. He thought thumbsucking to be a normal developmental phenomenon resulting from local irritation (like teething), maturation of hand-mouth coordination, fatigue and non-specific frustrations. Ilg and Ames[29] also regarded it as a natural activity, but they gave no explanation as to why some children become habitual

thumbsuckers and others do not. Benjamin Spock[30,31], besides giving credit to Levy, states that there may be other factors, like a constitutionally strong sucking drive. Reference to constitutional factors, although not explicitly stated, can also be found in the writings of Freud[9], and English and Pearson[25].

Social anthropological writings of Mead[21,22], Orlansky[32], and Davis and Havighurst[33] are also inconclusive. Even if there are differences in the incidence of thumbsucking among children of different cultures or sociocultural levels, it is obvious that only the way a child is reared can be etiological, and not the social level or the culture itself.

Though Gesell and Ilg[34], English and Pearson[25],and Ribble[23,24] have pointed out the relationship of thumbsucking to sleep, none has referred to a possible etiological connection. Gesell and Ilg wrote that if thumbsucking were related to sleep, its habitual pattern would be strong, and that it would therefore be abandoned by the child rather late or with more difficulty. Ribble emphasized the importance of the infant's need to suck while going to sleep, and even suggested that rythmic stimulation like rocking, lullabies, or sucking while the child goes to sleep may be helpful in preventing thumbsucking. In spite of these statements, however, which come close to explaining the etiological connection between sleep and thumbsucking, Ribble seemed to be inclined to view thumbsucking as a product of inadequate mothering or insufficient sucking.

This brief survey shows that the etiology of thumbsucking is still unknown. Our clinical and sociocultural observations suggested that there might be a direct etiological relation between thumbsucking and the ways children are allowed or induced to fall asleep. Therefore, the following study was made a preliminary step to explore this point together with other variables already investigated. The study will be continued through predictive longitudinal observations and recording.

Material and Methods

This study is based on data obtained from interviews, questionnaires and clinical evaluation. The subjects are described as follows: *Group I* (TS) consisted of 50 habitual thumb and/or finger suckers between ages one and seven. No atypical forms, such as excessive finger-mouth playing tendencies were included. *Group II* (NTS) consisted of 50 children between ages one and seven, who did not suck their thumbs or fingers to any striking degree. We considered a child as an habitual thumbsucker if he had made it a habit at least beyond 12 months of age. The mothers of groups I and II were interviewed in detail to obtain information for the variables listed below. These children were randomly selected from the pediatric clinic of the Hacettepe University.Children's Hospital in Ankara, Turkey.

None had applied for psychiatric examination or therapy and there were no pacifier users in these two groups. The social status, education and occupations of the parents of groups I and II were heterogeneous. *Group III*, the group of 'non-problem' children, comprised a total 250 children aged between 4 and 12, who were from a kindergarten and an elementary school in Ankara. None of these children had any psychiatric referral or treatment. *Group IV*, the group of 'problem' children, comprised 312 children between the ages of 4 and 14, who had been evaluated by the Child Psychiatry Unit of Hacettepe University Faculty of Medicine for various behavioral problems. Organic, psychotic and mentally retarded children were excluded. Evaluation of these children had been made by detailed family and developmental histories, therapeutic follow-up, and projective and psychometric tests. The subjects in groups III and IV were of urban middle or upper-middle class families.

In addition to these groups, a summary of a detailed study of seven families will be given in this paper to illustrate the presence of thumbsucking among siblings with particular reference to the variable that emerged as being significant.

The following variables were investigated: (1) ways of feeding, e.g. breast, bottle, cup; (2) duration (in months) of the specific way of feeding; (3) sucking until satisfaction versus time-limited sucking; (4) scheduled versus non-scheduled feeding; (5) strength of the sucking drive; (6) onset of thumbsucking; (7) sex distribution; (8) educational level of parents; (9) occupation of mothers; (10) attitudes toward physical contact and playing with children at home; (11) presence of serious disturbances in the mother-child relationship in problem children; (12) incidence of thumbsucking in problem and non-problem children; (13) the pre-sleep situation and ways of putting the child to sleep during infancy, e.g. sleeping alone after feeding, sleeping alone with a bottle, sleeping on the mother's lap while feeding, practice of rocking and lullabies.

Results and Discussion

Our findings regarding the relationship between thumbsucking and breast feeding are presented in Tables I and II, which show that the TS group had a significantly shorter period of breast feeding than the NTS group.

A comparison of the duration of breast feeding in thumbsuckers and non-thumbsuckers shows that there is a significant difference ($\pm = 4.00$, $p < 0.01$). Whereas, a comparison of total duration of breast and bottle feeding in both groups shows no significant difference ($\pm$ 0.31, $p > 0.05$). This finding can give the impression that there are more thumbsuckers among children weaned earlier from the breast in comparison to those weaned later.

TABLE I: Distribution of Thumbsuckers (TS) and Non-thumbsuckers (NTS) According to Form and Duration of Feeding

	TS				NTS		
Duration (months)	Essentially breast fed	Essentially bottle fed	Mixed feeding (breast-bottle)	Duration (months)	Essentially breast fed	Essentially bottle fed	Mixed feeding (breast-bottle)
0	8	13	21	0	5	34	39
1-3	12	0	0	1-3	1	0	0
4-6	16	0	0	4-6	9	0	0
7-9	9	3	3	7-9	11	2	1
10-12	2	14	11	10-12	10	4	4
13 >	3	20	15	13 >	14	10	6
Total	50	50	50	Total	50	50	50

TABLE II: Comparison of Thumbsuckers (TS) and Non-Thumbsuckers (NTS) With Respect to Duration of Breast and Bottle Feeding

	TS		NTS	
	$\bar{X}$	S.D.	$\bar{X}$	S.D.
Duration of breast feeding (months)	4.92	4.075	10.28	7.146
Duration of breast and bottle feeding (months)	13.58	6.271	13.98	6.528

This may seem to support Ribble and Mead who attributed the absence of thumbsucking in certain families or cultures to prolonged breast feeding in infancy. To arrive at a sound conclusion on this issue, however, the onset of habitual thumbsucking must be considered. If it usually starts and continues before weaning from the breast, then absence or shortage of breast feeding could not be a factor in its etiology. How can early or late weaning be related to thumbsucking if the habit is found to be acquired while the child is still on breast feeding?

Our investigation of breast-fed and bottle-fed children in regard to the onset of thumbsucking shows that among 50 thumbsuckers (TS) there were 13 children who were breast fed, and 11 of these children started thumbsucking before weaning from the breast. Eight were bottle fed and all of them started thumbsucking before weaning from the bottle. Twenty-nine children were both bottle and breast fed, and 20 of them started thumbsucking before weaning. Statistical analysis of this data ($X^2 = 8.595$, $p = < 0.01$) indicates that most habitual thumbsucking starts before weaning from the beast or bottle. Our finding

in this respect is in accordance with Levy, as reported earlier. Other explanations must therefore be sought to explain why there are more thumbsuckers among children relatively early weaned than those who are late weaned. This will be explained later.

Another important variable is scheduled versus demand feeding. It has been proposed, particularly by Levy, that long-interval scheduled feedings lead to a reduction in the child's sucking experience, causing non-nutritive sucking. In our study, a comparison of TS and NTS, according to scheduled versus demand feeding, shows that among 50 TS, 34 children were fed with scheduled form and 16 with demand form. Among 50 NTS, 23 children had scheduled feeding, and 27 were fed on a demand basis. Thus, there are significantly more schedule-fed than demand-fed children among TS ($X^2 = 4.08$, $p < 0.05$). In order to conclude whether or not scheduled feeding is an important factor, it is necessary to compare the number of TS with NTS in the total schedule-fed children. Among 57 schedule-fed children, there were 34 TS and 23 NTS. As the difference between these figures is not statistically significant, some other explanation must be sought for the finding that there are more schedule-fed children among TS than among NTS. This point too will be discussed later.

As for the length of individual feeding sessions, in Turkey, generally there are no limitations to the duration of breast or bottle feeding, and the mothers of our subjects stated that they invariably allowed their children to suck for as long as they wanted. This can be termed sucking-until-satisfaction. Only one mother said that she had tried to feed her baby with prescribed timing for the first three months and that her child was not a thumbsucker. Of 100 children, 99 were fed by the traditional sucking-until-satisfaction way, and of these, 50 were thumbsuckers and 49 were not. This does not support the findings of Levy, Davis, Roberts, Klackenberg and Yarrow[35] Besides, the view that thumbsucking is related to hunger (Gesell, Kunst) is not supported, since many children who are fed on demand and until satisfaction still become thumbsuckers.

Although it is extremely difficult to obtain reliable data on the strength of the sucking drive of infants, mothers were questioned carefully on their children's sucking appetite and strength. Information obtained on 91 subjects was clustered into two groups: good sucking drive and weak sucking drive. Of these 91 children, there were 42 TS and 36 of them (85.7 percent) were considered to have a strong sucking drive and six (14.3 percent) were considered to have a weak sucking drive*. Although these figures are not convenient for statistical comparisons, their percentages suggest that the NTS group do not have a sucking drive any weaker than the TS group.

* The authors have two children who had a strong sucking drive in infancy. Neither of them used pacifiers, nor were they thumbsuckers.

Sex distribution among TS and NTS did not show a significant difference. There were 27 females and 23 males in the TS group, and 22 females and 28 males in the NTS group. These figures support Levy's report that sex is not an important variable in habitual thumbsucking.

Another variable, the educational level of the parents, was investigated to see if there was any connection between TS and the maternal educational level, which is also reliably reflective of the sociocultural level in Turkey. In the TS group there were no illiterate mothers; 26 were high school and 15 were university graduates. In the NTS group there were 11 illiterate mothers, 16 high school graduates and five university graduates ($x^2 = 16.32$, $p < 0.05$). Although a significant difference was found between the two groups, the educational level could not be an etiological factor in itself, and it could only lead us to further questions. For example, mothers of higher education usually work, and, therefore, they may not always be at home. In the TS group, 11 were working mothers, 36 were housewives and the occupations of three mothers were unknown. Of the mothers in the NTS group, 10 were working mothers and 38 were housewives. These figures indicate that there is no significant difference between the number of working mothers and the number of housewives in both groups. Thus, it was felt that absence from home due to work could not be a related factor. The significance of the differences in educational levels will be explained later.

We tried to find out if there was any relation between thumbsucking and parental attitudes toward approval of physical contact and affectionate play with the child. The parents who took their children on their laps, played with them frequently, and who reported favoring such close contacts, were grouped as 'approving of physical contact'. Among 50 TS there were 18 children whose parents 'approved' of physical contact and 32 children whose parents 'disapproved' of physical contact. Among NTS there were 23 children whose parents 'approved' and 27 children whose parents 'disapproved' of physical contact. There is no significant correlation between parental attitudes toward physical contact and the presence or absence of thumbsucking ($x^2 = 0.661$, $p > 0.5$).

An inadequate mother-child relationship is usually implied as an etiological factor, both in case studies and in child psychopathology textbooks. In this study, the 'problem children' group from the Child Psychiatry Clinic were chosen as subjects to investigate this point because these children had been thoroughly studied. Methodologically, it is extremely difficult to study and define, in detail, the parent-child relationships of a large number of non-problem children, whereas, the parents of the clinical subjects are usually in a position to be carefully evaluated as to the quality of the mother-child relationship. Since thumbsucking usually becomes habitual during the first two years of life, special effort was made to investigate the quality of the mother-child relationship of the child's first two years. Of the

312 'problem' children, 201 used pacifiers and were therefore excluded from the study. The remaining 111 children's case histories were carefully reviewed, and the quality of the mother-child interaction was categorized. If the following conditions were found to have been present in the first two years of childhood, the mother-child relationship was qualified as 'inadequate or disturbed': (1) open rejection of the child; statements that the child was unloved; child delivered to the care of several mother substitutes; (2) severe marital discord resulting in the unhappiness of the mother and resentment toward the child; (3) severe neurosis or psychosis of the mother.

The mothers without the above characteristics were classified in this study as having established at least a relatively 'adequate relationship' with their children. In the 111 'problem children' there were 11 TS and 100 NTS. Of the 11 TS, six children had 'inadequate or disturbed' mother-child relationships and five had at least an 'adequate' relationship. Of the 100 NTS, 42 children had 'inadequate or disturbed', and 58 had 'adequate' mother-child relationships ($x^2 = 0.202$, $p > 0.05$). There was no significant difference between the two groups. This finding does not support the hypothesis that a poor mother-child relationship can be etiologically related to habitual thumbsucking. A separate comparison of the pacifier users with nonpacifer-users in the 'problem children' group did not reveal any significant difference.

As many psychiatrists and some known textbooks have regarded thumbsucking as a psychological problem, and an indication of neuroticism in children, we compared the incidence of thumbsucking in 'problem children' and 'non-problem' children. Although our subjects cannot be considered representative samples, both groups were from similar socioeconomic and cultural backgrounds and thus, comparisons could be made. Of the 250 'non-problem' school children, 141 children used pacifiers and, were therefore excluded and analyzed separately. In the remaining 109 children, there were 16 TS and 93 NTS. Of the 312 'problem children', the 201 pacifier-users were excluded and compared separately. Of the remaining 111 children, there were 11 TS and 100 NTS. No significant difference was found in the incidence of thumbsucking in the 'problem' and 'non-problem' children ($x^2 = 0.744$, $p > 0.05$). Similarly, the incidence of pacifier-use was not significantly different in these two groups. It was felt that the large number of children who used pacifiers in both groups might account for the relatively low frequency of thumbsucking in urban Turkish children (14-18 percent) as compared to 25 percent in the United States[10] and 30-50 percent in Scandinavia[4].

As a last variable, a careful inquiry was made of the pre-sleep condition and ways of putting children to bed during the first two years. The forms of falling asleep were classified as: (1) being left alone in their rooms to sleep on their own, after having been fed to satisfaction; (2) being fed by breast or bottle while going to

sleep in a crib or in the mother's lap; (3) being rocked in the mother's lap or in a cradle, or being sung lullabies while falling asleep (usually after completion of feeding).

The figures in Table III indicate an extremely strong relationship between thumbsucking and the way children are put to sleep. Ninety-six percent of the thumbsuckers had been left alone to fall asleep after having been fed. Of the NTS children, there was not a single child who was left to fall asleep alone or without a sucking opportunity while going to sleep. An additional attempt was made to test this finding by studying seven families selected on the basis of the following criteria: (a) each family had both TS and NTS children; (b) the age difference between siblings was rather low, in that the average age difference was 1 ½ years, the greatest being 2½ years (only one child); (c) these families did not use pacifiers; (d) the oldest child in these families was not older than seven. All variables investigated in our research groups were also studied in these families.

TABLE III: Distribution of Thumbsuckers (TS) and Non-Thumbsuckers (NTS) in Relation to Forms of Falling Asleep

	TS		NTS	
	n	%	n	%
Children left alone to fall asleep after being fed	48	96	0	0
Children provided with sucking experience, breast or bottle, to fall asleep	1	2	22	44
Children, after being fed, are rocked or sung lullabies to induce sleep	1	2	28	56
Total	50		50	

Two families had three children each, one TS and two NTS. Five families had two children each, one TS and one NTS. Thus, in these seven families there were seven TS and nine NTS. The only consistent finding was in the area of falling asleep, in that all TS were put to bed alone with no sucking opportunity other than their thumbs, and that all the NTS children had an opportunity to suck the breast or bottle while falling asleep. Two of these families are worth reporting: Family I had three children — a 5 year old boy, 2½ year old girl, and a 1½ year old boy. The two older children had been breast fed for four months and bottle fed for 30 months. The youngest child was not yet weaned at the time of investigation. They were all schedule-fed until satisfaction. It was found that the two older siblings had at least adequate physical contact and an adequate relationship with their parents, but the youngest child was considerably deprived. The mother had had long-term depression after this youngest child's birth, and the father had been away most of the day and

many nights as an intern in a hospital. There was no consistent mother substitute for the baby, who spent much time lying in bed with a bottle given to him before sleeping periods. This child, and the oldest one, who were regularly put to sleep in the mother's lap while sucking the breast or bottle, were not thumbsuckers. The thumbsucker in the family was the second child. It was after her birth that her parents, who were educated, were exposed to the recommendation of putting the child to sleep alone after having been fed.

Family VI had three children – 6 and 5 year-old girls and a 4 year old boy. The first two children were breast fed for nine months and the youngest for seven months. None had bottle feeding. They were all demand fed until satisfaction. Physical contact with babies was not highly approved in the family. There was no striking disturbance in the mother-child relationship with the two older children, but one could not easily say this with the youngest child, who was abruptly weaned at seven months, at a time when the mother had to leave for Europe to accompany the father because of the latter's severe illness. The child lost the breast feeding and the mother at the same time. The separation lasted about six months. During this period, the children were taken care of by the grandmother. In this family, the oldest child was regularly put to sleep alone in her crib after being fed, but the younger two children regularly slept in the mother's lap while sucking her breast. During the period of separation from the mother, the youngest child was regularly put to sleep by the grandmother, who rocked the baby in her lap and sang lullabies. The thumbsucker was the oldest child, and the other two children, one of which had a dramatic abrupt separation from the breast and the mother, were not thumbsuckers.

These case reports of families also strongly support our finding of the importance of the form of falling asleep as an etiological factor in thumbsucking.

Discussion and Conclusion

Our findings have to be considered provisional because of the question of reliability of data obtained through anamnestic methods. Nevertheless, material from different sources seem to lead to certain common findings, and therefore we feel justified in formulating the following etiological hypothesis of habitual thumbsucking. This hypothesis needs further evaluation through longitudinal studies which we plan to undertake. One of our findings was that there was significantly less thumbsuckers among breast-fed children, but that insufficient duration of breast feeding could not be a cause of thumbsucking since the habit was acquired while breast feeding was still continued. Another finding was that there were more schedule-fed children among TS than among NTS, but the difference between the numbers of TS and NTS was not significant in the total schedule-fed children. Therefore, it was felt that the connection could be an

indirect one. Another positive finding was that there were more thumbsuckers among children of educated mothers. Finally, it was found that thumbsucking and falling asleep alone, without a sucking opportunity or other rhythmic stimuli, were highly correlated. We propose the following explanation for these findings: educated mothers are likely to be more influenced by modern child-rearing techniques which include scheduled feeding and putting the child to sleep alone, have a better opportunity and more reason (as many work) to utilize the products of the modern baby-food industry, and tend to practice less breast feeding and more bottle and scheduled feeding than uneducated mothers. These mothers also tend to let their infants go to sleep alone after feeding. The more tradition-bound, uneducated mothers, breast and demand feed their babies until satisfaction, and generally put them to sleep either while feeding or by rocking and lullabies. We have aiready explained how breast and demand feeding, although found to be correlated with the absence of thumbsucking, could not be etiologically pertinent. Thus, the highly significant variable found in our study, i.e. the form in which the child is allowed or induced to fall asleep, seems to stand out as the etiological factor in thumbsucking. This needs further explanation.

Although during recent years, studies on the physiology and psychology of sleep have increased, our knowledge of this basic need, which consumes one-third of our lives, is rather limited. It is beyond the scope of this paper to review sleep studies. Although certain physiological aspects and varying levels of sleep in infancy have been investigated[28,36,37], very little is known on the drive distribution, particularly of the sucking drive, in the infant's organism during sleep or pre-sleep. Whatever physiological or biochemical mechanisms are involved, it is generally accepted that from the cerebral, physiological and behavioral standpoints sleep is a regressive activity during which there is relative dominance of the more primitive cerebral functions and inhibition of the higher ones[36,38]. From a psychological standpoint too, sleep is considered to be a regressive phenomenon, and in psychoanalytic literature, it has been regarded as a state in which the ego regresses to more primitive levels[39]. Peiper states that the sucking activity of the child is one of the most primitive functions, and that the sucking center is in the immediate neighborhood of other vital centers in the medulla oblongata. It is known that an infant's sucking can be aroused as a 'vacuum activity' without any external stimuli or hunger stimulus from inside. According to Peiper, this vacuum activity, frequently observed during infancy, can be seen in later childhood during 'light sleep'. Thus, sucking as a primitive reflex activity, occurs during the regressive state of sleep or light sleep. An analogous condition is observed in insulin coma, during which there is a gradual progressive dissolution of the cerebral functions. In the initial stage there is facilitation of subcortico-diencephalic activity associated with primitive involuntary movements, among

which sucking can be mentioned, together with depression of higher cerebral and cerebellar functions[40]. Similarly, it is quite possible that the sucking reflex is stimulated, and the sucking drive intensified while going to sleep.

There is also the question of mouth-hand coordination in thumbsucking. Again according to Peiper, this is easily stimulated in children, and even in adults, when cerebral functions are in a regressive state. It can therefore be assumed that while falling asleep both the sucking drive and mouth-hand coordination are highly stimulated. This would explain why thumbsucking can easily start while going to sleep, and why it is particularly difficult for the child to relinquish it during the falling asleep period.

A similar explanation can be given on the basis of the psychological significance of sleep. Considering sleep as a regression of the ego to a more primitive state, the ego's relative autonomy from the id is decreased, and the organism is in increased drive tension. As sucking is one of the more primitive and important drives in infancy, its stimulus value would be expected to increase in sleep, resulting in an intensified need to seek a drive-satisfying object. Thus, a relationship between sucking and sleep on both physiological and psychological levels can be defined. While falling asleep, the intensification of the sucking drive and the stimulation of mouth-hand coordination create a favourable ground for thumbsucking. If the infant goes to sleep while sucking the breast, bottle, or pacifier, the sucking drive will be satisfied, and the stimulation of mouth-hand coordination will not be used for thumbsucking. Similarly, if the infant is rocked or if his sense organs are rythmically stimulated (rocking, lullaby or the mother's lap) the sucking drive and mouth-hand association will be detoured, leading to a lessened perception of these internal stimulations, and to smooth sleep with less internal drive demand. It is also possible that these external stimuli may serve other purposes, such as that of assuring the infant of the mother's presence while he falls asleep, which can be perceived as gradual separation from her, or as being left alone if the child falls asleep in her absence. Children who are left alone without the breast, bottle, pacifier or other stimuli offering gratification while falling sleep, develop habitual thumbsucking which will gradually be generalized to other behavioral areas of increased drive tension (e.g. hunger, fatigue, frustration). While the onset of thumbsucking is causally related to the way of falling asleep, its relinquishment is more difficult and delayed in the pre-sleep and sleep stages than that of thumbsucking occurring elsewhere.

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SERUM IgD CONCENTRATIONS IN IMMUNODEFICIENCY DISEASES*

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Summary: Sanal Ö, Ersoy F, Tezcan İ, Yeniay İ. (Immunology Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Serum IgD concentrations in immunodeficiency diseases. Turk J Pediatr 32: 175-182, 1990.

Serum IgD levels were determined in 66 patients with well-defined primary immunodeficiency diseases. The two major groups of patients consisted of those with ataxia-telangiectasia (38 patients) and those with selective IgA deficiency (11 patients). The ataxia-telangiectasia patients tended to have higher serum IgD levels while no significant difference was found in the serum IgD levels of the selective IgA deficiency patients when compared with the controls. No correlation was found between the IgD levels and the presence of frequent infections in both patient groups or the associated disorders present in the selective IgA deficiency patients. The percentage of low serum IgD phenotype in the normal subjects was similar to that described in the literature. *Key words: serum IgD, immunodeficiency diseases, low IgD phenotype.*

The role of serum IgD in the immune system is still unclear, and therefore cannot usually be determined routinely in clinical laboratories. There are few studies describing IgD concentrations in immunodeficiency diseases[1-3].

In this study we determined serum IgD concentrations in 66 patients with various primary immunodeficiency diseases.

Material and Methods

Venous blood samples were obtained from 66 patients with well-defined immunodeficiency diseases and from 33 healthy age-matched controls. The study population consisted of patients with immunodeficiency diseases. There were 38 patients with ataxia-telangiectasia (AT), 11 with selective IgA deficiency, five with

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common variable immunodeficiency (CVID), five with Hyper-IgM syndrome (HIgM), three with X-linked hypogammaglobulinemia (XLA), one with selective IgM deficiency, one with Chèdiak-Higashi syndrome (CH), one with chronic mucocutaneous candidiasis (CMCC), and one with severe combined immunodeficiency (SCID).

Serum IgD concentrations were measured by the radial immunodiffusion technique using commercial plates (Behringwerke; Germany).

The Mann-Whitney *U* test was used for statistical analysis. Since it has been reported that 13-14 percent of normal individuals also have low serum IgD levels (low serum IgD phenotype)[4-6], the median and geometric mean values and the Mann-Whitney *U* test were calculated either with or without the zero IgD values.

Results

The serum IgD concentrations of the AT patients were found to be significantly higher than the controls ($p = 0.018$; Tables I-III; Fig. 1) by the Mann-Whitney *U* test. Serum IgD was undetectable in nine of 38 AT patients (23.6%) and in six of the 33 controls (18.1%). The difference between these two groups was not significant. Of the 38 patients with AT, 18 had low or undetectable serum IgA levels. Although the number of patients with undetectable IgD levels was higher in the IgA deficiency group than in the normal IgA group (33.3% vs. 15.0%), the difference between these two groups was not found to be significant. In ten families there were 24 AT patients, all siblings. Four of these families had three AT children each, and six families had two AT children each. Of these 24 patients, four patients from three families had undetectable serum IgD levels. Two of three affected siblings in one family had undetectable IgD levels while two patients with undetectable IgD levels had AT siblings with normal IgD levels.

AT patients with normal IgA levels had significantly elevated serum IgD levels when compared with the controls ($p = 0.0001$), while AT patients with IgA deficiency did not differ significantly ($p = 0.3$) when patients with zero IgD levels were included. But when the patients with zero IgD levels were excluded, AT patients with low IgA levels had significantly higher IgD levels than the controls, such as the patients with normal IgA levels ($p = 0.014$; $p = 0.0002$). No significant difference was found between AT patients with normal or decreased IgA levels when evaluated either with or without zero IgD levels. Serum IgD concentrations in AT patients did not show any correlation with the concentration of other Ig isotypes (IgG or IgM) or the presence of recurrent infections.

TABLE I: Serum IgD Concentrations of Patients With Immunodeficiency Diseases

Group	n	Age (yrs)	Serum IgD (u/ml) Range	Median	Geometric mean
Ataxia-telangiectasia	38	4-23	0-440	84.5 (115)*	20.64 (107.8)*
a. normal IgA	20	4-16	0-440	95 (115)	39.44 (113.33)
b. IgA deficiency	18	5-23	0-410	51 (100)	10 (100.38)
Selective IgA deficiency	11	2-10	0-240	15 (47)	4.83 (44.36)
X-linked hypogammaglobulinemia	3	5-18	0-105	0	
Common variable immunodeficiency	5	6-15	0-10	0	
Hyper – IgM syndrome	5	2-17	0-147	0	
Controls	33	2-12	0-120	49 (53)	16.27 (50.3)

* Numbers in parenthesis are the values obtained when zero IgD values were excluded. *Statistical analysis* : AT (total) - control $p = 0.018$, AT (IgA normal) - control $p = 0.0001$, AT (IgA low) - control $p = 0.3$, AT (IgA normal) - AT (IgA low) $p = 0.11$

Since it has been reported that 13-14 percent of normal individuals have low serum IgD levels (low serum IgD phenotype), the Mann-Whitney *U* test was used with or without zero IgD values and the results did not differ statistically except for AT patients with low IgA and the controls.

In the selective IgA deficiency patient group, serum IgD levels and the number of patients with undetectable serum IgD levels did not differ significantly when compared with the controls (36.3% vs 18.1%). Again serum IgD levels did not seem to correlate with other Ig isotypes or associated disorders.

Serum IgD was undetectable in the patients with SCID, HIgM syndrome, CVID and XLA with the exception of one patient in each of the latter three disease groups. However, IgD levels were normal in patients with CH or selective IgM deficiency, and high in patients with CMCC.

TABLE II: Serum Immunglobulin Concentrations of AT Patients With Normal IgA Levels

	Age (yrs)	IgG (mg/dl)	IgM (mg/dl)	IgA (mg/dl)	IgD (u/ml)
MP	8	1130	200	118	0
EK	15	1130	414	162	440
AÖ	15	963	299	210	410
OÇ	5	1000	190	117	188
ÖK	13	1310	88	130	84
IY[a]*	4	1140	160	56	230
MY[a]	9	802	290	118	35
ED	11	1560	200	84	75
SŞ[b]	16	1250	402	135	190
OŞ[b]	15	1370	208	252	115
SY	14	1190	243	162	0
MT[c]	8	1900	290	162	18
ST[c]	7	1250	243	101	125
HT[c]	14	1250	200	144	137
BaB[d]	9	1170	113	110	160
BB[d]	2	1100	167	94	85
NB[d]	21	963	130	42	85
AA[e]	26	1100	110	84	0
KA[e]	6	1650	175	126	63
LÖ[f]		463	184	49	105

* Small letters indicate sibling pairs.

TABLE III: Serum Ig Concentrations of AT Patients With Low IgA Levels

	Age (yrs)	IgG (mg/dl)	IgM (mg/dl)	IgA (mg/dl)	IgD (u/ml)
AE	23	2110	252	0	0
AA[g]	5	1900	445	0	85
OA[g]	13	1250	343	< 42	410
MP	8	1130	200	0	0
DH[h]	11	1430	200	0	0
MH[h]	10	2260	252	0	251
EÇ	16	1690	370	< 42	19
SA	7	2340	448	0	35
IS	9	2260	448	0	199
KAG[k]	5	963	160	< 42	60
AG[k]	6	1500	170	< 42	315
OG	9	1560	243	0	42
GB	6	700	243	< 42	0
ÖT[l]	7	3770	145	< 42	160
ÖzT[l]	8	3770	90	0	0
RA[e]	18	1150	109	< 42	0
ZÖ[f]	10	1300	237	< 42	63
HÖ[f]	9	550	175	< 42	115

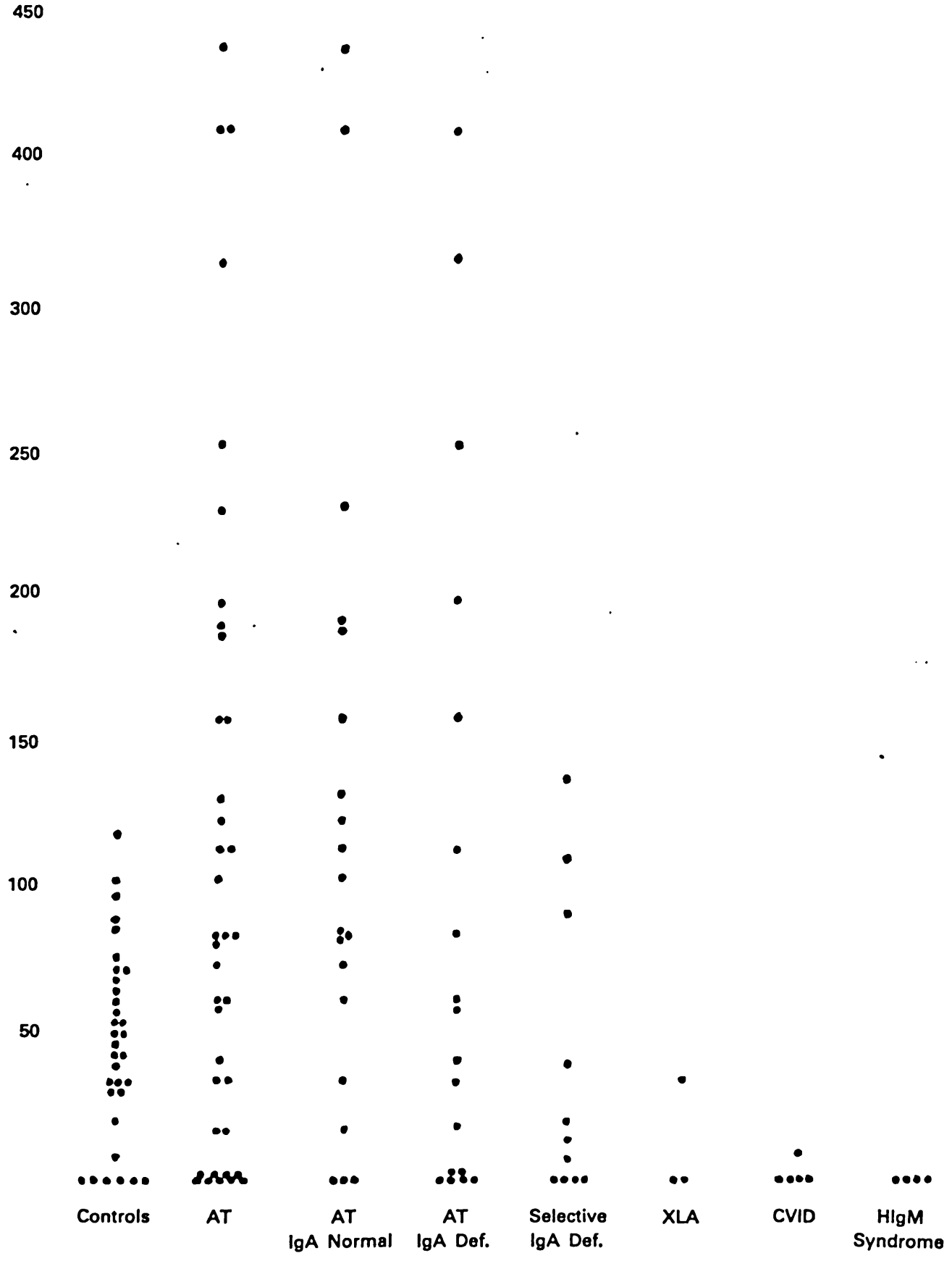

Fig. 1: Serum IgD concentrations (u/ml) in various immunodeficient patients and controls.

Discussion

Since the exact role of serum IgD in the immune system is still unclear, this Ig isotype has been studied less thoroughly than others in various disorders. In this study, we determined IgD levels in 66 primary immunodeficiency patients (38 AT patients) and in 33 healthy age-matched controls. Serum IgD was undetectable in 18.1 percent of normal children, and the percentage of low IgD sera was similar to the values earlier reported[4-6]. Nine of 38 AT patients (23.6%) also had undetectable serum IgD. The difference between the control and patient groups was not significant in this respect. The pattern of segregation of low serum IgD in AT sibling pairs was compatible with a mode of autosomal recessive inheritance of low serum IgD phenotype and with crossing-over. AT patients tended to have higher IgD concentrations, and the difference between controls and AT patients was found to be significant ($p = 0.018$). When AT patients were evaluated according to their serum IgA levels, the number of patients with undetectable serum IgD was higher in the IgA deficient group than in the patients with normal IgA levels (33.3% vs 15%), but the difference was not significant. In contrast to AT patients with normal IgA levels, the IgD values in patients with IgA deficiency did not differ significantly when compared with the controls, but the difference was significant when zero IgD values were excluded. Since low IgD values (low IgD phenotype) have been reported in 13-14 percent of normal individuals, it is impossible to ascertain, without knowing the IgD values of other family members, whether patients have low IgD or come from families with low IgD phenotype. Buckley and Fiscus[1] have reported elevated median IgD values in patients with AT but the difference was not significant. McFarlin et al[2] found high IgD levels in some of their AT patients. Since no difference has been found between patients with high and normal IgD values in respect to frequent infections and levels of IgG or IgM, chronic antigenic stimulation alone does not seem to be responsible for high IgD values. In addition some immunodeficient patients who had recurrent infections did not have high IgD values. Production of specific IgD antibody has been reported infrequently in infection[4]. Increases in serum IgD are not common. Hodgkin's disease and AIDS are among the diseases in which IgD has been found to be high[7-9]. In patients with bacterial and fungal infections (e.g. tuberculosis, leprosy, aspergillosis) IgD may be elevated but no consistent correlation exists between increased IgD and chronic infection[1].

Conflicting results have been reported regarding serum IgD concentrations in patients with selective IgA deficiency. While Buckley and Fiscus[1] found depressed levels, Plebani et al[3] found normal values in this patient group. In the present study, the difference between the patients and control groups was found to be insignificant. Again serum IgD concentrations did not show any correlation with the associated diseases in IgA deficiency patients. Thus our data did not reveal a compensatory increase in serum IgD in patients with IgA deficiency.

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DETECTION OF INTRACARDIAC LEFT - TO - RIGHT SHUNTS IN CHILDREN BY CONTRAST ECHOCARDIOGRAPHY AND THE RADIONUCLIDE TECHNIQUE*

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Summary: Özme Ş, Özer S, Caner B, Bekdik C, Saraçlar M, Özkutlu S. (Departments of Pediatrics and Nuclear Medicine, Hacettepe University Faculty of Medicine, Ankara Turkey). Detection of intracardiac left-to-right shunts in children by cardiac echocardiography and the radionuclide technique. Turk J Pediatr 32: 183-195, 1990.

This study was carried out in the Departments of Pediatrics and Nuclear Medicine at Hacettepe University Faculty of Medicine between April 1986 and March 1988 with the aim of detecting left-to-right shunts in 70 patients with isolated ventricular septal (VSD) defect, isolated atrial septal defect (ASD) and patent ductus arteriosus, by using the radionuclide technique together with contrast echocardiography. In some patients, the results were confirmed by both cardiac catheterization and angiocardiography. Most of the data were confirmed during surgery. A good correlation was found between the results of contrast echocardiography and radionuclide angiography. The difference between the QP/QS value and the grade of positive contrast effect was tested statistically and "p" was found to be less than 0.001. Therefore, we conclude that these methods could be applied together to determine the indication for surgery in cases with ASD or VSD. *Key words: intracardiac left-to-right shunts, contrast echocardiography, radionuclide technique.*

The radionuclide technique is used for rapid and safe detection, and quantitation of intracardiac shunts in pediatric patients. It is a noninvasive procedure which delivers low radiation so that it can be repeated, if necessary. Recent studies using this technique have shown a good correlation when estimating letf-to-right shunting according to the Fick method[1].

Another noninvasive method is echocardiography which has found a wide field of application in medicine during the last 20 years. This method is preferred over the others since it is non-traumatic, easy, inexpensive and can be repeated as frequently as necessary[2-4]. Furthermore its reliability has been proven by angiographic and pathologic studies[5]. When compared to oximetry, peripheral vein contrast echocardiography is a much more specific method in demonstrating shunts at septal defects[6,7]. Contrast studies using two-dimensional echocardiography have detected a right-to-left (positive) shunt or a left-to-right (negative) shunt at the atrial level in patients with atrial septal defect and at the ventricular level in patients with ventricular septal defect[8-10].

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In this study, two-dimensional echocardiography and the radionuclide technique were used together to detect and evaluate intracardiac shunts. In some patients, the results of both studies were confirmed by cardiac catheterization and angiocardiography. In addition, most of the data were substantiated surgically.

Material and Methods

The aim of this study carried out between April 1986-March 1988, in the Departments of Pediatrics and Nuclear Medicine at the Hacettepe University Faculty of Medicine was to detect left-to-right shunts in 70 patients with isolated ventricular septal defect (VSD), isolated atrial septal defect (ASD) and patent ductus arteriosus (PDA) using cardioechography, cardiac catheterization and the radionuclide technique in combination. Since the radionuclide method proved to be unsuccessful in 12 patients, the remaining 58 patients formed the study group. A control group of 10 children (with no heart disease) were compared with the study group.

The cases were divided into three groups according to the methods used. The control group comprised 10 subjects in which only radionuclide angiography was performed. Group A comprised 45 subjects in which both contrast two-dimensional echocardiography and radionuclide angiography were carried out. Group B comprised 13 subjects in which contrast two-dimensional echocardiography, radionuclide angiography and cardiac catheterization were used. There were 43 males and 37 females, and their ages ranged between one and 17 years (Table I).

TABLE I: Distribution of 68 Cases According to Age and Sex

	Control	Group A	Group B
Girl	3	21	9
Boy	7	24	4
Total	**10**	**45**	**13**
Age (yrs)	3-7	1-15	4-16
Mean (yrs)	9.72 ± 0.63	8.47 ± 0.51	9.76 ± 0.89

The patients with left-to-right shunts did not have any valvular insufficiency or findings of congestive heart failure.

Two-dimensional echo studies were performed using a Toshiba SSH-60A echocardiograph equipped with 3.75 and 5 mHz transducers. The images were recorded on video tape for further evaluation. The contrast material consisted of 2-10 cc of 3% saline or 5% dextrose injected intravenously into a peripheral vein in patients with either atrial septal defect or ventricular septal defect. The injection was repeated at least three times in each case. The passing of the

contrast material from the right atrium into the left atrium or from the right ventricle into the left ventricle was evaluated as a "positive contrast" while non-contrast blood passing from the left atrium to the right atrium or from the left ventricle to the right ventricle was termed a "negative contrast". A positive contrast was quantitated in four grades while a significant negative contrast effect was graded as three negative or four negative[8-10]. Grade three positive and grade four positive contrast effects were considered definitive evidence of an atrial or ventricular septal defect (Figs. 1-4).

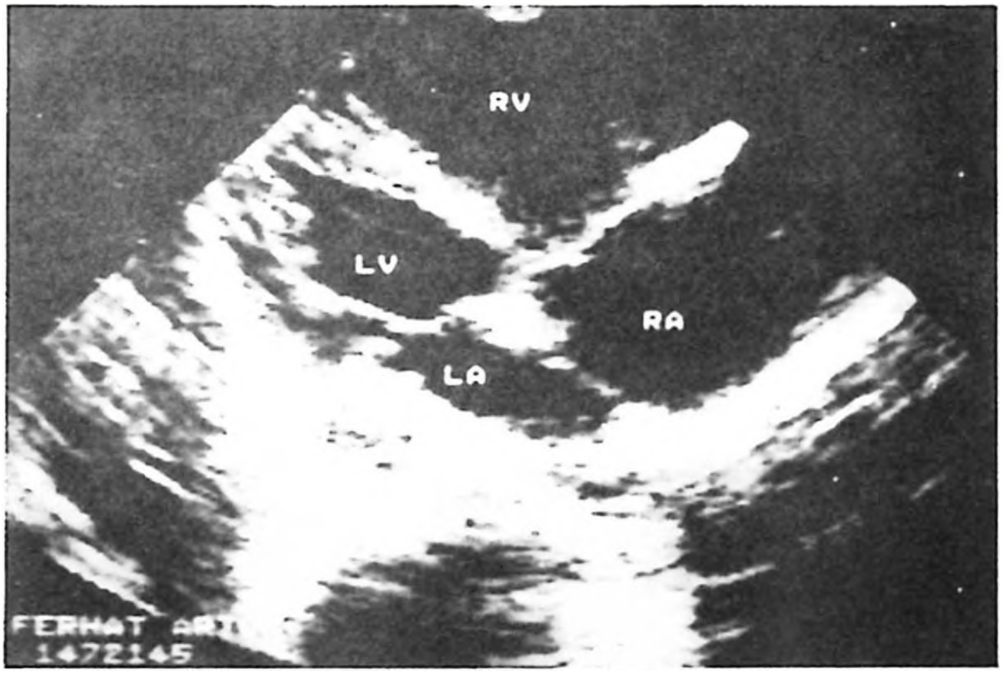

Fig. 1: Apical four-chamber view.

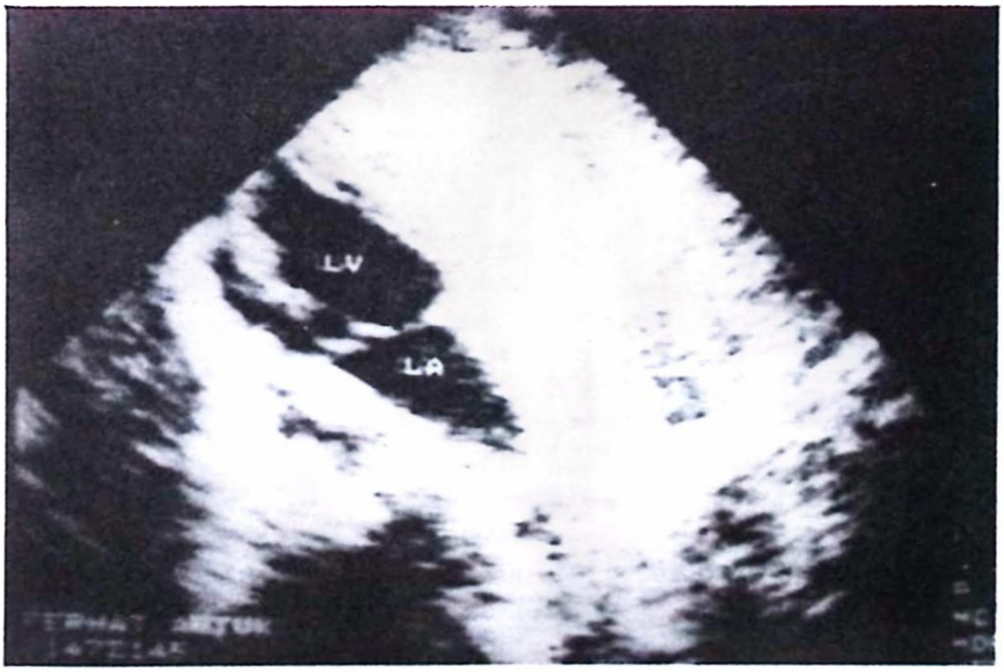

Fig. 2: Contrast material is seen in the right atrium and the right ventricle.

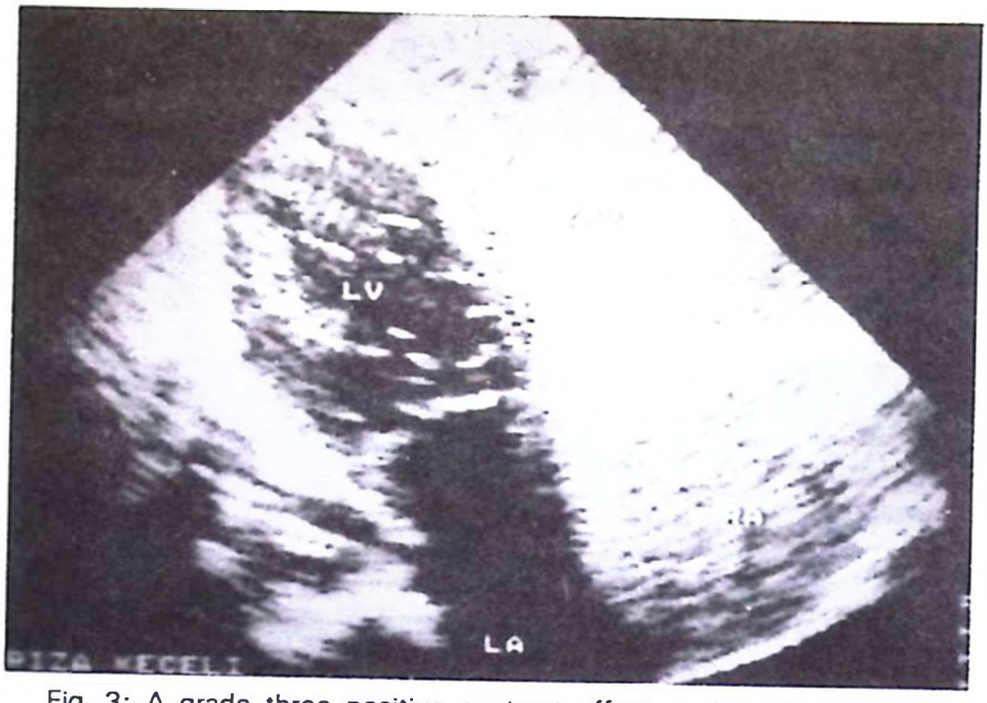

Fig. 3: A grade three positive contrast effect in the left ventricle.

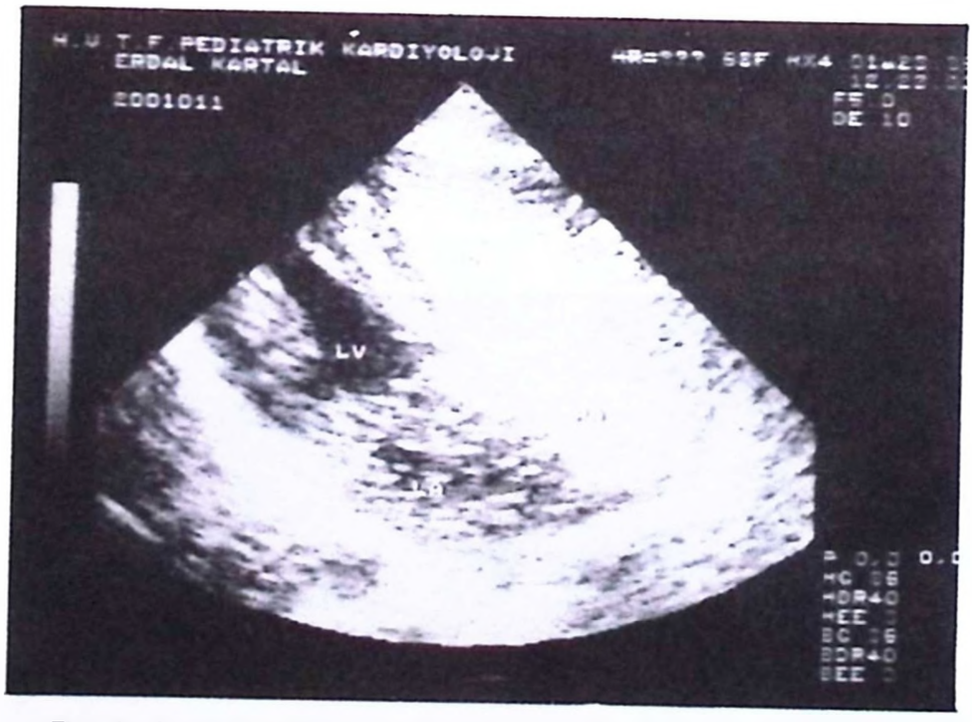

Fig. 4: A grade three positive contrast effect in the left atrium.

70 patients with left-to-right shunts and 10 controls were studied by radionuclide angiography using either the Siemens Scintiview II camera or the Toshiba GCA-501 S digital camera. Radionuclide angiography was performed under the computerized gamma camera with the patients in a supine position. We used the

gamma function area rate method in our study[11-15]. After administering a bolus of intravenous ^{99m}Tc sodium pertecnetate, as the radionuclide material, curves of time-activity were obtained from the areas taken on the chest. By analyzing these histograms by the gamma function method, the pulmonary flow/systemic flow (QP/QS) ratio was calculated. A value of up to 1.20 was considered normal while values greater than this were regarded as definite evidence of a left-to-right shunt[1].

Results

Twelve out of 80 cases (15%) were excluded from the study because of unsuccessful radionuclide estimations: there was bolus failure in nine patients, uncooperativeness in two patients, and a registration fault in one patient.

The QP/QS values of the 10 children in the control group were found to be between 1.05-1.15 (average 1.07 ± 0.09) using the radionuclide method.

Table II illustrates the distribution of 58 patients with left-to-right shunts according to diagnosis. Group A consisted of 36 cases with ventricular septal defect, five with secundum atrial septal defect and four with patent ductus arteriosus. Group B consisted of six cases with ventricular septal defect, four with secundum atrial septal defect and three with patent ductus arteriosus (Table II).

TABLE II: Distribution of 58 Patients With Left-to-Right Shunts

	Group A	Group B
VSD	36	6
ASD	5	4
PDA	4	3
Total	45	13

In group A, four of 36 cases with VSD showed a grade three or four positive contrast effect and the radionuclide QP/QS values ranged between 1.70-3.60 (average 2.40 ± 0.14) in these patients. As a result of these findings all the patients underwent surgical closure for ventricular septal defect. These procedures were successful in all patients operated on and the defects were large. Another three cases with VSD showed a grade two or one positive contrast effect. We saw no positive contrast effect in the 19 cases with VSD. Radionuclide angiography revealed that the QP/QS values ranged between 1.10-1.80 (average) 1.40 ± 0.04) in these 22 patients. According to this data, we decided that surgical repair was not indicated in these 22 patients.

A grade three or four positive contrast effect was found in the four cases with atrial septal defect. The radionuclide QP/QS values varied between 1.93 and 2.94 (average 2.34 ± 0.23). Accordingly, all four cases with ASD underwent atrial septal defect closure. The surgical results confirmed that the defect was large. We could not find any positive contrast effect in one case with ASD whose QP/QS value was 1.20, as measured by the radionuclide technique; catheterization was performed in this case. The patient was operated on and the defect was not large.

The QP/QS values of four patients with PDA ranged between 1.25-1.67 (average 1.47 ± 0.22) for the right lung and 1.30-1.89 (average 1.63 ± 0.14) for the left lung. Contrast echocardiography was not used in these cases. All of these patients underwent surgery (Table III).

The radionuclide QP/QS values were found to be between 1.70 and 3.60 (average 2.39 ± 0.13) in a total 18 cases (14 VSD, 4 ASD). These cases also showed a grade three or four positive contrast effect. They underwent surgical closure for atrial or ventricular septal defects. In 23 cases (22 VSD, 1 ASD), the radionuclide QP/QS values ranged between 1.10 and 1.80 (average 1.39 ± 0.04), and they showed a grade two or one positive contrast effect. It was thus decided that all the VSD cases should be followed up. After catheterization and angiography, the ASD case was operated on. When the difference between the mean QP/QS value and the grade of positive contrast effect was tested statistically, "p" was found to be less than 0.001 (Table IV; Fig. 5).

There were 13 cases (6 VSD, 4 ASD, 3 PDA) in group B (Table V). Cardiac catheterization, radionuclide angiography and contrast echocardiography were performed in combination in each patient with VSD or ASD. However, in the patients with PDA, only cardiac catheterization and radionuclide angiography were used.

Two out of six patients with VSD showed either a grade three or a grade one positive contrast effect, and the QP/QS value was found to be 2.70 and 2.40 in the catheterization and 2.40 and 2.70 in the radionuclide angiography. We decided that surgical repair was indicated in these patients. Another patient with VSD showed a grade two positive contrast effect and QP/QS values of 1.20 in the catheterization and 1.34 in the radionuclide angiography. We could not find any positive contrast effect in three of the six cases with VSD. In these three patients the QP/QS values were between 1.00-1.70 (average 1.34 ± 0.20) in the catheterization and 1.29-1.50 (average 1.39 ± 0.05) in the radionuclide angiography. Surgery was not recommended, and these four patients were managed conservatively. The remaining two patients with VSD underwent surgery for ventricular septal defect closure. During the operation the sizes of the defects were found to be between 1.15 cm.

TABLE III: Data of 45 Patients Studied by Two-Dimensional Echocardiography and Radionuclide Angiography (Group A)

Diagnosis	Number of Patients	Positive Contrast Effect in Echocardiography	Radionuclide QP/QS	Treatment
VSD	7	+4	2.04 – 3.60 (2.78 ± 0.19)	Surgery
VSD	7	+3	1.70 – 2.70 (2.05 ± 0.12)	Surgery
Total	14	(+4, +3)	1.70 – 3.60 (2.40 ± 0.14)	Surgery
VSD	1	+2	1.80	Clinical follow-up
VSD	2	+1	1.43 – 1.67 (1.55 ± 0.11)	Clinical follow-up
VSD	19	No positive contrast effect	1.10 – 1.60 (1.37 ± 0.03)	Clinical follow-up
Total	22	+2, +1, or no positive contrast effect	1.10 – 1.80 (1.40 ± 0.04)	Clinical follow-up
ASD	1	+4	2.94	Surgery
ASD	3	+3	1.93 – 2.50 (2.34 ± 0.27)	Surgery
Total	4	(+4, +3)	1.93 – 2.50 (2.34 ± 0.23)	Surgery
ASD	1	No positive contrast effect	1.20 (For left lung)	Surgery
PDA	4	--	1.30 – 1.89 (1.63 ± 0.14)	Surgery
Total	**45**			

TABLE IV: Comparative Data of Radionuclide QP/QS Values and Degree of Positive Contrast Effect in Echocardiography

Degree of Positive Contrast Effect in Echocardiography	x	$S_{\bar{x}}$	n	t
VSD (+4, +3)	2.40	0.14	14	
				6.38 $p < 0.001$
VSD (+2, +1, no positive contrast effect)	1.40	0.04	22	
VSD (14), ASD (4) (+4, +3)	2.39	0.13	18	
				7.23 $p < 0.001$
VSD (22), ASD (1) (+2, +1, no positive contrast effect)	1.39	0.03	23	

(41 patients with ASD or VSD in Group A)

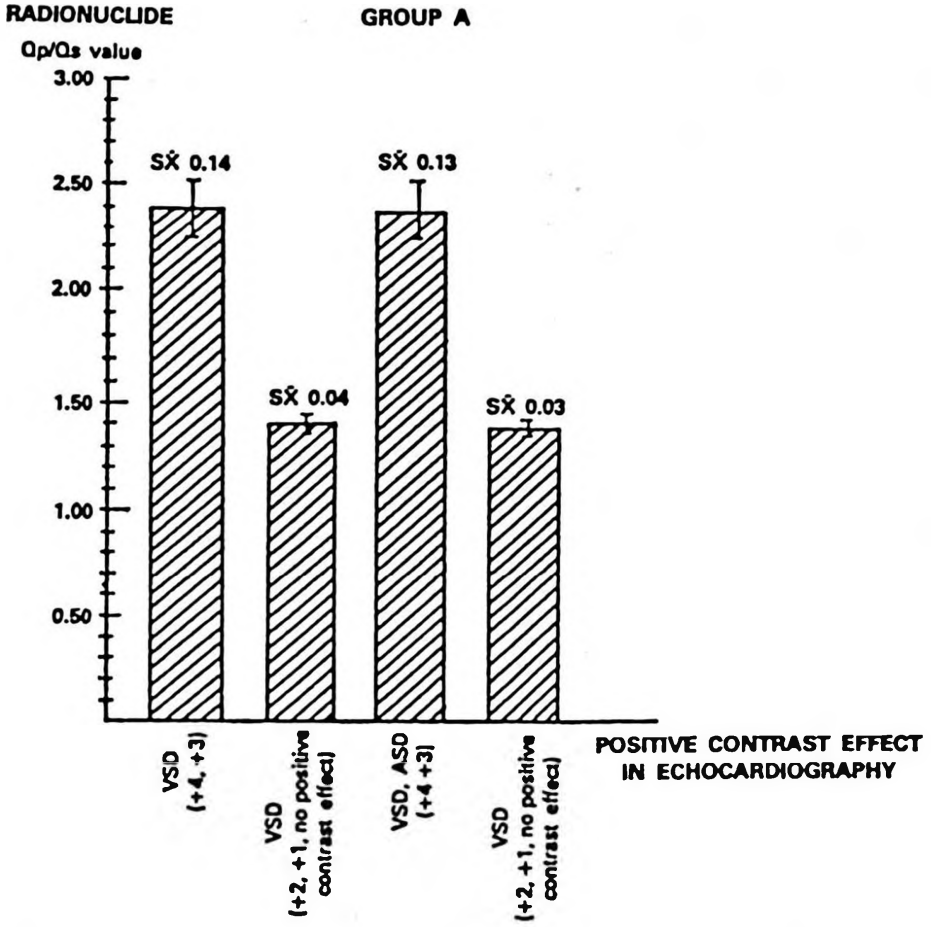

Fig. 5: Comparative values of radionuclide QP/QS vs. degree of positive contrast effect in echocardiography.

Two of the four patients with ASD showed a grade three positive contrast effect. In addition the QP/QS values ranged between 1.60-1.90 (average 1.75 ± 0.14) in the catheterization and 1.70-2.60 (average 2.15 ± 0.44) in the radionuclide angiography. In the other two cases associated with ASD, no contrast effect was observed. Their QP/QS values ranged between 1.60-2.50 (average 2.05 ± 0.44) in the catheterization and 1.90-3.00 (average 2.45 ± 0.54) in the radionuclide study. The size of these defects varied between 1.5-3 cm.

The radionuclide QP/QS values in the patients with PDA were calculated for the left lung. The patients were operated on.

Catheterization performed on patients in group B revealed QP/QS values which varied between 1.00-2.70 (average 1.84 ± 0.15). However this ratio was found to be between 1.29-3.00 (average 2.02 ± 0.08) in the radionuclide angiography (Table V).

TABLE V: Data of 13 Patients Studied by Two-Dimensional Echocardiography, Radionuclide Angiography and Cardiac Catheterization (Group B)

Diagnosis	Number of Patients	Positive Contrast Effect in Echocardiography	Radionuclide QP/QS	Cardiac Catheterization QP/QS	Treatment
VSD	1	+3	2.40	2.70	Surgery
VSD	1	+1	2.70	2.40	Surgery
VSD	1	+2	1.34	1.20	Clinical follow-up
VSD	3	No positive contrast effect	1.29 – 1.50 (1.39 ± 0.05)	1.00 – 1.70 (1.34 ± 0.20)	Clinical follow-up
ASD	2	+3	1.70 – 2.60 (2.15 ± 0.44)	1.60 – 1.90 (1.75 ± 0.14)	Surgery
ASD	2	No positive contrast effect	1.90 – 3.00 (2.45 ± 0.54)	1.60 – 2.50 (2.05 ± 0.44)	Surgery
PDA	3	—	1.62 – 2.60 (2.17 ± 0.28)	1.00 – 2.70 (1.84 ± 0.15)	Surgery
Total	13		1.29 – 3.00 (2.02 ± 0.08)	1.00 – 2.70 (1.84 ± 0.15)	

When the differences between the QP/QS values calculated by radionuclide angiography and oximetry during cardiac catheterization were tested statistically, they were not found to be significant ($p > 0.05$) in 13 patients (Table VI; Fig 6).

In this study, contrast echocardiography was used in 51 cases with VSD or ASD for detection and evaluation of intracardiac shunts. This procedure was successful in most of the patients. However, in two cases with ASD, and in one case with VSD from group B, the QP/QS values were found to be above 1.2 by catheterization while in radionuclide angiography either no positive or a grade one

positive contrast effect was observed in contrast echocardiography. It is concluded that contrast echocardiography demonstrated 5.8% false negative results in 51 patients with septal defect.

TABLE VI: Differences Between QP/QS Values Calculated by Radionuclide Angiography and Oximetry During Cardiac Catheterization Tested Statistically

Group B (13 Patients)

$X_D = 0.18$
$S_D = 0.11$
$t = 1.151$
$p > 0.05$

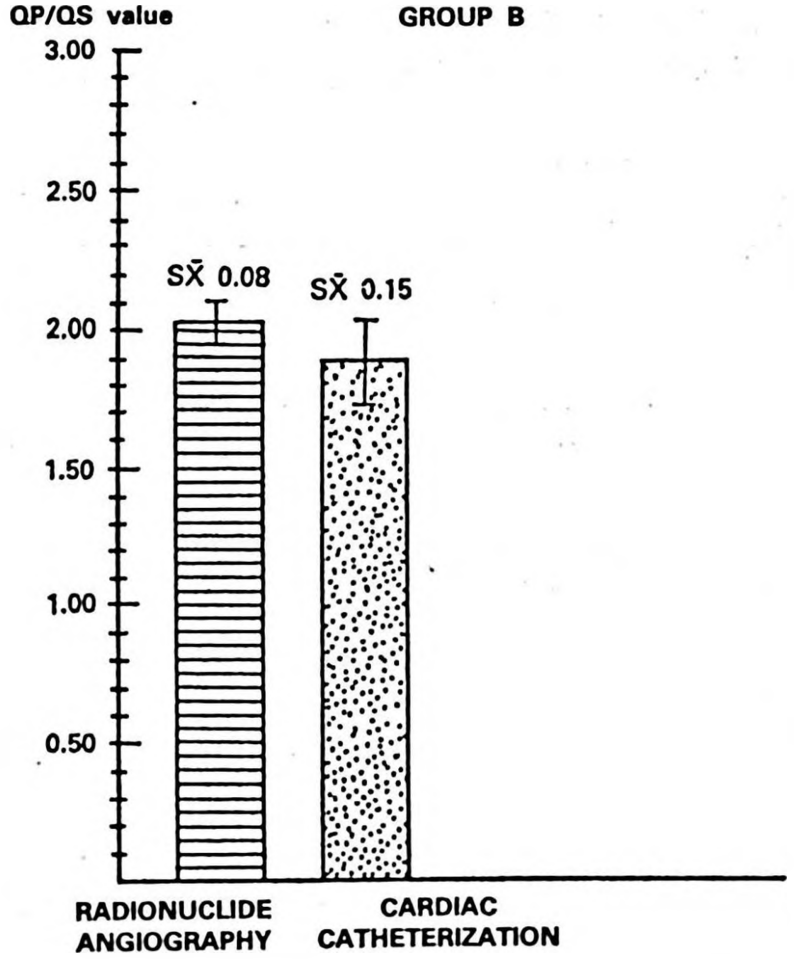

Fig. 6: QP/QS values in radionuclide angiography and cardiac catheterization.

Discussion

Cardiac catheterization and angiocardiography, which are the best means for visualizing the morphologic and functional properties of the heart in a living organism, maintain their importance and reliability in the face of advancing knowledge and techniques. However these methods require a well-trained team and a careful laboratory study. In addition, they carry some risks for the patient and the examiner[2]. Hemodynamic and angiocardiographic studies have shown that in ASD patients without complications there is only right-to-left shunt of small magnitude during the early systolic period[7]. In ASD patients, who undergo two-dimensional echocardiography, it has been observed that after injection into the right side, visualization of the contrast substance in the left atrium or left ventricle is very specific for left-to-right shunts[3,4,8-10,16]. Contrast echocardiography in patients with VSD has shown that the flow of the contrast substance from the right ventricle to the left at ventricular level occurs during the isovolumetric relaxation period of the ventricle (early diastole, after the closure of the aortic valve, and before the opening of the mitral valve)[8].

In this article we discussed two noninvasive techniques, namely, two-dimensional echocardiography and radionuclide angiography used in combination to deterimine the need for surgical intervention in our patients. 41 patients with VSD or ASD (group A) were studied. The degree of positive contrast effect was compared with the QP/QS values found by the radionuclide angiography. The difference between the two results was found to be significant ($p < 0.001$).

After a thorough search of the literature, we found that there have been no reports of studies performed in which both techniques were used in combination. There are some reports, however, that compare hemodynamic studies with the results of contrast echocardiography in adult ASD patients[8-10]. In addition, there are documented studies which show that it is possible to have a positive contrast substance flow from right to left at ventricular level in patients with a right ventricle/left ventricle pressure ratio of more than 0.50 or 0.71[8,17]. The QP/QS values of the 13 patients with VSD, ASD and PDA in group B were determined using catheterization and radionuclide angiography. When the results of the two methods were compared, no significant difference was found between the two groups ($p > 0.05$). These findings correlate with the results found in the literature. In the research done by McIlveen et al[12] the number of small shunts could not be estimated by oximetry, however, they were able to demonstrate them all by using radionuclide angiography. Askenazi et al[13] found a high correlation between the two studies in their investigation of 105 patients, and Sorensen and Starling[18] confirmed this correlation. Our study showed a good correlation between the QP/QS values obtained from catheterization and radionuclide angiography. All of these studies prove the sensitivity and reliability of the radionuclide method. The

results demonstrate that radionuclide techniques are most valuable in detecting simple cardiac defects such as isolated ASD or VSD. The definition of more complex malformations usually requires more invasive diagnostic methods.

In our study two noninvasive methods, contrast echocardiography and radionuclide angiography were used in combination to determine the indication for surgery in VSD or ASD cases. A good correlation was found between the results of the two techniques. We conclude that these methods can be applied together easily and safely for definite detection and quantitation of left-to-right shunts especially in isolated ASD or VSD cases.

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WHOLE BOWEL IRRIGATION IN CHILDREN: PROLONGED POST-IRRIGATION DIARRHEA DUE TO ISOTONIC SALINE*

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Summary: Şenocak ME, Büyükpamukçu N, Hiçsönmez A. (Department of Pediatric Surgery, Hacettepe University Faculty of Medicine, Ankara Turkey). Whole bowel irrigation in children: prolonged post-irrigation diarrhea due to isotonic saline. Turk J Pediatr 32: 197-200, 1990

Whole bowel irrigation (WBI) was performed in 60 children aged two to 16 yrs (mean 5.1 ± 0.5 yrs) in preparation for surgery (n: 59) and rectoscopy (n: 1). Isotonic saline (n: 43) and lactated Ringer's solutions (n: 17) were infused for irrigation. Vital signs remained stable during the procedure. Negligible electrolytic alterations were encountered. In general, WBI was well tolerated by all the patients. Two (3.3%) patients had abdominal cramps, vomiting was observed in nine (15%) and edema developed in one (16%).

The results of the preparation were assessed as satisfactory in 45 cases (75%), adequate in 10 cases (16.6%) and poor in 5 cases (8.3%). Diarrhea, as a complication of saline, has not been reported previously in the literature, but was observed in 32 of our cases (74.4%), and lasted 2-5 days (mean 3.38 ± 0.7 days) after irrigation. In addition, it is noteworthy that bile-stained intraluminal clear fluid was seen only in the patients who had been irrigated with lactated Ringer's solution. Our research related to this observation is continuing. *Key words: whole bowel irrigation, colonoscopy, rectoscopy, colonic surgery, diarrhea.*

Whole bowel irrigation (WBI) was first developed for the treatment of cholera[1]. Hewitt et al[2] described their experience using WBI as a newer method of bowel preparation. They achieved rapid and effective cleansing of the colon by irrigating the intestinal tract with large volumes of saline or lactated Ringer's solutions[2,3].

Since Hewitt et al[2] first reported WBI in 1973, many studies comprising a large series of adults have been carried out, in which good tolerance, promptness and efficacy of the method have been observed[4]. We found only a few published reports describing the application of this procedure in childhood[3-5]. The purpose of this article is to report our experience using WBI in 60 children and to discuss the results.

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Material and Methods

This study includes children who underwent elective colorectal surgery or endoscopy between January 1986-June 1987. Indications for WBI are given in Table I.

TABLE I: Indications for Whole Bowel Irrigation

Procedure	No of Patients
Colostomy closure	38
Hirschsprung's disease	
Swenson's operation	7
Duhamel's operation	5
Hemicolectomy	1
Colonic interposition	1
Colotomy and polyp excision	1
Myectomy	4
Perineal pull-through	2
Rectoscopy	1
Total	60

WBI was performed in 60 patients aged between two to 16 years, who had no evidence of cardiac disorders, renal failure, cirrhosis or intestinal obstruction. The patients were admitted one day before the procedure was to be performed. Dietary restrictions were not recommended. A nasogastric tube was placed into the stomach and metoclopramide hydrochloride (Metpamide^{R}) was given (0.3 mg. per kg) intramuscularly 30 minutes before irrigation to initiate gastric emptying and to prevent abdominal cramps. Forty-three of the patients were irrigated with isotonic saline solution, while the others received lactated Ringer's solution. Antibiotics were not added to the solutions which were heated to 37 °C and administered via a nasogastric tube at a rate of 1m/kg/min for 30 minutes after the defecation material was clear.

Weight, hemoglobin, hematocrit, blood electrolytes, and urine density were determined before, during and after irrigation. Vital signs (heart beat, arterial blood pressure, body temperature) were monitored and recorded per 15 minutes. Observed complaints including nausea, vomiting, epigastric fullness and abdominal colic were also recorded. The adequacy of the preparation was assessed by direct inspection of the colon. The results were evaluated as either satisfactory (no fecal residue present), adequate (little residue), or poor (considerable residue). All the patients were prepared and operated on under the same conditions. Post-operative observation included clinical signs of irrigation-related complications.

Results

The first stool was usually passed 30-90 minutes after the initiation of irrigation (mean 61 ± 2.9 min). The clear fluid evacuation time changed and ranged between 60-270 minutes (mean 128 ± 7.9 min). The mean time of total irrigation was 222 ± 0.126 minutes. 2-11 liters (mean 3.88 ± 2.43 l) of irrigant were infused (mean 223 ml/kg). Preparation was completed without any discomfort in 48 patients (80%), two patients experienced abdominal cramps, vomiting was observed in nine patients and edema in one patient. Vital signs were normal. There were no significant changes in weight, serum electrolyte, hemoglobin or hematocrit values during and after irrigation. In some cases, urine density decreased slightly at the end of the procedure.

Preparation was assessed as satisfactory in 45 cases (75%), adequate in 10 cases (16.6%), and poor in 5 cases (8.3%). Bile-stained fluid was detected in all the patients irrigated with lactated Ringer's solution. Diarrhea was observed 2-5 days after preparation in 32 patients (74.4%) who had been irrigated with isotonic saline. The defecation rate was 4-6 times daily (mean 4.66 ± 0.4).

Discussion

Traditional methods are time consuming, difficult and frequently inadequate in cleansing the colon[4]. WBI is the best alternative to the usual methods used in children[4]. Many irrigants have been recommended[4,6]. We preferred using isotonic saline and lactated Ringer's solutions because they are inexpensive and readily available. In addition, infusion of large volumes of these solutions were well tolerated. Since the absorbed volume was minimal, no significant hemodynamic or electrolytic alterations were encountered. Edema was only observed in one patient, and disappeared spontaneously. According to our experience, the administration of a diuretic is usually unnecessary in children.

The administration of neomycin and/or erythromycin may lead to pseudomembranous colitis, as described by Weidema et al[7]. Therefore, we did not add these drugs to the irrigants nor did we administer them orally. Excessive bile-stained intraluminal clear fluid was detected in the patients who had been irrigated with lactated Ringer's solution. We cannot ascertain the reason for this, but it is known that lactated Ringer's solution may produce a choleretic effect. We believe that in order to explain this occurrence, further investigation is required, and our research concerning this subject is continuing.

As far as we know, continual post-irrigation diarrhea has not been reported. It is considered a complication of saline and is explained by the prolonged purging effect of an irrigant due to the release of cholecystokinin and pancreozymin from the intestinal mucosa[6].

WBI is effective in rapidly evacuating drug overdoses and/or ingested toxic foreign bodies (e.g. iron, tricyclic antidepressants, alkaline battery) from the gastrointestinal tract[3,8,9]. WBI has also been administered to prepare the colon for double contrast barium enema[4]. None of our patients were irrigated for these reasons. Our study illustrated that WBI provides excellent preparation for colonic surgery and endoscopy, and that the preoperative admission time is reduced by 2-3 days. The procedure was well tolerated by our patients, and only prolonged diarrhea was a complication of isotonic saline irrigation. Thus, we decided to use lactated Ringer's solution in WBI.

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EXERCISE – INDUCED VENTRICULAR TACHYCARDIA IN CHILDREN*

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Summary: Çeliker A, Oto A, Oktay A, Özer S, Özme Ş, Karamehmetoğlu A, Oram E, Uğurlu Ş. (Hacettepe University Institute of Child Health, Ankara, Turkey). Exercise-induced ventricular tachycardia in children. Turk J Pediatr 32: 201-206, 1990

Two children with exercise-induced tachycardia, one with idiopathic long-QT syndrome, are presented. The patients were evaluated by exercise testing and electrophysiologic study. From the onset of treatment with the beta-blocking agent, pindolol, the patients have been symptom-free. These findings emphasize that children with syncope must be evaluated by ECG, exercise testing, 24-h Holter-monitoring, and finally, electrophysiological study. *Key words: tachycardia, exercise-induced, children.*

Exercise-related ventricular tachycardia is an uncommon finding in children. Current knowledge is based on reports of series comprising small numbers of patients. In a relatively large series, Bricher et al[1] found exercise-related tachycardia to have a frequency of approximately 0.8 percent among a referral population of children with cardiac disease. Although tachycardia, which occurs in children during exercise, is generally well tolerated, it is well known that in some cases it may cause syncope and even result in sudden death[2]. In this report we describe two children with unexplained syncope associated with exercise-induced ventricular tachycardia.

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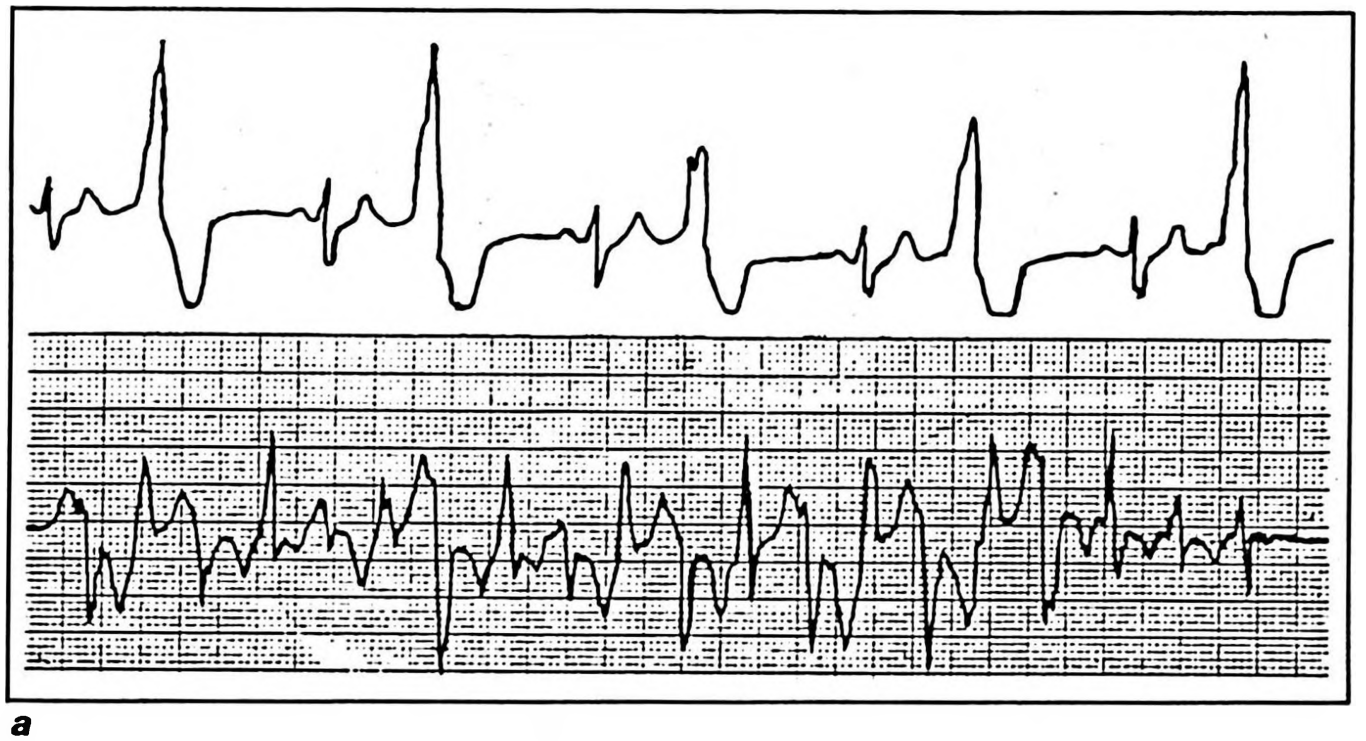
Case Reports

Case 1

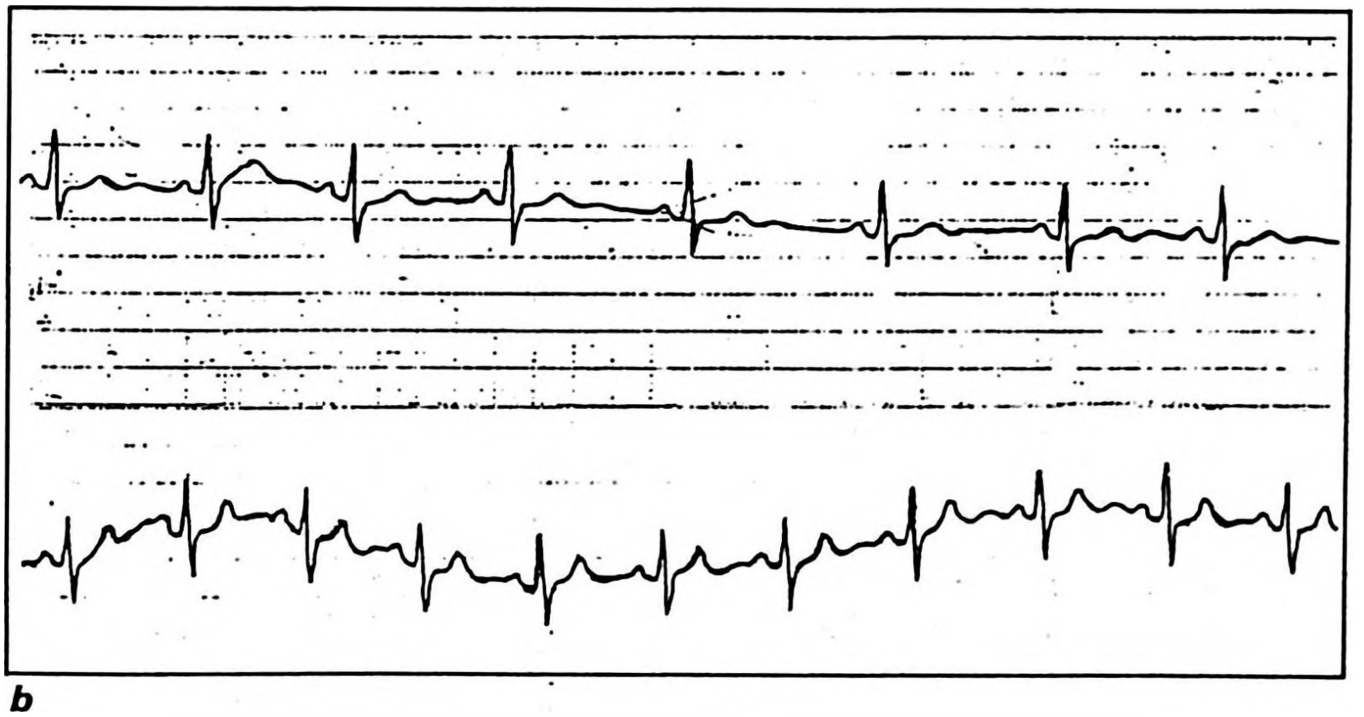
A 14-year-old boy with the diagnosis of unexplained syncope who was followed up for four years had a VVI (ventricular pacing sensing inhibiting) permanent pacemaker implanted at the age of 13. Despite the presence of pacemaker back-up, he continued to have fainting episodes and was reevaluated. Physical examination revealed that there was only an apical late systolic murmur grade I/VI. ECG was normal, apart from a sinus bradycardia. Echocardiography revealed no structural abnormality. Neurological evaluation showed no disorder. The permanent pacemaker was removed and an electrophysiologic study was performed which revealed no abnormality. An exercise test was performed because of a probable association between exertion and syncope, and it revealed unifocal ventricular premature beats and short runs of ventricular tachycardia (Fig. 1a.b). Pindolol (Visken^{R}) therapy was instituted and the dosage was gradually increased to 45 mg bid. The medication was well tolerated and the syncopal attacks completely disappeared. The patient started to play basketball on the school-team, and was a successful student. During the four-year follow-up period he showed normal physical and psychological growth.

Case 2

A 9-year-old boy with the diagnosis of unexplained syncope was followed up for three years. Despite antiepileptic treatment, there was no improvement in his fainting episodes. A careful examination of the history revealed that there was a possible relationship between the fainting and exertion. According to the family history, the parents of the child were close relatives. In addition, two of the patient's male cousins, both siblings, had died of unexplained syncope, one at 15 years of age and the other at 12 years of age. Moreover, the patient's father had had palpitations and attacks of dizziness upon exertion, but had never used any medication for these conditions. Physical examination revealed normal physical findings. Neurologic examination was also unremarkable. Electrocardiographically, the QTc interval was 420 milliseconds. Two-dimensional echocardiography was normal. An electrophysiologic study was performed and revealed no abnormality except for a prolonged QTc interval (Fig. 2). A simple controlled exercise test, consisting of jumping, precipitated a bout of ventricular tachycardia and syncope. Pindolol (Visken^{R}) in a dose of 5 mg b.i.d., was started and 24-h Holter-monitoring showed the patient to be free of ventricular tachyarrhythmias. The patient, diagnosed as having idiopathic long QT syndrome, has been syncope-free for two years.



a



b

Fig. 1: The top of the panel shows ventricular bigeminy and exercise-induced multiform ventricular tachycardia. (a) after treatment with pindolol ventricular bigeminy disappeared, and exercise could not provoke ventricular tachycardia (b).

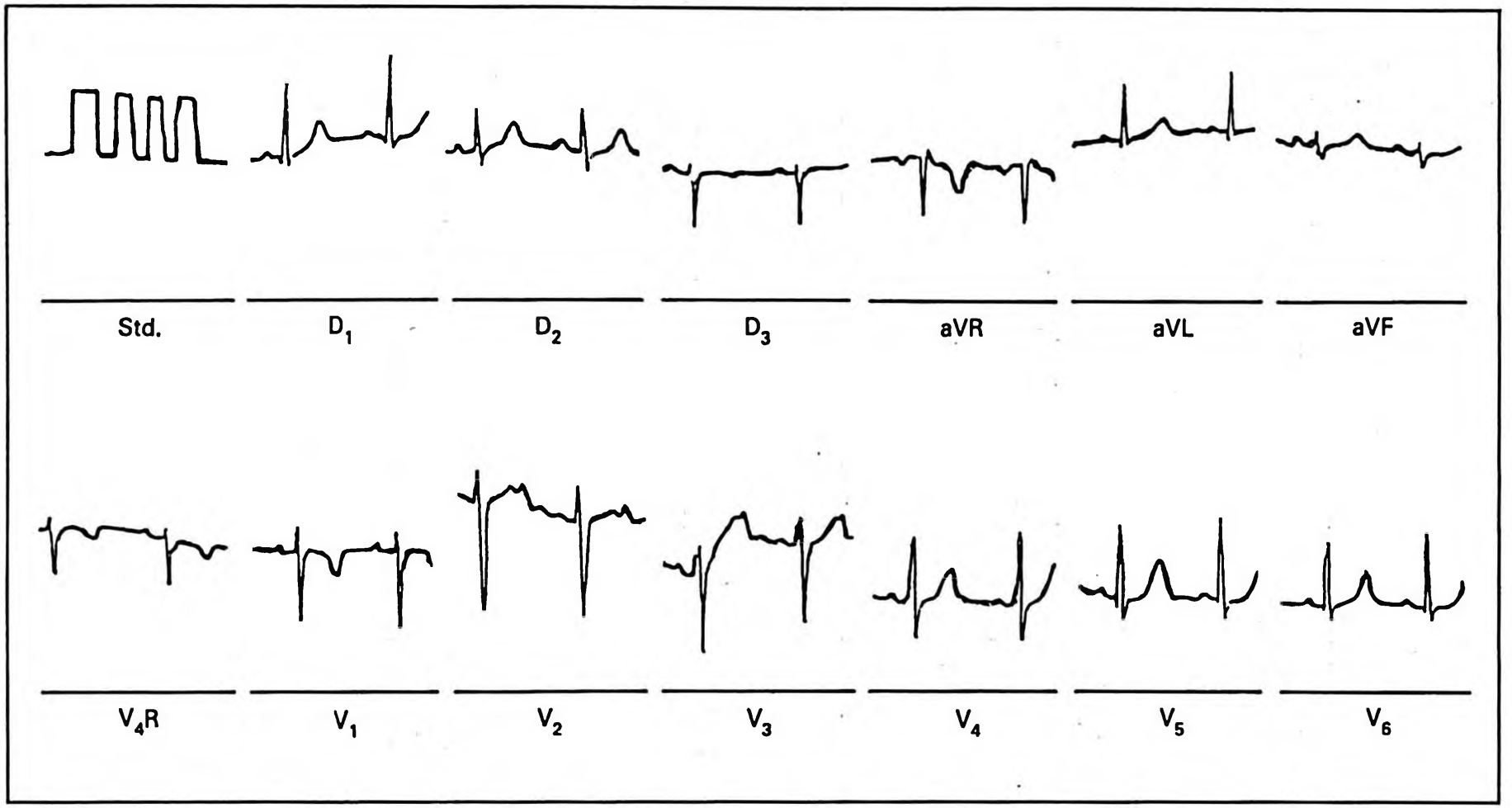


Fig. 2: The rhythm strip revealed a normal sinus rhythm and a corrected QT interval of 420 milliseconds.

Discussion

Ventricular arrhythmias in children are uncommon, especially in the absence of congenital structural heart disease or other predisposing factors[3-5]. The diagnosis of ventricular tachycardia in children is commonly an incidental finding in asymptomatic patients[6]. Idiopathic ventricular tachycardia is generally believed to carry a favorable prognosis, though the natural history and the need for treatment still remains controversial[7-9]. However, patients with exercise-related ventricular tachycardia may be at an especially high risk of sudden death, and antiarrhythmic therapy has been recommended, even in asymptomatic patients[1,10].

Exercise increases sympathetic tone and promotes secretion of catecholamines. Consequently, exercise enhances diastolic (phase 4) depolarization, improves membrane conductivity, shortens refractory periods of all cardiac tissues,and activates the adenylate cyclase-cyclic AMP system, thereby increasing transmembrane calcium influx. Therefore, exercise can theoretically provoke tachyarrhythmias via all three major mechanisms: re-entry, automaticity and triggered rhythmic activity. Patients with exercise-induced tachycardia generally do not have excessive secretion of catecholamines. These findings have led investigators to suggest the presence of a low sympathetic threshold[11]. Sung et al[12] have demonstrated that beta-adrenoreceptor blockade is especially effective in suppressing ventricular tachycardia. From a clinical standpoint, it is thus quite reasonable to initiate beta-blocker therapy in patients with exercise-induced ventricular tachycardia unless clinical findings indicate otherwise[13]. In selective cases, electrophysiologic studies are needed to define the underlying mechanism of this abnormality and to select an effective pharmacological agent[14,15]. Our first case had exercise-induced tachycardia, and a beneficial effect was achieved with beta-blockade, which is consistent with the above-mentioned data. Since we could not demonstrate any anatomic substrate either by echocardiographic or electrophysiologic studies, and because there was no clinical evidence for increased sympathetic activity, we propose a low sympathetic threshold as the cause of the ventricular arrhythmia.

Idiopathic long QT syndrome is a ventricular repolarization abnormality characterized by autosomal recessive or dominant inheritance. The diagnosis of this disease is made basically by measuring the corrected QT interval (QTc), which extends beyond the normal limits for age. Affected individuals have ventricular tachycardia and syncope induced by exercise and stress[2]. Electrophysiological studies are not usually helpful, however, they may be valuable in doubtful cases to rule out other possible causes[14,15]. Treatment is based on the administration of beta-blocker drugs. Some patients may experience syncope despite this medication and require high thoracic left sympathectomy[2]. The present case has been on pindolol for two years and has remained symptom-free. If drug tolerance develops in this patient, a sympathectomy might be planned as a more definitive approach.

In conclusion, occult arrhythmias are important causes of syncope in some children with both structurally normal hearts and negative neurologic evaluation. Children with negative findings for non-cardiac causes of syncope should be evaluated by ECG, 24-h Holter-monitoring, maximal exercise testing, and a detailed cardiac electrophysiologic study. These recommendations are especially important in children with exercise-induced syncope because of the fatal nature of the outcome related to this arrhythmia[16].

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HEMOPHILIC PSEUDOTUMOR: A CASE REPORT*

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Summary: Sarıkayalar F, Tanrıöğer N, Ünsal M, Özsoylu Ş. (Hacettepe University Institute of Child Health, Ankara, Turkey). Hemophilic pseudotumor: a case report. Turk J Pediatr 32: 207-210, 1990

Hemophilic pseudotumor has been defined as a progressive cystic swelling involving muscle which is produced by recurrent hemorrhage and accompanied by roentgenographic evidence of bone involvement. Pseudotumor is a rare complication of hemophilia, and, therefore, we present a case of a six-year-old male hemophiliac with a cyst in the left distal radius. *Key words: bone and joint changes, hemophilia, hemophilic cyst of bone.*

The term hemophilic pseudotumor describes a progressive cystic swelling involving muscle which is produced by recurrent hemorrhage and accompanied by radiographic evidence of bone involvement[1]. Masses develop most commonly in the pelvis, thigh or calf and consist of a slowly expanding encapsulated coagulum of chronic and acute hemorrhage[2,3]. In this paper, we describe a hemophiliac with a cyst in the left distal radius.

Case Report

A six-year-old boy was admitted to the hospital with the complaint of swelling of the left arm. The diagnosis of Factor VIII deficiency was established when he was two years of age. He had suffered a trauma of the left arm nine months ago. Although, he had been symptom-free in recent months, a swelling appeared on the same site of his arm.

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Physical examination revealed no abnormalities except for swelling and skin necrosis on the distal part of the left arm (Fig. 1). Laboratory examination revealed a hemoglobin level of 11.5 g/dl, white blood cell count 11200/mm^3, and differential count within normal limits. The prothrombin time was 14 sec and partial thromboplastin time 100 sec. The platelet count was 175000/mm^3. He had mild hemophilia type A, with Factor VIII being more than five percent.

Roentgenograms showed a hemophilic pseudotumor in the distal part of the left radius (Fig. 2).

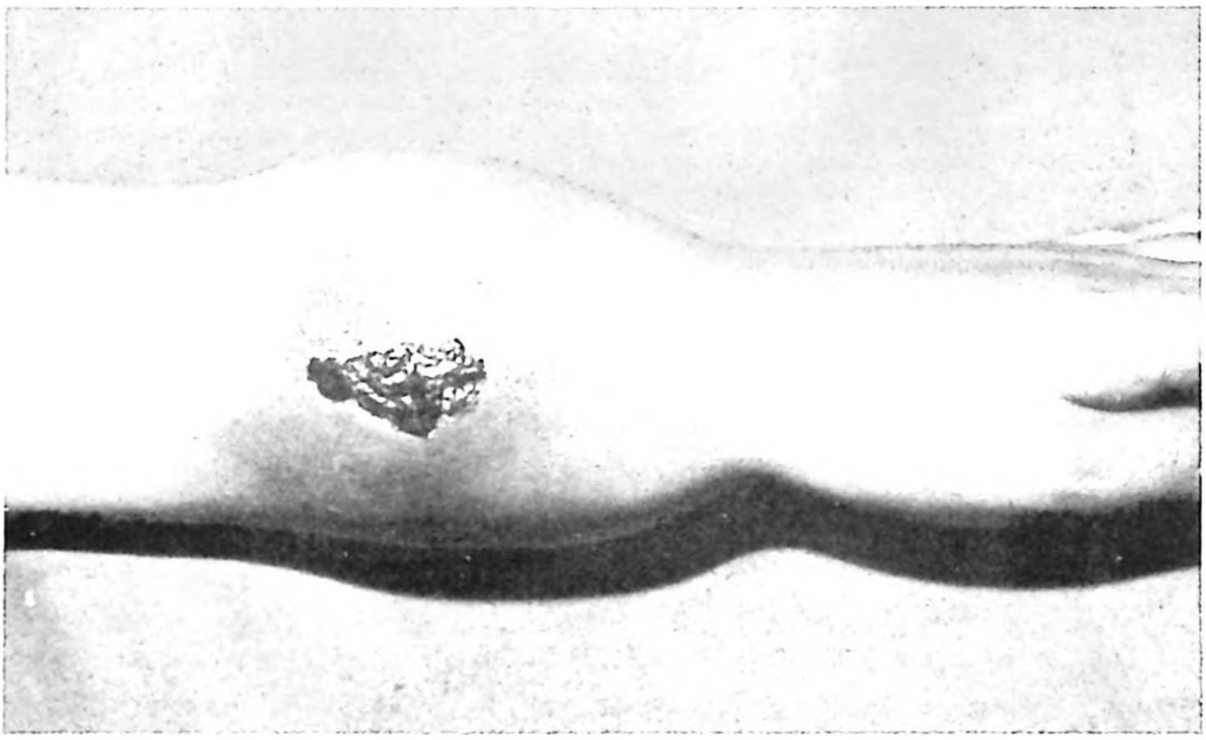

Fig. 1: Swelling and skin necrosis on the distal part of the left arm.

Fig. 2: Hemophilic pseudotumor on the distal part of the left radius.

Discussion

Pseudotumor is an unusual complication of hemophilia[3]. Gunning[4] estimated that one percent of severe hemophiliacs may have pseudotumors. However, its pathogenesis is not fully understood, and confirmed trauma is a factor in some patients[2].

Bone destruction has undoubtedly also played a role in the formation of pseudotumors, particularly in cases preceded by fracture. Intraosseous hemorrhage may also be a factor in the development of the hemophilic cyst, and with continued or repeated hemorrhage, these cysts may then increase in size causing expansion of the bone and thinning of the bony cortex. Reported cases indicate that lesions occur most commonly in the femur. However, they have also been reported in the pelvis, tibia, small bones of the hand, feet, calcaneus, humerus, olecranon and radius[2]. These lesions may also occur in more than one bone[3].

A pseudotumor can remain asymptomatic and unchanged for decades and then may suddenly be the site of bleeding and perforation. Fernandez de Valderrama[1] is of the opinion that there are three main types of hemophilic cysts involving muscle which can be defined by their mode of origin and subsequent course. Gilbert[5] described two types of pseudotumor: a proximal type located in the pelvis and a distal type tumor localized mainly in the hands and feet. The former type appears mainly in adults, while the latter, with a better prognosis, appears only in children.

Gross pathologic examination of these pseudotumors has revealed thick-walled cysts filled with old clot and serosanguinous fluid. The walls of the cysts are extremely rigid, firm, and thick. Microscopic examination has revealed multiple organizing hematomas consistent with both recent and old hemorrhage[6].

Characteristic roentgenographic features of a soft tissue mass containing coarse calcifications, periosteal elevation, new bone formation in the configuration of bony "struts", and varying degrees of bone destruction are usually sufficiently distinctive to indicate the diagnosis[2].

Non-invasive imaging of these lesions by computerized tomography and sonography have proved useful in diagnosis and in planning treatment[6-9]. Early periosteal elevation resembles that of osteomyelitis, Ewing's sarcoma and metastatic neuroblastoma. Also, the osteolytic bone destruction which occurs resembles the lesions seen in primary bone sarcomas, tuberculosis, coccidioidomycosis, echinococcosis, aneurysmal bone cyst, giant cell tumor, plasmacytoma (myeloma) and metastatic neoplasms[2].

Hemophilic pseudotumors have been treated surgically, conservatively, and with radiation therapy. Prior to the availability of Factor VIII transfusions, surgical treatment was usually fatal[4]. Surgery appears to be the treatment of choice when

the lesions have been present for many years and non-surgical management is unsuccessful[4]. Needle or aspiration biopsies may result in chronic fistulous tracks and surgical scars that fail to heal, in addition to increasing the possibility of secondary infection[2]. Brant and Jordan[10], who believe that doses of 1000 to 2000 rads result in an endarteritis in an acutely bleeding hematoma, have noticed regression of the soft tissue mass in acute lesions. However, radiation was ineffective in the treatment of pseudotumors with longstanding bone changes that had been present for years[2]. Our patient refused hospitalization, and no specific surgical treatment was given.

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DIABETES MELLITUS, DIABETES INSIPIDUS, OPTIC ATROPHY AND DEAFNESS (DIDMOAD SYNDROME)*

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Summary: Saatçi Ü, Söylemezoğlu O, Özen S, Yordam N, Saatçi O. (Intensive Care Unit, Department of Pediatrics, Hacettepe University Institute of Child Health, Ankara, Turkey). Diabetes mellitus, diabetes insipidus, optic atrophy and deafness (DIDMOAD syndrome). Turk J Pediatr 32: 211-215, 1990

Two patients with diabetes mellitus (DM), diabetes insipidus (DI), optic atrophy (OA), deafness (D) and dilatation of the urinary tract-the so-called DIDMOAD syndrome are presented. In one of the patients, the presenting components were DI and OA. In the second case, DM was the first manifestation to be diagnosed, and in this patient the course of the syndrome was complicated by associated epileptical activity disorders, and later septicemia. The admission of these patients led us to review the literature describing this syndrome. *Key words: diabetes mellitus, diabetes insipidus, hydronephrosis, neuronal degeneration.*

In 1938, Wolfram[1] published a report from The Mayo Clinic describing the incidence of diabetes mellitus (DM) and optic atrophy (OA) in four siblings. Since then, the association of juvenile diabetes mellitus, diabetes insipidus (DI), optic atrophy and sensorineural deafness (D),known as DIDMOAD or Wolfram syndrome, has become more frequently recognized. DIDMOAD syndrome has a B autosomal recessive mode of inheritance[2,3], and, therefore, can be expected to occur more often in our country, where the rate of consanguinity is high. For this reason, more attention should be given to evaluating patients with DM or DI.

Hydronephrosis, hydroureter, and dilatation of the urinary bladder are often associated with DIDMOAD syndrome[3-5]. Since the onset is in childhood, and urinary tract dilatation is responsive to treatment, components of this syndrome should be searched for more often. This report describes two cases with DIDMOAD syndrome.

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Case Reports

Case 1

A 14-year-old boy, the seventh child in the family, was admitted to the Hacettepe University Children's Hospital with complaints of hyperglycemia and ketosis. The first-born child in the family, diagnosed as having DM type I, had died at the age of thirteen. The patient was the result of a normal delivery. He had had complaints of polyuria and polydypsia since he was nine years old. At the age of eleven, a diagnosis of diabetes mellitus was established, and he received desamino-D-arginyl vasopressin (DDAVP) in a dose of 5 μg b.i.d. by nasal insufflation. Examination of the fundi, at the time, revealed bilateral optic atrophy, however, no signs of retinopathy were noted. Ultrasonography demonstrated bilateral hydronephrosis and hydroureter. Renal function was normal and creatinine clearance 110 ml/min. On the patient's last admission, glycosuria associated with a fasting blood glucose of 400 mg/dl and ketosis were noted.

TABLE I: Clinical Presentation of the Patients

	Case No. 1	Case No. 2
Sex	M	F
Age (yrs)	14	11
Height (percentile)	5	5
Weight (percentile)	5	5
Age (yrs) at onset of		
Diabetes mellitus	14	7
Diabetes insipidus	11	11
Neurosensory hearing loss	14	11
Dilatation of urinary tract	Yes	Yes
Electroencephalogram	Normal	Subcortical instability and dysrrhythmia
Brain scan	Normal	Cortical atrophy and infarcts
Abnormal audiogram	Yes	Yes
Abnormal VER	Yes	Yes
Abnormal BAER	Yes	Yes
Family history of DM	Yes (Type I)	Yes (Type II)
Endogenous creatinine clearance	Normal	Impaired
Parental consanguinity	Distant	First cousins

The patient's condition was subsequently stabilized with the daily administration of a combination of 16 units NPH and 8 units crystalline insulin. Neurological examination was normal, except for the presence of optic atrophy.

An audiogram indicated bilateral sensorineural hearing loss. Skull x-rays, CT scan and electroencephalography were completely normal. Visual-Evoked Response (VER) and Brain Stem Auditory-Evoked Response (BAER) revealed bilateral optic atrophy and sensorineural deafness, respectively. Since polyuria and polydypsia were still present, the dose of DDAVP was increased to 10 μg/day.

Case 2

An 11-year-old girl, the first-born child of healthy parents who were first cousins, was admitted to the Hacettepe University Children's Hospital in a ketoacidotic state. The patient was the result of an uncomplicated delivery and had a normal early childhood. When evaluated at age seven, the diagnosis of DM was established, and insulin treatment was initiated. She complained of progressive visual and hearing deterioration in the last few months.

Physical examination on admission revealed a severely ill child in a ketoacidotic coma. The blood pressure was 110/60 mm Hg. She was severely dehydrated, had Kussmaul respiration, and was spastic with diminished deep tendon reflexes. Funduscopic examination showed bilateral optic atrophy but there was no evidence of diabetic retinopathy. In addition to hyperglycemia, ketonemia and metabolic acidosis, her renal function was impaired. Laboratory studies revealed a BUN of 108 mg/dl, serum creatinine 6.5 mg/dl, uric acid 10.6 mg/dl, calcium 7 mg/dl, and phosphate 7.4 mg/dl. Creatinine clearance was 20 ml/min/1.73 m^2. Ketonuria and 8-10 white blood cells per high magnification field were noted in the urine sediment with a specific gravity of 1001. The hemoglobin was 6.75 g/dl and the blood film revealed hypochromia. The white blood cell count was 31,000/mm^3, with 86% neutrophils. Urine osmolality was found to be 170 mOsm/kg H_2O and serum osmolality 300 mOsm/kg H_2O. Skull x-rays were normal. CT scan of the brain showed cortical atrophy and infarcts which were interpreted as diabetic angiitis. The electroencephalogram showed diffuse epileptiform activity and dysrrhythmia. VER and BAER revealed bilateral abnormal P response consistent with optic atrophy and sensorineural deafness, respectively

The patient was treated with intravenous insulin therapy, appropriate fluid and electrolyte solutions and antibiotic therapy for the urinary infection. Despite the antibiotic treatment, we were unable to control an overwhelming infection. Her clinical condition deteriorated and gross intestinal bleeding began. She died on the nineteenth day of admission, due to hypovolemic septic shock.

Discussion

DIDMOAD syndrome has become an entity which is frequently observed in diabetic patients. Besides the four main features associated with this syndrome, namely, diabetes insipidus (DI), diabetes mellitus (DM), optic atrophy (OA) and sensorineural deafness (D), various other disorders including ataxia, neurogenic bladder, epilepsy, infantilism, retinal pigmentation, congenital heart disease, myocarditis, cataract and obesity have also been noted[6].

Many patients have been reported to have OA prior to the onset of DM which supports the primary nature of optic involvement. In fact, primary optic atrophy without retinitis pigmentosa may be regarded as a specific sign of the syndrome, and deserves special attention. In our patients, progressive OA without retinitis pigmentosa was one of the main features but diabetic retinopathy was not present.

The occurrence of hydronephrosis, hydroureter, and an enlarged bladder has been previously described in this syndrome[3,7-9]. Minimal signs of peripheral neuropathy and an absence of obstruction are factors usually attributed to DI [9]. Hydronephrosis and hydroureter are well known complications of DI. In the series reported by Balci et al[7,8], one patient had both hydronephrosis and hydroureter, which were detected years after the onset of DI. Although renal function in DI is well maintained, it has been shown that it may eventually become impaired. As described in the literature, endogenous creatinine clearance has been found to be decreased in some cases, as in our second patient[5].

HLA-typing studies have been carried out on patients with DIDMOAD syndrome to see if any similarities exist between this syndrome and insulin-dependent diabetes mellitus. The results and the absence of islet cell antibodies suggest that the pathogenesis of DM in DIDMOAD syndrome is different[10].

Cremers et al[5] reported deafness in 39 of the 88 patients reviewed in the literature up to 1977. The audiograms of our patients revealed bilateral sensorineural deafness, and BAER confirmed the results. So far, the reports do not clearly indicate the involvement of afferent fibers from the middle and upper cochlear coils[3].

In 1976, Gunn et al[11] described another four patients with DM, OA, DI and sensory nerve deafness. They suggested that this clinical syndrome might be systemic degeneration involving the optic nerve, supraoptic and paraventricular nuclei and the eighth cranial nerve, and that the association of DM could be through the APUD cell series.

On the other hand, clinical and necropsy studies give good evidence of a specific neuronal degeneration as the pathogenesis of DI, OA and deafness. There are also some reports which suggest a direct neuronal degenerative process in the

pathogenesis of the dilatation of the urinary tract. The correlation of DM with these proposals and the explanation of the etiology of this entity remain obscure. New cases, however, might serve to shed light on the pathogenesis of this syndrome.

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CEREBELLAR INFARCTION: COMPUTED TOMOGRAPHY, MAGNETIC RESONANCE AND IMP – SINGLE PHOTON EMISSION TOMOGRAPHY FINDINGS*

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Summary: Caner B, Caner H, Toyoma T, Ishii Y. (Department of Nuclear Medicine, Hacettepe University Faculty of Medicine, Ankara, Turkey). Cerebellar infarction: computed tomography, magnetic resonance and imp-single proton emission tomography findings. Turk J Pediatr 32: 217-224, 1990

In this report, a rare case of a child with cerebellar infarction (CI) confirmed by vertebral angiography, magnetic resonance imaging (MRI), computed tomography (CT) and N-isopropyl-p^{123}-I-iodoamphetamine single photon emission tomography (IMP-SPECT) is presented. It was concluded that although all imaging modalities could demonstrate CI, MRI is superior to the other methods because of its fine display of anatomical detail, its lack of bony artifacts and its ability to show infarction in early stages. *Key words: cerebellar infarction, magnetic resonance, N-isopropyl-p-^{123}I-iodoamphetamine (IMP-SPECT), computed tomography (CT).*

Cerebellar infarction is often difficult to diagnose clinically. Moreover, isolated cerebellar infarction is rarely seen in children[1]. This report describes a child with cerebellar infarction proved angiographically. We correlated the findings obtained from computed tomography (CT), magnetic resonance imaging (MRI) and N-isopropyl-p-^{123}I-iodoamphetamine single photon emission tomography (IMP-SPECT).

Case Report

An eight-year-old boy suddenly developed dizziness, aggravated by movement, nausea, vomiting and difficulty in talking. He had unremarkable family and past histories. Because his symptoms persisted without any improvement, he was referred to the Fukui University Hospital. Examination revealed that the patient was uncomfortable from persistent dizziness. He had pallor but was alert and oriented. His speech was slightly slurred. The blood pressure was 110/68 mm Hg,

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and the pulse rate was 84 beats/min and regular. The visual fields were intact and the pupils were of the same size and reactive. The extraocular movements were normal. There was no pathological reflex. Cerebellar tests were slightly poor, mostly on the left side. Blood chemistry results including an analysis of serum immunoglobulin, ASO and CRP were all within the normal range.

The patient had a CT scan evaluation on the second day of admission, which revealed two focal low intensity lesions of the cerebellum without hydrocephalus (Fig 1). Magnetic resonance (MR) scanning was performed on the seventh day using a Yokogawa Medical 0.35T superconducting system. T1 and T2-weighted images were obtained with a spin-echo pulse sequence. T2-weighted images showed abnormally bright signal intensity involving the territories of the left posterior cerebellar arteries (PICA) and left and right superior cerebellar arteries

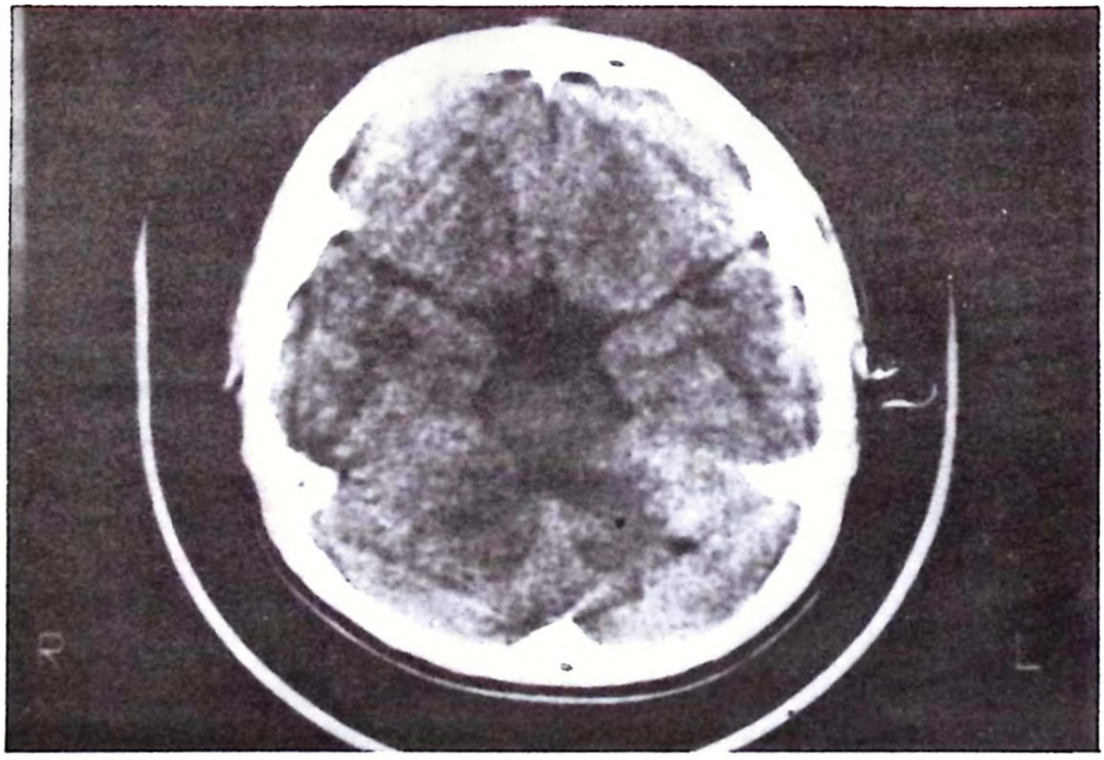
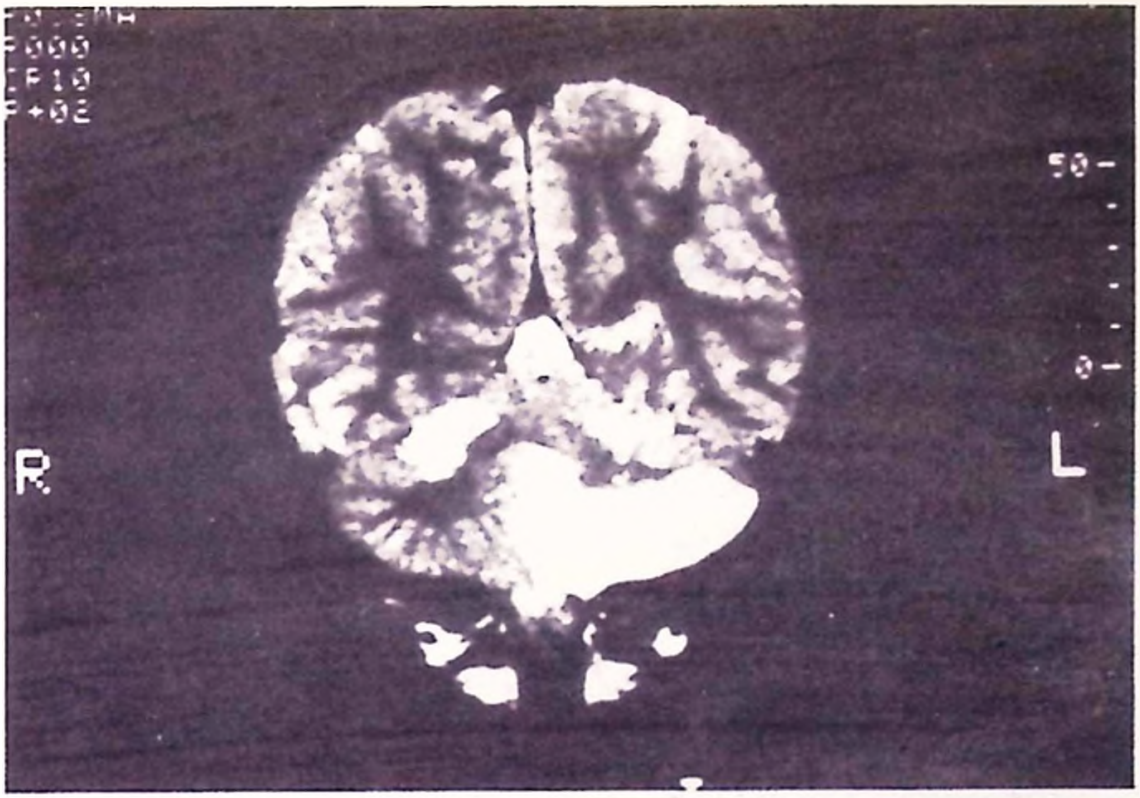
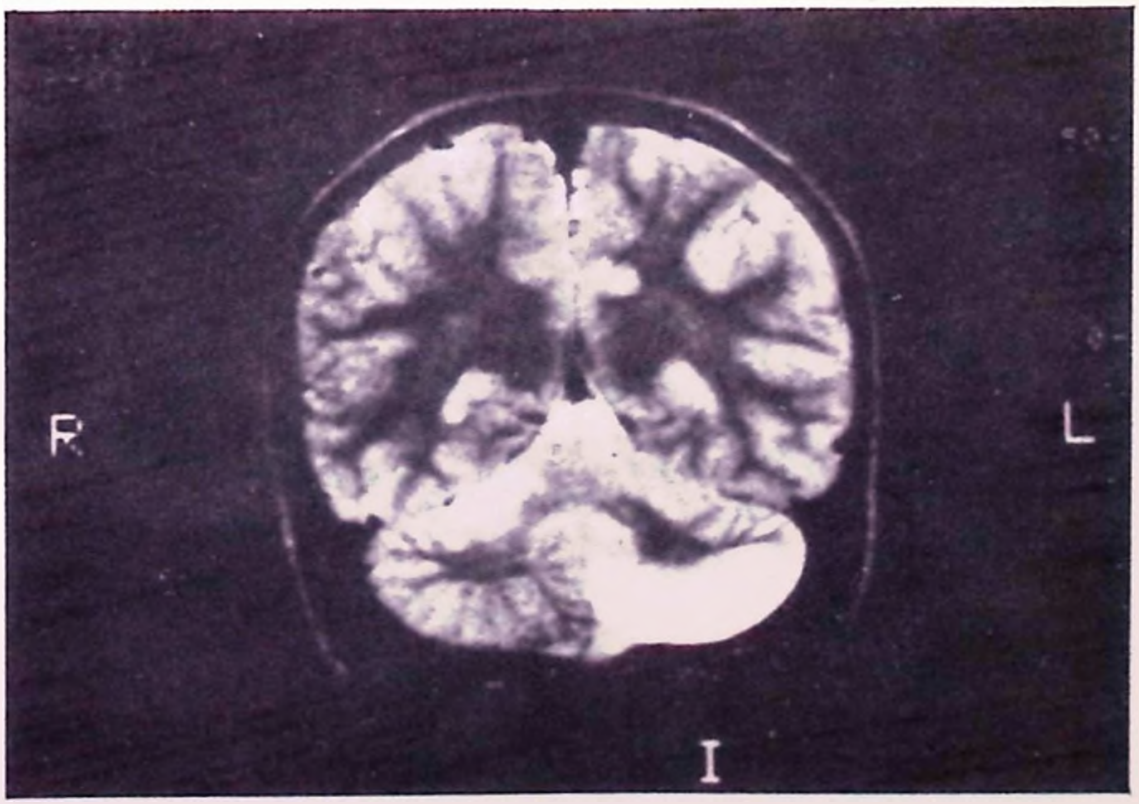


Fig. 1: CT demonstrates ill-defined areas of low density in both cerebellar hemispheres.

(SCA) (Fig 2a). Four days following the MR study, the patient underwent IMP-SPECT study. N-Isopropyl-p-^{123}I-iodoamphetamine (IMP) was obtained from Nihon-Medi Physics (Japan). 3 mCi IMP was injected i.v and SPECT images were obtained using a low energy parallel hole collimator (General Electric Model; 400AC Starcam, USA) at 30 min postinjection. A total 60 frames were recorded (30 sec/each). In this study, the left cerebellum could not be visualized, and



a



b

Fig. 2(a): T2-weighted coronal MR image showing high intensity areas involving the territory of left PICA, right SCA and left SCA. (b): Follow-up study revealed that high intensity areas were smaller compared to the previous study.

decreased activity of the right cerebellum was noticed (Fig 3a). Vertebral angiography performed on the eleventh day revealed that the left SCA and posterior cerebral artery were spastic and that the left PICA and right SCA were

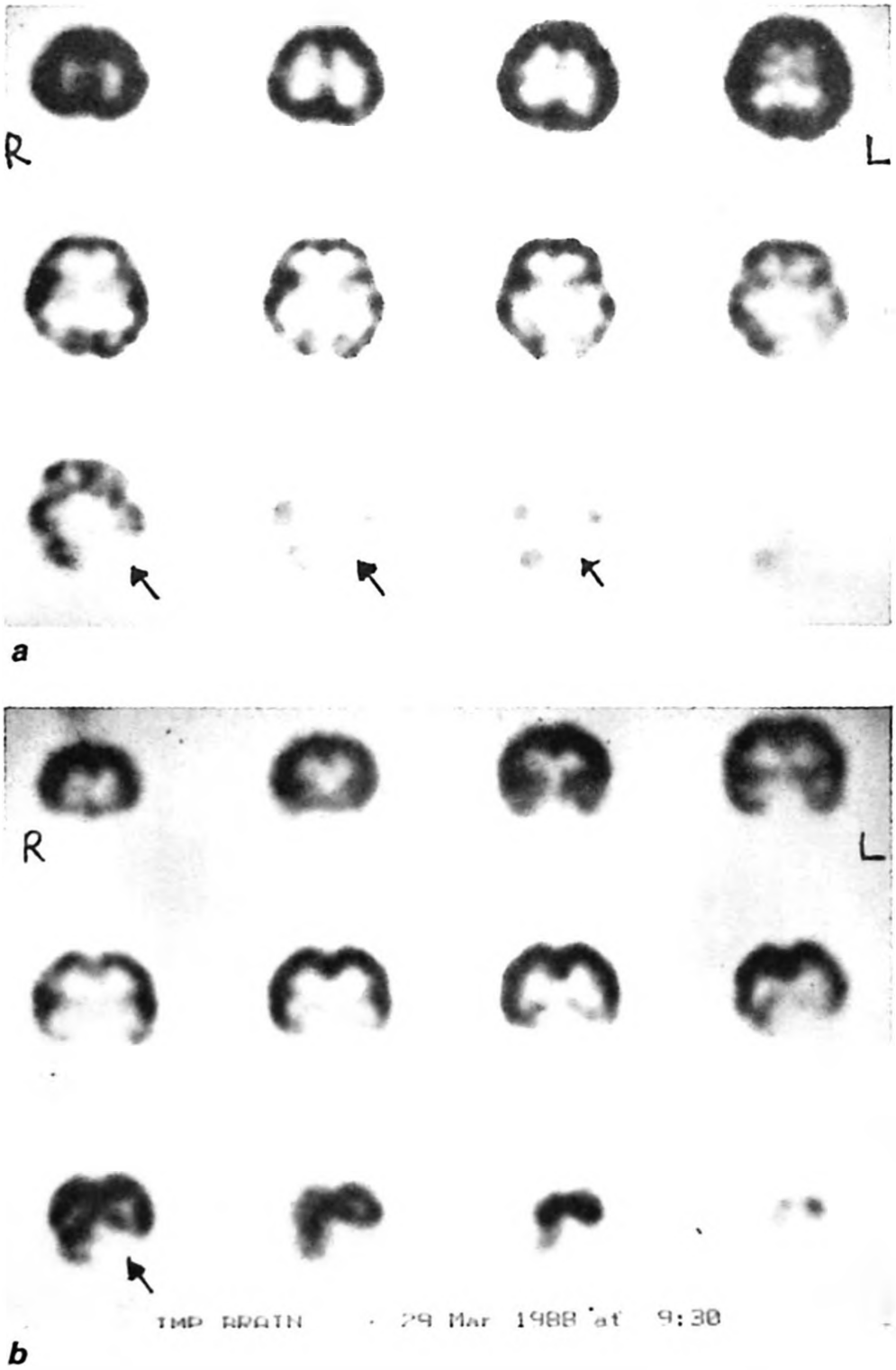
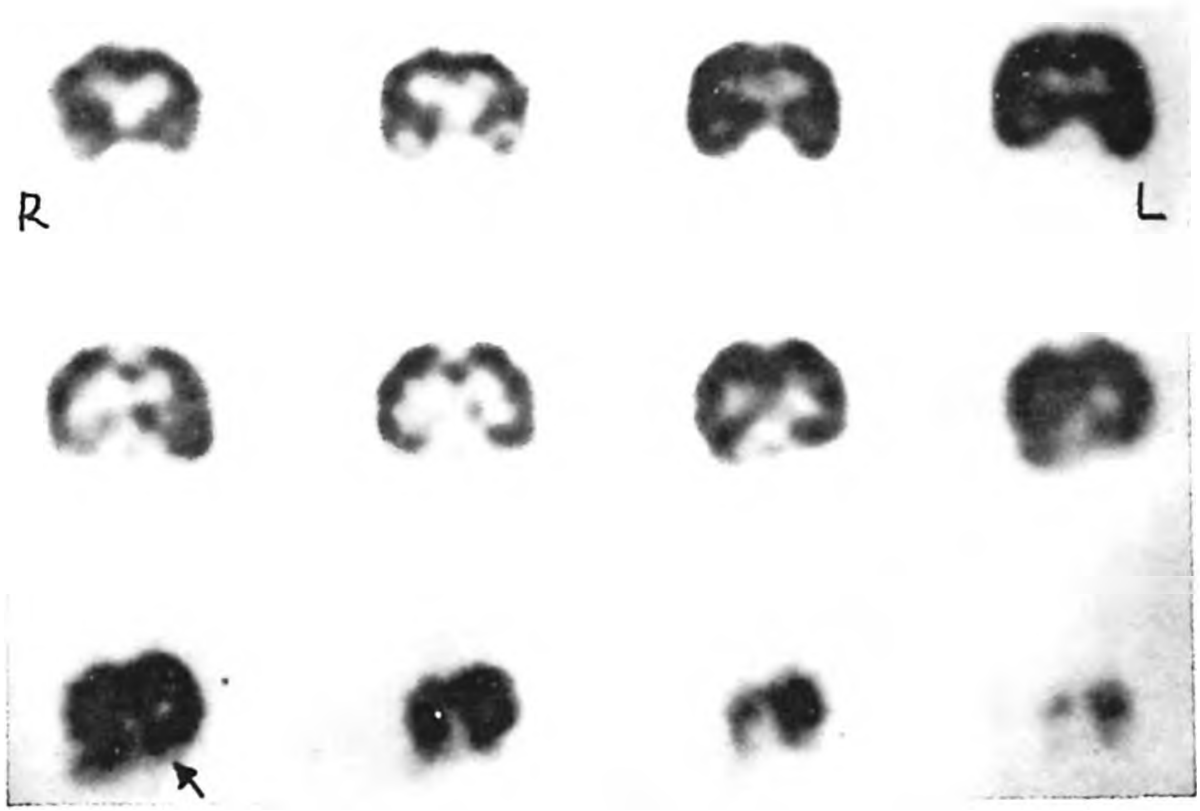


Fig. 3(a): Transaxial and coronal IMP-SPECT images. Note nonvisualization of the left cerebellum and faint visualization of the right cerebellum (arrows). (b): Follow-up study. The left cerebellar hemisphere is faintly visible (arrows).



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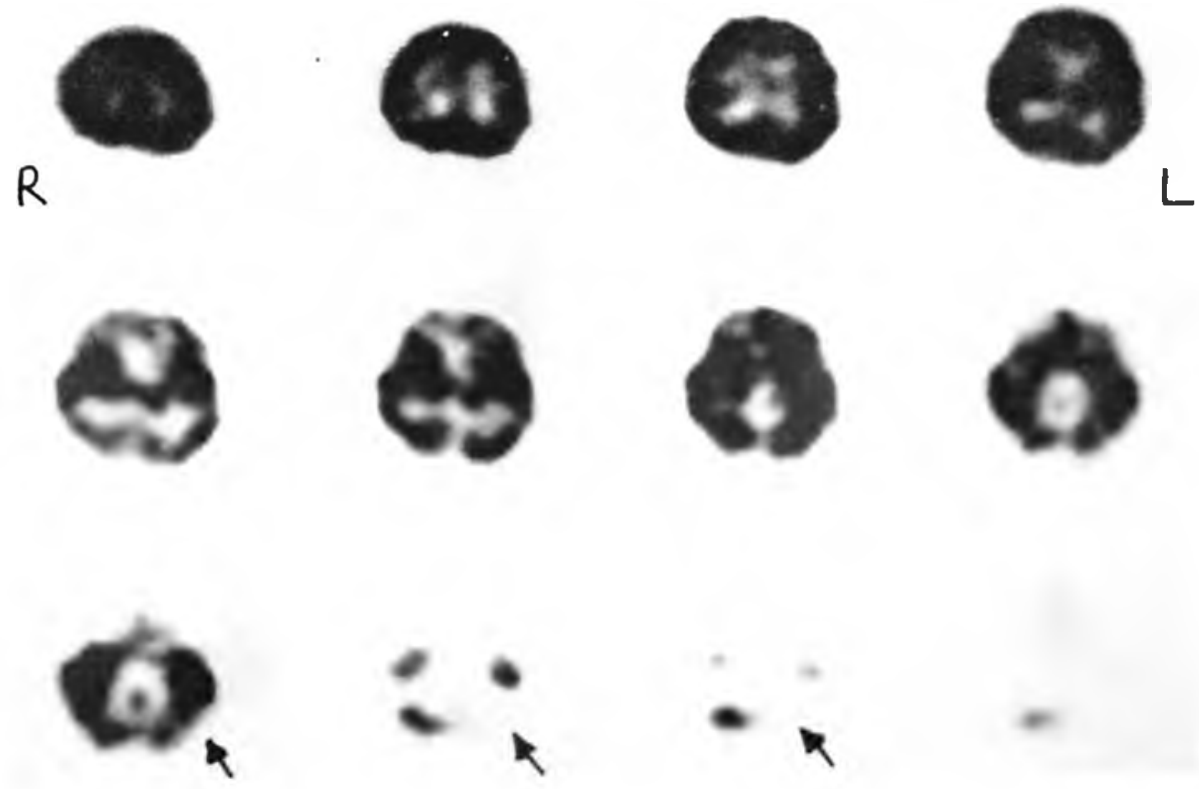

occluded (Fig 4a). There was no remarkable change either in clinical status or upon neurologic examination during the time interval of the tests. The second IMP-SPECT taken on the thirty-sixth day revealed that the defective area in the right cerebellar hemisphere had become smaller and that the left hemisphere could be visualized very faintly compared to the previous study (Fig 3b). The second MR scan taken on the thirty-eighth day showed that the high intensity areas seen on both cerebellar hemispheres had become smaller (Fig 2b). At the follow-up vertebral angiography performed on the fortieth day, the left PICA could not be visualized, there were no abnormalities of the left SCA, left posterior cerebral artery or right SCA (Fig 4b). On the forth week of admission, the patients's clinical status showed moderate improvement, and he was discharged with mild residual slurred speech on the 45th day of admission.

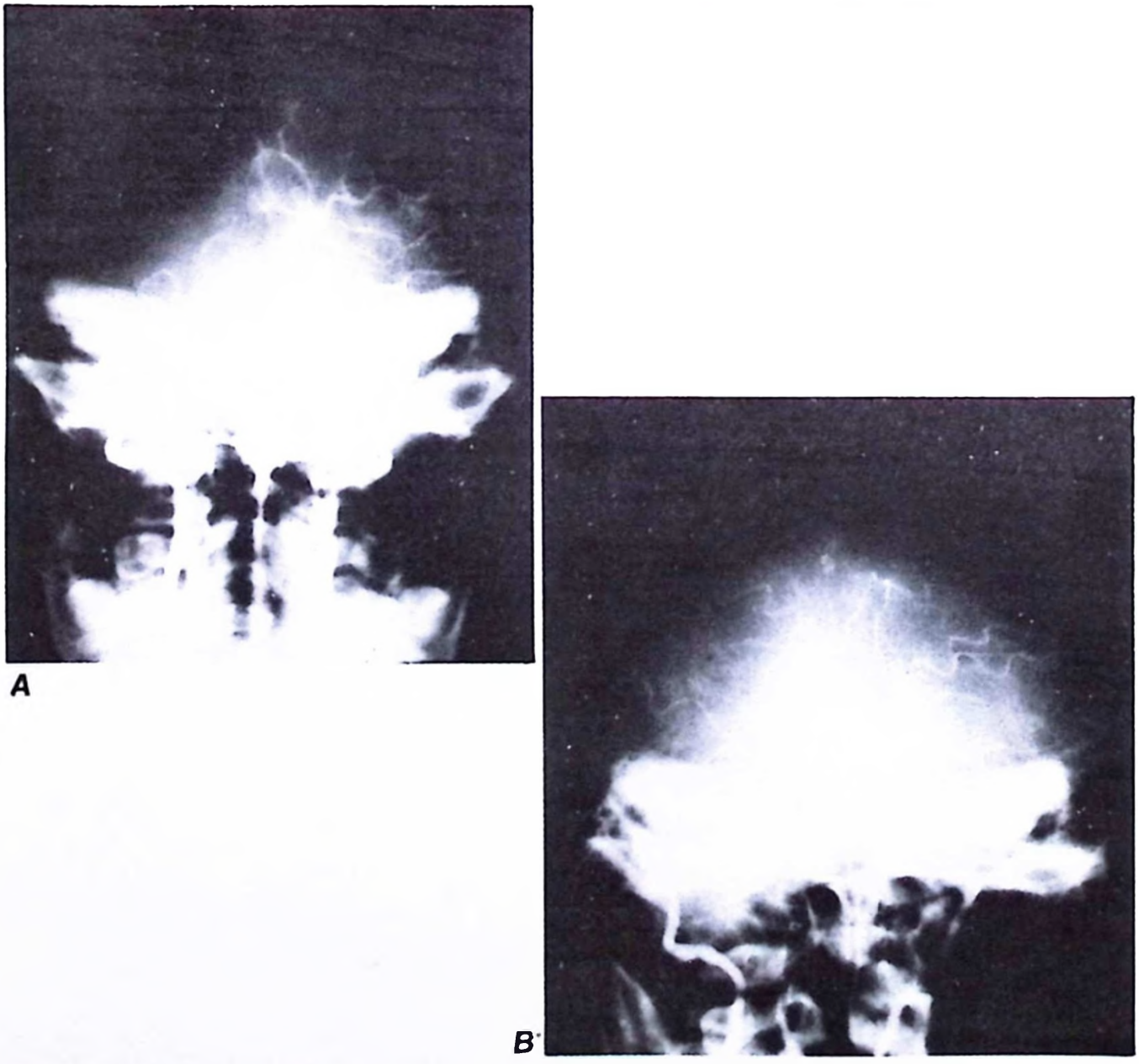

Fig. 4(a, b): First and follow-up vertebral angiographies of the patient. See text for explanation.

Discussion

Isolated cerebellar infarction is a rare occurrence not only in childhood but also in adulthood. The clinical features of cerebellar infarction cover a wide spectrum, mimicking symptoms and signs from acute labyrinthitis to a rapidly expanding posterior fossa mass lesion with brain stem and cerebral dysfunction[2,3]. It has been concluded in various studies that cerebellar infarction is uncommon, but the true incidence is not known[4,5]. In children, acute cerebellar ataxia, acute labyrinthitis and drug intoxication may result in the onset of acute cerebellar signs and symptoms[6,7]. In a number of previous reports, trauma to the vertebral artery and chiropractic manipulations have been implicated in this condition[8,9].

The diagnosis of cerebellar infarction had a poor prognosis in the pre-CT scan era, and postmortem studies show that the diagnosis was often overlooked. The introduction of CT has made it possible to rapidly distinguish cerebellar infarction from hemorrhage[10]. But it has been reported that the correlation between angiographic and CT localization of the infarction is not good, and that CT has limited resolution in the posterior fossa because of the presence of bony artifacts[11]. Moreover, CT is often normal in the first 48 hours after an ischemic infarction even with high resolution scanners[12]. In our case, low density areas were noticed in both cerebellar hemispheres. Since MRI has no bony artifacts and infarctions can be visualized earlier, information obtained by MRI is superior to that of CT[13-15]. In our case, the high intensity areas on the cerebellar hemispheres were more on the left side, indicating that the cerebellar infarction was clearly detected. Information obtained by MRI regarding the extent and localization of the lesion was much better than that obtained by CT. With the introduction of IMP-SPECT, it has become possible to evaluate brain perfusion noninvasively[16]. Single photon scanning with intravenously administered I-123 amines or ^{99m}Tc labelled amines such as ^{99m}Tc-HMPAO is innocuous to the patient, requires a low level of cooperation and can be performed by nuclear medicine personnel familiar with SPECT. To our knowledge, no significant morbidity has been reported with IMP-SPECT. The distribution of IMP mainly reflects the regional cerebral and cerebellar blood flow on the images taken immediately postinjection. Decreased tracer accumulation indicates the presence of ischemia. In the present case, perfusion defects were clearly demonstrated by IMP-SPECT, with anatomic information inferior to that of MRI. Follow-up study of IMP-SPECT revealed that perfusion to the involved areas was better than in the previous study, supporting the follow-up angiographic data. The second MRI successfully demonstrated that the high intensity areas became smaller, indicating either a resolving of vasospasm, edema and/or recanalization of some occluded vessels. Angiography is a classical imaging modality which evaluates a cerebellar infarction, but it may not show the exact location of the cerebellar infarction because the distribution of

vascular territories in the cerebellum is quite variable. Moreover, infarcts may involve only some part of a vascular territory, but fortunately clinical history, CT, IMP-SPECT and MR follow-up studies always help in establishing the correct diagnosis.

In conclusion, MRI is the method of choice for evaluating cerebellar infarction, but it is not routinely available. Moreover, patients with resuscitation devices cannot undergo MR evaluation. Although anatomic information obtained by IMP-SPECT is inferior to that of MRI, it can demonstrate perfusion abnormalities of the cerebellum and is valuable in its follow-up.

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15 January 1990

To the Editor,

I feel the need to bring to your attention an explanation concerning the article by Durak et al., entitled "A Case of Parathyroid Adenoma With Brown Tumors Diagnosed by ^{20}Thallium-^{99m}Technetium Subtraction Scintigraphy" *(Turk J Pediatr* 31:151, 1989). In this paper, a 15-year-old girl with primary hyperparathyroidism due to a parathyroid adenoma, who was reported to have been diagnosed and treated at Hacettepe University Faculty of Medicine, was presented. From this case report, as far as we could understand, the main topic was the successful use of scintigraphy in confirming the definitive diagnosis, localizing the parathyroid adenoma and the detection of Brown tumor by ^{201}Thallium uptake.

In fact, the patient (A.G., N.205850) was admitted to our clinic with complaints of fatigue and a swollen chin. The diagnosis of hyperparathyroidism was first suspected after the microscopic examination of the bone biopsy at our pathology department. Then, the patient was sent to the Hacettepe University Faculty of Medicine for parathyroid scintigraphy. The scintigraphic findings of the case were reported to be compatible with an ectopic parathyroid; but this finding was actually the result of thallium accumulation in the biopsy-diagnosed Brown tumor located at the right corpus of the mandible, as the primary lesion was due to an adenoma of the ectopic parathyroid gland.

On March 16, 1988, the patient was operated on, and a tumoral mass was found underneath the inferior pole of the right thyroid lobe between the trachea and esophagus. The other parathyroids were observed to be normal. Postoperatively, the inevitable complication, hypocalcemia, occurred which was managed by the administration of calcium gluconate, calcium lactate and vitamin D. The clinical symptoms and the bone lesions improved[2] dramatically following this regimen. The patient is still being followed by us.

To summarize: a. the diagnosis and the treatment of the patient, except for the scintigraphy, was carried out at Gazi University Faculty of Medicine.

b. Moreover, the diagnosis of Brown tumor was essentially established by bone biopsy before the scintigraphic study, and parathyroid adenoma was diagnosed by pathological examination of the surgical specimen. Therefore, we want to stress the conflict between the title and the content of this article.

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A reply to the above letter follows:

19 March 1990

To the Editor,

The patient described in the article, "A Case of Parathyroid Adenoma With Brown Tumors Diagnosed by ^{201}Thallium-^{99m}Technetium Subtraction Scintigraphy" was referred by the Department of Pediatrics of the Gazi University Faculty of Medicine to the Department of Nuclear Medicine of the Hacettepe University Faculty of Medicine with an epicrisis, and was admitted as an outpatient to be evaluated by parathyroid scintigraphy. There is no mention in our text about the treatment of the patient.

According to the epicrisis, it was also requested that a search be made for ectopic parathyroid tissue. ^{201}Thallium-^{99m}Technetium Subtraction Scintigraphy (TTSS) was performed immediately, and a focal area of ^{201}Thallium (^{201}Tl) accumulation was found below the inferior pole of the right thyroid lobe. This area was described in the beginning of the report, which was sent to the clinic. As stated in the letter dated January 15,1990, the surgeon found the adenoma to be at exactly the same site as we had described.

There were also multiple sites of ^{201}Tl accumulation in the bones which were proven to be Brown tumors by biopsy. After a review of the literature on nuclear medicine, it appeared that the accumulation of ^{201}Tl in Brown tumors had not been reported up to that date (March, 1988). In other words, this finding was probably the first in the literature. But, in light of the epicrisis, it was also found necessary to inform the clinic about the possibility of an ectopic focus at the right half of the corpus mandibulae.

The originality of the finding relating to nuclear medicine was verbally conveyed to the patient's clinic but, the proposal of a collaborated publication of the case was not accepted. This refusal has ended the contact between the departments. Therefore, we were not able to inform the attending physician of the retrospective evaluation of the lesion on the mandibulae as a Brown tumor, and neither could we obtain further information on the patient's laboratory or clinical data. A year later, the same misinterpretation of a Brown tumor located at the sternum as an ectopic focus was published by Yang C J et al. in the *Journal of Nuclear Medicine* (30:1264,1989), and thus we missed the opportunity of publishing it earlier.

Returning to 1988, we decided to publish our own finding, emphazising only the nuclear medicine aspects, without any clinical concern. The originality of this report was only based on the ^{201}Tl uptake by Brown tumor, because TTSS in the detection of parathyroid adenoma is a well known procedure in clinical nuclear medicine.

Our department finds it appropriate to publish an original finding retrospectively, if it is not published by any other department after a certain time interval, for the benefit of those in the medical profession.

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ANNOUNCEMENTS

MEETINGS

ROME, 30 SEPTEMBER - 4 OCTOBER 1990

THE EUROPEAN SOCIETY OF PEDIATRIC NEPHROLOGY CONGRESS (ESPN '90)

Inquiries to : Progress
Promozione Congressi S.r.1.
Via Carlo Conti Rossini, 58
00147 ROME, ITALY

ROME, 1 OCTOBER 1990

THE EUROPEAN SOCIETY FOR PEDIATRIC HEMATOLOGY AND IMMUNOLOGY (ESPHI) CYTOKINES IN HEMATOLOGY, IMMUNOLOGY AND ONCOLOGY SATELLITE MEETING IN CONJUNCTION WITH THE ANNUAL SIOP MEETING

Inquiries to : Secretariat
Prof. G. Prindull
Universitäta Kinderklinik
Robert Koch Str. 40
3400 Göttingen
GERMANY

ROME, 2 - 5 OCTOBER 1990

XXIInd MEETING OF THE INTERNATIONAL SOCIETY OF PAEDIATRIC ONCOLOGY (SIOP)

Inquiries to : Organizing Secretariat
Progressi in Medicina S.r.l.
Via Bartolomeo Gosio 102-00191
ROME, ITALY

CARTAGENA, 3 - 7 OCTOBER 1990

THE COLOMBIAN PEDIATRIC SOCIETY AND THE AMERICAN ACADEMY OF PEDIATRICS PAN AMERICAN AND LATIN CONGRESS OF PEDIATRICS (ALAPE),

Inquiries to : Prof. Ernesto Plata Rueda
World Trade Center
Carrera 8 A, No.99.51 OF.207
6005 BOGOTA 8, COLOMBIA

CHIBA, JAPAN, 4 - 10 NOVEMBER 1990

THE JOINT CONVENTION OF THE 5th INTERNATIONAL CHILD NEUROLOGY CONGRESS AMD THE 3rd ASIAN AND OCEANIAN CONGRESS OF CHILD NEUROLOGY

Inquiries to : Secretariat of the Joint Convention of the 5th
and 3rd AOCCN
c / o Simul International Inc,
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Akasaka 1 - chome, Minato-ku
TOKYO 107, JAPAN

TOKYO, 4 - 10 NOVEMBER 1990

THE 3rd ASIAN AND OCEANIAN CONGRESS OF CHILD NEUROLOGY

Inquiries to : Dr. Yukio Fukuyama
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Kowa Bldg. No.9,8 - 10
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TOKYO 107, JAPAN

MONTREUX, 3 - 6 JULY 1991

FIFTH CONGRESS OF THE INTERNATIONAL ASSOCIATION FOR ADOLESCENT HEALTH

Inquiries to : IAAH Cinquieme Congres
Office du tourisme
Case Postale 97
CH - 1820 MONTRUEX, SWITZERLAND

JERUSALEM, 30 AUGUST - 4 SEPTEMBER 1992

IX CONGRESS OF THE INTERNATIONAL PEDIATRIC NEPHROLOGY ASSOCIATION

Inquiries to : Secretariat
IX Congress of the International Pediatric Nephrology Association
P.O. Box 50006
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