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# Familial Corpus Callosum Agenesis*

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Congenital agenesis of corpus callosum was first described by Reil[1] in 1912. Several cases with normal physical and mental development were also reported in the literature.[2-4]

This anomaly can be seen in complete or partial forms. Most of the reports are on isolated cases. Familial occurence is rare and there were only five familes reported until 1973. This paper reports three siblings in the same family with this rare anomaly. It is also the first family ever published in Turkey.

**Case Histories:** The patients were the 3rd, 4th and 5th siblings of consanguinous parents. Case I, a 6 year old male was admitted to Hacettepe Children's Hospital with the chief complaints of inability to hold his head, to sit up, to walk and to see. He was third child of the family and was born after an uneventful and full term pregnancy. Delivery was normal and spontaneous. He had developed jaundice on the fifth day of life which lasted for 40 days. The parents were second cousins. Their first child, a son, had similar symptoms and died due to an infectious disease when he was 4 years old. The 2nd sibling who was also a male, was reported healthy. Family history was also negative (Figure 1).

The parents noticed that the child had developed some stiffness on the extremities when he was three months old. At later stages he was different from other children and was retarded mentally and motorwise. He also had generalised seizures occasionally.

Physical examination of the patient revealed his weight to be 9.8 kg, height 82 cm, head circumference, 46 cms, and chest circumference was 44 cm. He was uninterested in his surroundings; his extremities were spastic and he had clenched fists and crossed legs. He also had mild hypertelorism (Figure 2).

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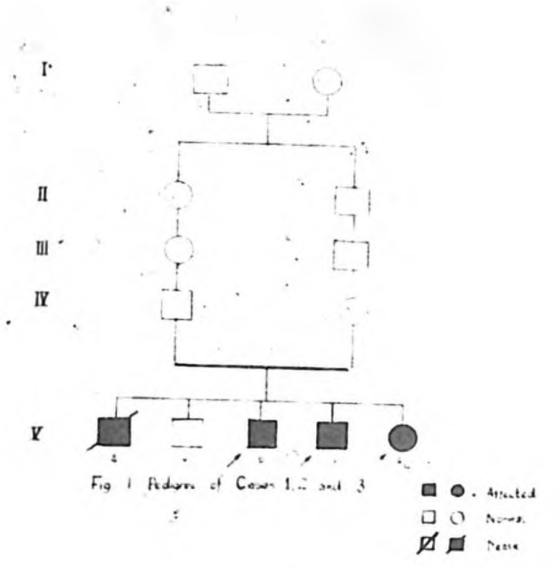


**Figure 1**

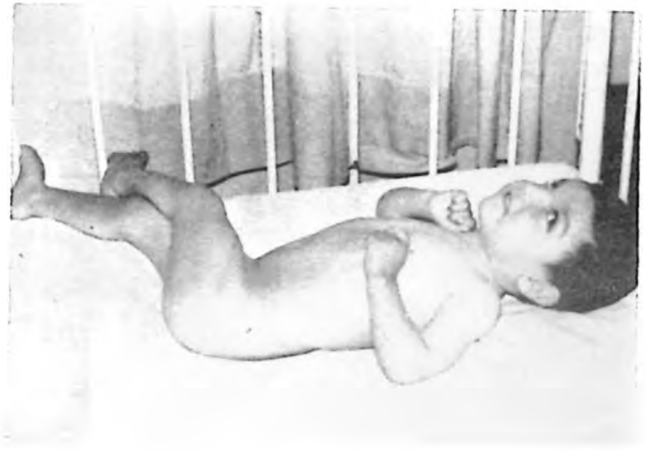

**Figure 2**

Eye ground examination showed bilateral primary optic atrophy and fine retinal pigmentation was observed. There was neither visual nor auditory response. DTR were bilaterally hyperactive on four extremities. No pathological reflexes were elicited. He had a hyperthrophic right index finger and bilateral hip dislocation (Figure 3). There were also undescended testises. The rest of the systems were within normal limits.

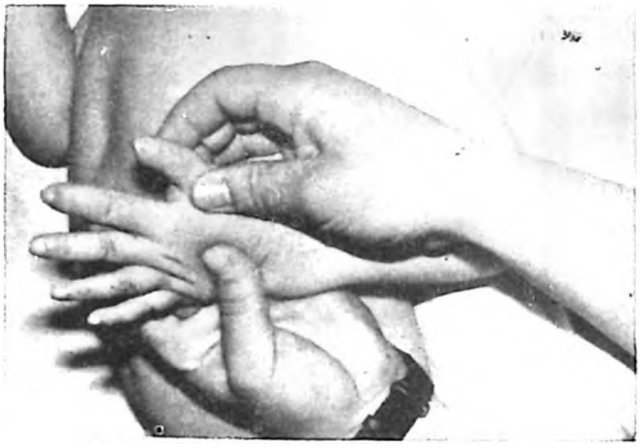

**Figure 3**

Laboratory data showed normal hemogram and urinalysis. Total lipids were 840 mg/dl, cholesterol 192 mg/dl, Ca 9.3 mg/dl, P 4.5 mg/dl alkaline phosphatase 6 BU, and CSF protein 24 mg/dl. Urinary and serum amino acids and mucopolysaccaride levels were normal. There was no metachromatic material in the urine. Some metachromatic lipid particles at the sural nerve biopsy could not be evaluated properly. Brain biopsy material was unsatisfactory. The chromosome analysis was normal for male (46, XY). Bone age was at the two years level. EEG showed generalized disturbance and an active centroencephalic myoclonic epileptiform activity. Pneumoencephalogram showed enlargement of the lateral ventricles, widening of the interventricular space and upward displacement and enlargement of third ventricle. There was also bilateral cortical atrophy. These findings were interpretted as positive signs of the agenesis of Corpus Callosum (Figure 4, 5).

Case II. The male sibling of the first case was admitted when he was 4 years old. He also had developed some spasticity of his extremities after three months of age. He was unable to hold his head and to sit up and he had no vision on admission (Figure 6).

Physical examination showed his weight to be 7.2 kg, height 72 cm, head circumference 44.5 cm and the chest circumference 46 cm. He was uninterested in his surroundings, had a generalized spasticity and was not able to hold his head. He also had bilateral primary optic atrophy but no retinal pigmentation. He had a normal facial appearance. DTR were hyperactive bilaterally and there were no pathological reflexes. The rest of the examination was normal.

**Figure 4**

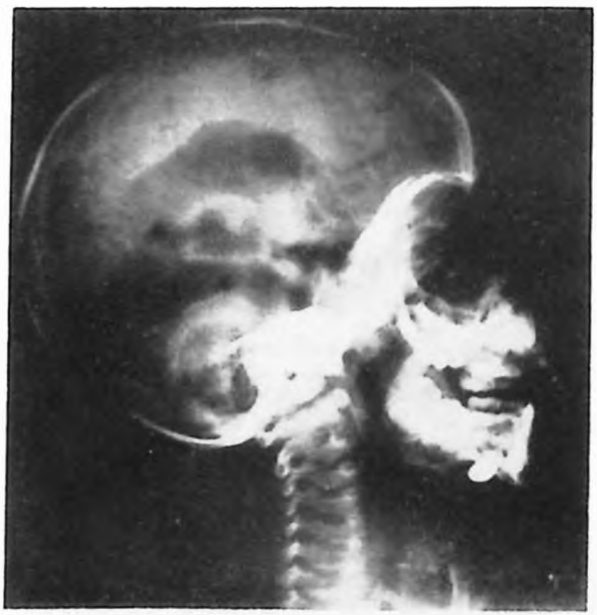

**Figure 5**

Laboratory data showed normal hemogram and urinalysis. Biochemical tests results were within normal limits as with the first sibling.

There was no metachromatic material in the urine. Sural nerve biopsy was not specific. EEG showed generalized slow wave activity and unlocalized spikes.

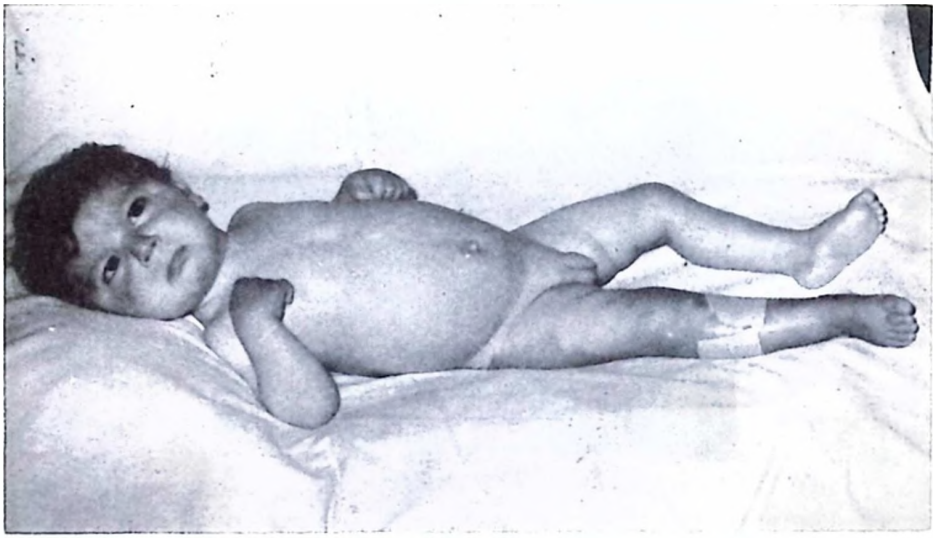

**Figure 6**

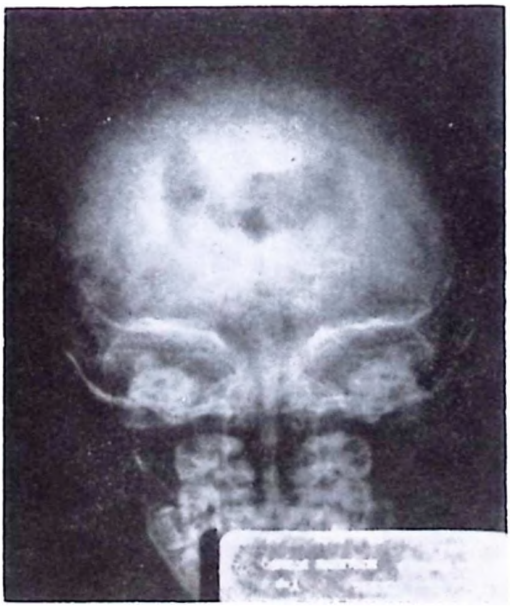

**Figure 7**

Pneumoencephalogram showed widening of the lateral ventricles, upward displacement and enlargement of the third ventricle. There was an increased amount of air in the basal cisterns and sulcis (Figure 7).

Case III. The youngest sibling of the family was brought to the hospital when she was 4 months old for a routine checkup. Pregnancy with this child was normal and the delivery was uneventful. Physical examination showed her weight to be 6.3 kg, height 56 cm, head circumference, 40 cm and the chest circumference 41 cm. Her anterior fontanel was normal and she had no head control. She had bilateral horizontal nystamus and primary optic atrophy. There were no retinal pigmentation. She also had a generalized spasticity and hyperactive DTR (Figure 8).

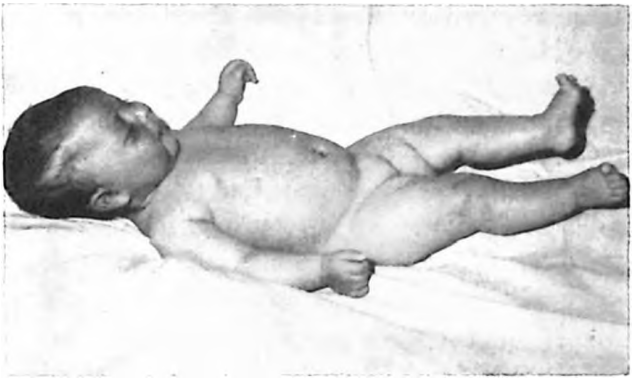

**Figure 8**

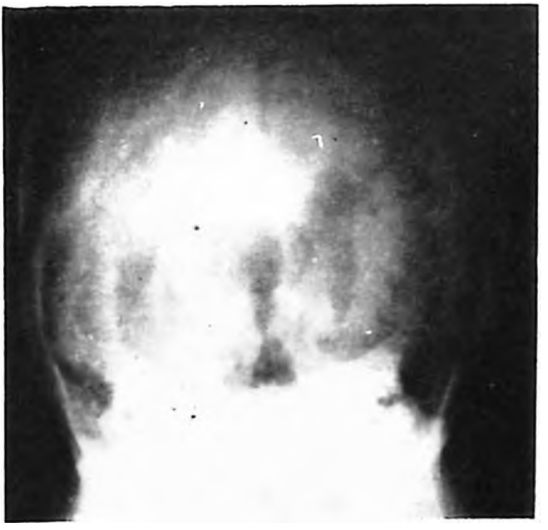

**Figure 9**

Laboratory data was normal for hemogram and urinalysis. Her biochemical and amino acid investigations were also normal. EEG showed generalized dysrythmia and some localized disturbance in the left posterior regions.

Pneumoencephaglogram was also compatible with the findings of the agenesis of Corpus Callosum (Figure 9). No biopsy was obtained from the sural nerve of this patient.

*Discussion*

Most of the cases of this anomaly were published as sporadic cases, rarely as familial cases. All these cases were proved by pneumoencephalogram or by post mortem investigation.[2, 5, 11-14]

Our patients showed similar signs. Their history of pregnancy and delivery was normal. The first two cases had obvious physical and mental retardation, microcephaly and severe spasticity. The youngest patient was only four months old on admission. She also had some spasticity and was not able to hold her head. All three cases had primary optic atrophy and visual defects. The first case had retinal pigmentation whereas the others did not. Seizures were seen only in the first patient.

Previous reports did not reveal specific typical clinical signs for these patients.[1, 5] Some authors claim that the associated abnormalities were the cause of clinical signs and symptoms.[1, 4, 5] But our patients showed most of these signs together. Some of these cases have associated with chromosomal aberrations such as trisomy D, E and translocation on group B cases.[15-17] Our patients had normal caryotypes. The etiology of this anomaly is still unknown.[5, 11, 18]

Familial cases were first reported in 1952 by Zellweger.[6] He diagnosed this condition on two brothers and reported a third male sibling in 1958 by Ziegler.[9] These three brothers had intractible convulsive seizures during infancy. Two of them underwent pathological examination and agenesis of Corpus Callosum CCA and hydrocephaly were reported. Two sisters with severe mental and physical retardation and agenesis of Corpus Callosum were reported by Naiman and Fraser,[7] in 1955, after pneumoencephalographic investigations. Menkes[8] descirbed a family with five male cases of CCA and claimed that they showed a sex-linked inheritance. Two of these cases were brothers and had severe mental retardation and convulsions. The post-mortem investigation showed increased lipid content of the brain tissue especially in the fractions of cholesterol and cerebroside. Shapira and his colleaques[10] reported two sisters with CCA and mental retardation and convulsions.

Most of these cases are males. But sporadic occurence in females gives an impression that the mode of inheritence is autosomal and recessive.

### *Conclusion*

All the cases with physical, mental and motor retardation convulsions, primary optic atrophy and positive family history must force us to think of the possibility of agenesis of Corpus Callosum and other congenital CNS malformations. Air studies are still the best investigations method to reveal the anomalies. Further investigations such as electromicroscopy and histopathological methods may reveal some uncovered information about these cases.

### *Summary*

Three siblings with agenesis of Corpus Callosum were described. Their chief complaints were motor weakness, mental retardation and spasticity which were more obvious after three months of age. Physical examination showed primary optic atrophy, increased muscle tones, spasticity, and mental and motor retardation. Pneumoencephalograms showed increased ventricular size, widening of the interventricular space and cortical atrophy. EEG's were disturbed generally. An autosomal recessive type of inheritence was accepted as the mode of inheritance.

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