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AICARDI SYNDROME*

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Aicardi syndrome was first reported in 1965 by Aicardi, Lefebvre and Lerique-Koechlin[1] in a brief paper entitled "A new syndrome: Spasm in flexion, callosal agenesis, ocular abnormalities"[1]. Later, in 1969, Aicardi et al[2] gave a more detailed description of the syndrome, and at present more than 100 cases have been reported[3].

Several authors had described the syndrome's characteristics before the name was coined by Aicardi[4,5]. In 1949 Sabin and Feldman[6] reported cases with chorioretinopathy associated with other evidence of ocular cerebral damage or defects, including agenesis of the corpus callosum not due to toxoplasmosis.

Findings in the syndrome are female sex, agenesis of the corpus callosum, infantile spasms, specific chorioretinopathy, mental subnormality and characteristic electroencephalographic (EEG) changes.

We believe the following report of a patient with the Aicardi syndrome is the first reported case in Turkey.

Case Report

A 43-day-old girl brought to Hacettepe University Children's Hospital had been born at term to a 20-year-old primigravida after an uneventful pregnancy except for a flu-like illness in the first trimester. There was no history of physical or mental defects or neurologic disorders in the family. Labor and delivery had been spontaneous. At birth the patient was reported to be cyanotic for a period of two minutes with infantile spasms following shortly. On the day of admission to the hospital she weighed 3,500 g, her head circumference measured 36 cm, and she seemed unaware of her environment despite normal vital signs. Low-set ears, ocular hypertelorism, short neck, scoliosis, marked hypotonicity with diminished tendon jerks and frequent

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spasm-type convulsions were observed during examination (Figure 1). Ophthalmologic examination revealed bilateral "lacunar" chorioretinopathic lesions with sharp borders, little pigment, and yellowish-white color (Figure 2). The pupilla of the microphthalmic right eye was key-hole shaped, with colobomata.

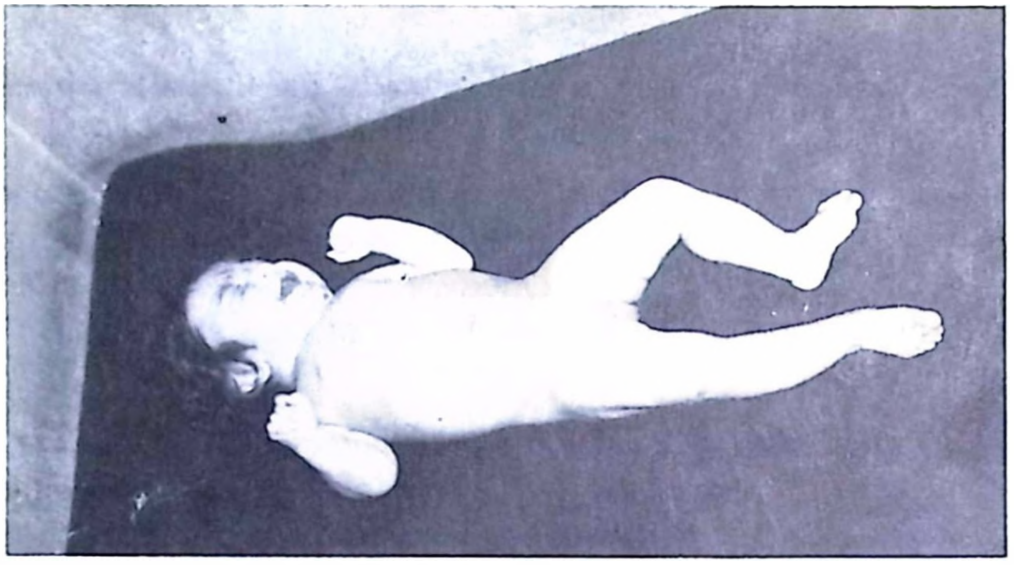

Figure 1

Photograph of the patient at 3 months of age.

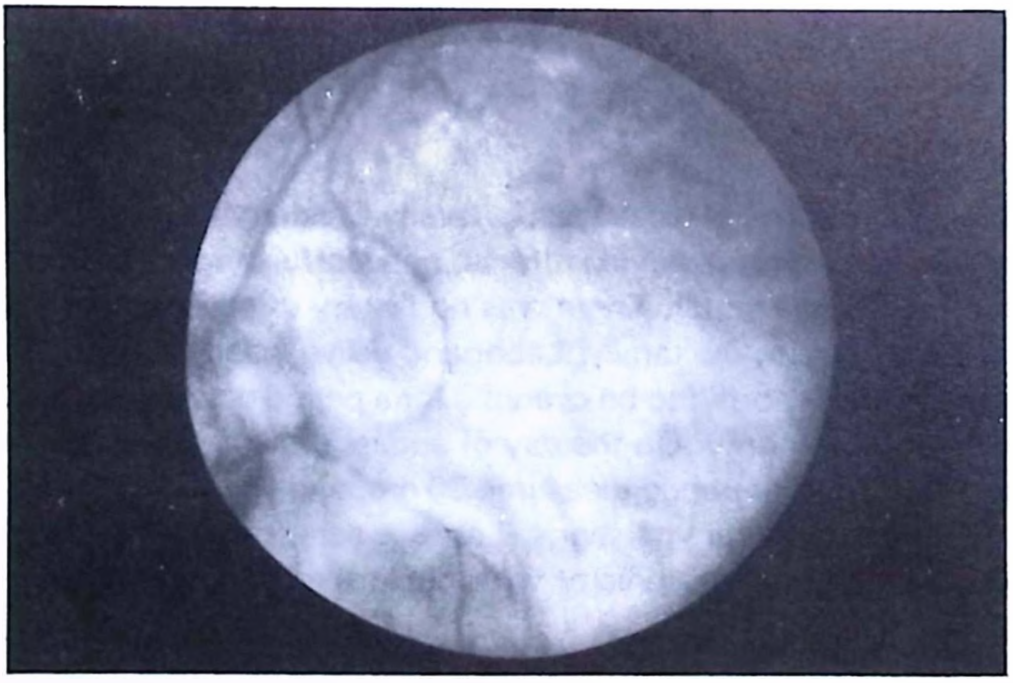

Figure 2

Left retinal photograph of the patient showing typical "lacunar" chorioretinopathic lesions of the Aicardi syndrome, with sharp borders, little pigment, and yellowish-white color. Age 3 months.

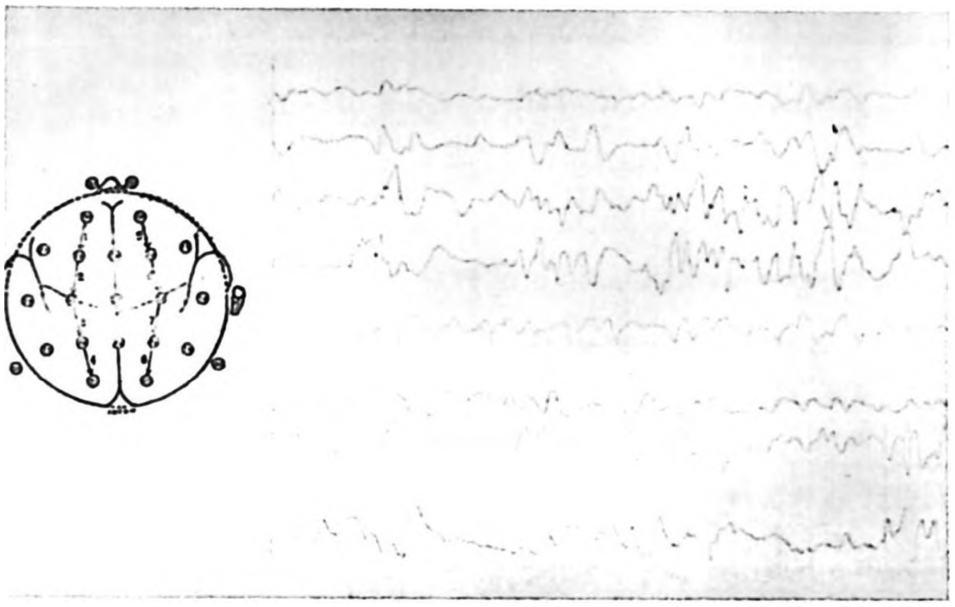

Figure 3

EEG showing asynchrony. Age 1.5 months.

Laboratory data: EEG revealed interhemispheric asymmetry with discharges of sharp waves and 1-2 cy/sec slow wave activity dominating the left and occasionally the right hemisphere (Figure 3). The pneumoencephalogram demonstrated agenesis of the corpus callosum accompanied by deformities of the ventricles (Figures 4-6). Spinal x-rays were unremarkable. Normal studies included: CBC, urine analysis, serum calcium, alkalene phosphatase, phosphorus, and blood sugar levels, cerebrospinal fluid (CSF), blood and urine amino acid screening, PPD, Sabin-Feldman, VDRL, and rubella antibody titration.

Phenobarbital (5 mg/kg/day) and prednisone (2 mg/kg/day) were partially effective in controlling convulsions.

Discussion

In Table I below we have grouped the features of the Aicardi syndrome under two headings: necessary constituents and expected features.

The salient features of the Aicardi syndrome present in this case are female sex, agenesis of the corpus callosum, infantile spasms, bilateral chorioretinal lacunae, characteristic EEG changes, mental subnormality, and hypotonicity.

All patients reported with Aicardi syndrome so far have been females except for the male case of Curatolo[3], and there have been no affected siblings. Aicardi et al[2] referred to the syndrome as "hologynic inheritance" transmitted exclusively by

TABLE I

FEATURES OF THE AICARDI SYNDROME

A. Necessary constituents

1. Agenesis of the corpus callosum (probably a *sine qua non* for the syndrome).
2. Pathognomonic chorioretinopathy (bilateral punched-out depigmented zones of atrophy in the pigment epithelium, described as "lacunes" or "chorioretinal lacunae").
3. Seizures (often like infantile spasms).
4. Mental subnormality.

B. Expected features

1. Female sex.
2. Hypsarrhythmia, independent bioelectric activity of the two hemispheres, or variable EEG records.
3. Other ophthalmic abnormalities (microphthalmia, colobomata, iris synechia, and optic atrophy).
4. Skeletal abnormalities (scoliosis; fusion of vertebrae, block vertebrae, hemivertebrae, butterfly vertebrae, spina bifida, abnormal ribs, and abnormal costovertebral articulations; facial and skull asymmetry, plagiocephaly; increased interorbital distance).
5. Hypotonicity or spasticity.
6. Other cerebral pathology (ectopic cortical grey matter; lissencephaly; microgyria; plexus papilloma; abnormal cerebellum with deficient vermis and tonsils; absence of epiphysis; abnormalities of ventricles).
7. Other miscellaneous anomalies (low hair line over the forehead; cleft palate; incomplete development of the superior helices of ears, low set ears; overlapping of the third finger over the second finger, clinodactyly of the fifth finger, camptodactyly of the third finger with the absence of the distal interphalangeal crease; biseptate vagina; two vessels in the umbilical cord; Arnold-Chiari malformation; Dandy-Walker syndrome, facial asymmetry; microcephaly).

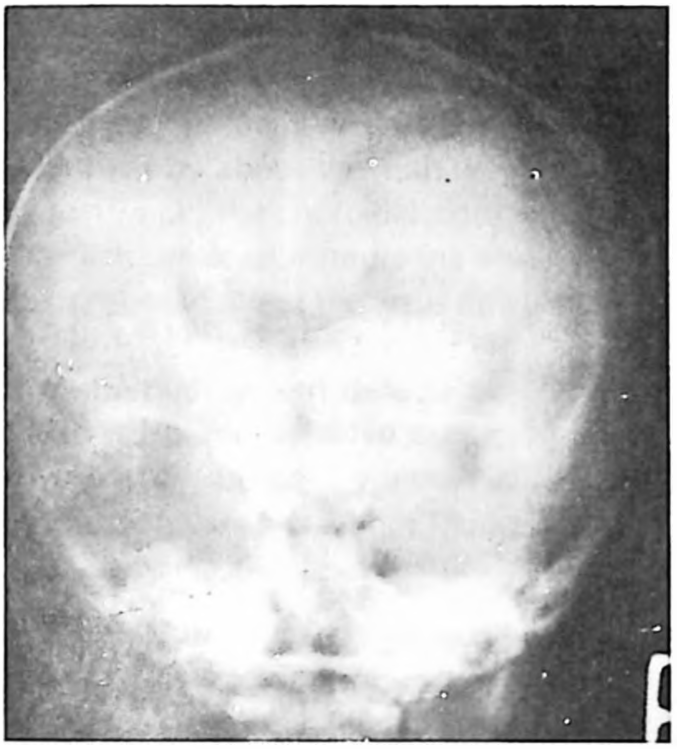

Figure 4

Figures 4, 5, 6

Pneumoencephalograms demonstrate agenesis of the corpus callosum with ventricular anomalies. Age 1.5 months.

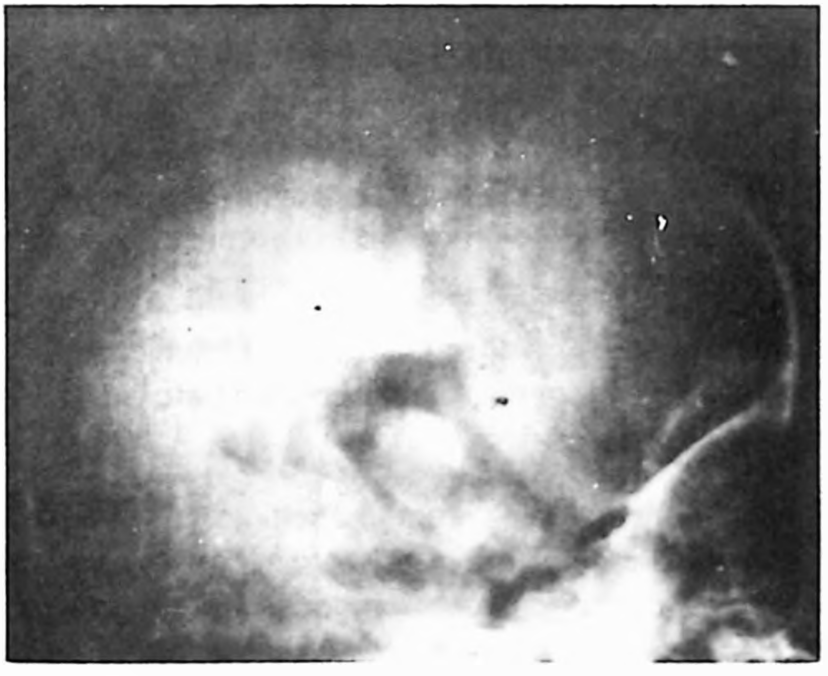

Figure 5

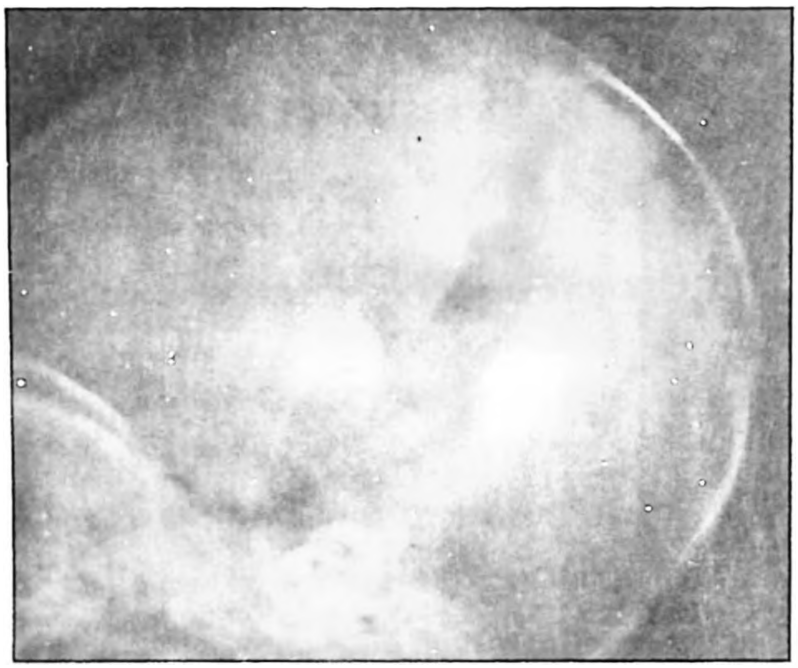

Figure 6

the female through genes located on X chromosomes [7]. But given the report on a male patient with Aicardi syndrome[3] we put the female sex findings, under the heading "expected constituents." The first genetic possibility is an X chromosomal dominant inheritance with manifestations in the heterozygote and lethal in the male[5]. A second likely explanation is an extrachromosomal inheritance[5]. The possibility of a multipe gene effect with a greatly increased tendency to appear in females is also pointed out[8]. All reported cases are sporadic and probably due to new mutations[5]. After identifying the syndrome in a male patient, Curatolo[3] suggests the need to reconsider the genetic aspects of the malformation.

Bogdanoff et al[9] described an infant with central nervous system and multiple eye deformities as possible sequelae to the prenatal use of drugs, including LSD. Influenza attack in early pregnancy was considered a possible offending external agent in a patient with Aicardi syndrome[10], and this may apply to our patient's mother. Among Jones and Smith's fetal alcohol syndrome series, case number 2, the offspring of a chronic alcoholic, revealed in necropsy agenesis of the corpus callosum and other central nervous system abnormalities [11].

Infantile spasms are documented in all but one of the fifteen cases in Aicardi's original series [2]. Variable seizure patterns usually occurred before the onset of infantile spasms, as in Dennis and Bower's case[8].

In 1956, Brihaye had described clinically and pathologically what may have been an Aicardi syndrome case, where post-mortem examination revealed a grossly abnormal brain in which the corpus callosum, trigone and septum pellucidum were absent[8]. In 1976, de Jong et al[5] described the clinical and pathological findings of

two Aicardi syndrome cases with no pineal glands. They concluded that since the epiphysis cerebri was important as a clock for sexual development, its absence might be incompatible with the development of a male fetus. The corpus callosum is formed by about the 16th week of gestation. The retinal pigment appears in the fourth week; the choroidal pigment appears and closure of the papilla takes place in the fifth week of intrauterine life. The pathogenetic agent, which may be exogenous, should affect the fetus between the third and fifth month of intrauterine life or earlier [5,8,12]. It is also believed that agenesis of the corpus callosum and other central nervous system defects are part of a gross cerebral pathology. Migrational failure of primitive nerve cells during fetal development results in ectopic cortical grey matter. In cases where this failure is complete, the neuroblasts remain at the embryologic site of origin (subependymal). This is believed to be the case in the Aicardi syndrome[8], but despite investigations the syndrome's pathogenesis remains unclear[12].

In the differential diagnosis, congenital infections have to be excluded. Certain associated abnormalities referred to as congenital infections would make a diagnosis of the Aicardi syndrome less likely. The associated features include glaucoma, cataracts, keratitis or conjunctivitis, long-bone changes, intracranial calcifications, congenital heart disease, skin lesions, deafness and a pleocytosis in the CSF[13]. As mentioned by Willis and Rossman[13], the importance of this diagnostic distinction is threefold. Although mental subnormality is one of the Aicardi syndrome's necessary constituents, it may be absent with the congenital infections. Congenital syphilis and toxoplasmosis are now specifically treatable, unlike the Aicardi syndrome. The genetic pattern of the Aicardi syndrome brings forth the importance of family planning.

We believe that a retrospective search for cases of Aicardi syndrome among patients with congenital infections and infantile spasms now accepted as idiopathic would show the syndrome to be more common than currently reported.

Summary

A case of Aicardi syndrome is described. The salient features are female sex, agenesis of the corpus callosum, pathognomonic chorioretinopathy, seizures, and mental subnormality. The authors suggest that the incidence of the syndrome may be higher than expected.

Acknowledgement

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