

### Aicardi Syndrome

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The Aicardi Syndrome (AS) was first described in 1965(1), as an association of three main features: infantile spasms, peculiar chorioretinopathy and agenesis of the corpus callosum. A number of additional developmental defects such as vertebral and costal abnormalities, and subependymal heterotopias have been recorded in association with the 3 main features and vary in different patients. Although AS has become recognized as a specific clinical entity over the past two decades, there is only one case report as yet from India(2). Recognition of the entity is important for counselling the parents. The report of a girl with AS is being presented.

#### Case Report

A child was brought at 4 years of age with complaints of poorly controlled seizures and marked developmental delay.

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She was born full term by a normal vaginal delivery of a non-consanguineous marriage. There were no adverse antenatal or perinatal factors. From the 15th day of life, she started having occasional twitching movements of the right side of the face and hands. At 4 months of age, she had repeated myoclonic jerks of the limbs followed by typical infantile flexor spasms. The EEG done then, showed a graph consistent with interictal record of generalized seizures with focus over right temporo-parietal region and runs of polyspikes. She continued to have myoclonic seizures, and of late started having tonic clonic movements, and some times atonic spells. She had received various anticonvulsants and also ACTH and prednisolone, but continued to have recurrent seizures.

Parents reported that the child had shown a gross delay in her development right from early infancy. There was no family history of a similar disorder.

Clinical examination showed a hypotonic child with microcephaly (head circumference 46 cm) and gross developmental delay. She was unable to sit without support, showed little interest in the surroundings, and did not get excited by visual or auditory stimuli. She could recognize her family members and reach out for gross objects; pincer grasp was absent. She could vocalize but did not have any meaningful speech.

There was no specific focal neurological deficit; deep tendon reflexes were depressed. Other systems were essentially normal.

On ocular examination, the child showed poor fixation. Anterior segment

examination was unremarkable. On funduscopy, in both eyes there were characteristic well defined, circular, hypopigmented lacunae varying in size from one fourth to four disc diameters. The lesions were clustered around the optic disc, decreasing in size and number as they extended into the periphery of the fundus. The right optic nerve head was tilted. There was a halo of peripapillary choroidal atrophy around the optic disc in both the eyes. On fluorescein angiography the lesions exhibited transmission defects without late hyperfluorescence demonstrating these areas to be deficient in retinal pigment epithelium and choroidal atrophy (*Figs. 1 & 2*).

The EEG showed a background of 15-16 Hz (10-20 uv), fast beta activity superimposed on 4-5 Hz (60-70 uv) theta activity and runs of polyspikes. CT Scan revealed agenesis of the corpus callosum. (*Figs. 3 & 4*). Roentgenographic examination of the chest and vertebral column did not reveal any abnormality.

The child was started on Nitrazepam 2.5 mg BD (0.5 mg/kg/day). Counselling was given to the parents, on regular follow up for a year, the child showed little developmental progress. She could sit without support and stand with support. There was still no meaningful speech. Her seizures were, however, controlled.

## Discussion

Aicardi syndrome is considered in the diagnosis of infantile spasms in females. Seizures generally start early in life, 68% cases presenting at less than 3 months of age. Almost all patients have infantile spasms. These may be preceded, accompanied or followed by other seizure types(3) as seen in this case. EEGs are always abnormal. The commonest abnormality described is pseudoperiodic discharges

occurring asynchronously over both hemispheres, with suppression-burst pattern. Hypsarrhythmia often atypical has been described in 18% cases. The EEG abnormalities tend to become less characteristic over a period of time, and the pseudo-periodicity and asynchrony may even disappear; the paroxysmal activity often evolves into diffuse or multifocal discharges(3).

Motor and mental retardation is present in all patients, is apparent from an early age, and is almost always severe. Most patients establish little social contact, and language development is absent or extremely limited. All these features were present in this child. Gross hypotonia, hemiplegia and bilateral pyramidal tract signs are the neurological abnormalities described. Head circumference is generally normal at birth, but microcephaly is acquired later(3). The skull may be asymmetrical.

Most children show poor visual fixation. Ocular anomalies, like microphthalmos, microcornea, strabismus or persistent pupillary membrane may be obvious in some cases. However, the ophthalmoscopic picture known as 'chorioretinal lacunae' is pathognomonic. The lesions are seen as yellowish white, round areas with sharp borders, multiple in number and clustered around the optic disc. The diameter of the lesions vary from a small fraction to five to six times the disc diameter(4). The ocular findings are almost always bilateral but the eyes may not be equally affected. The lacunae are quite distinct in appearance, shape and pigmentation from inflammatory chorioretinopathy even then the two lesions had been confused in the past(5).

Fluorescein angiography has been reported only in one previous study(6) and suggests that the retina itself is normal, and the abnormalities affect only the choroid

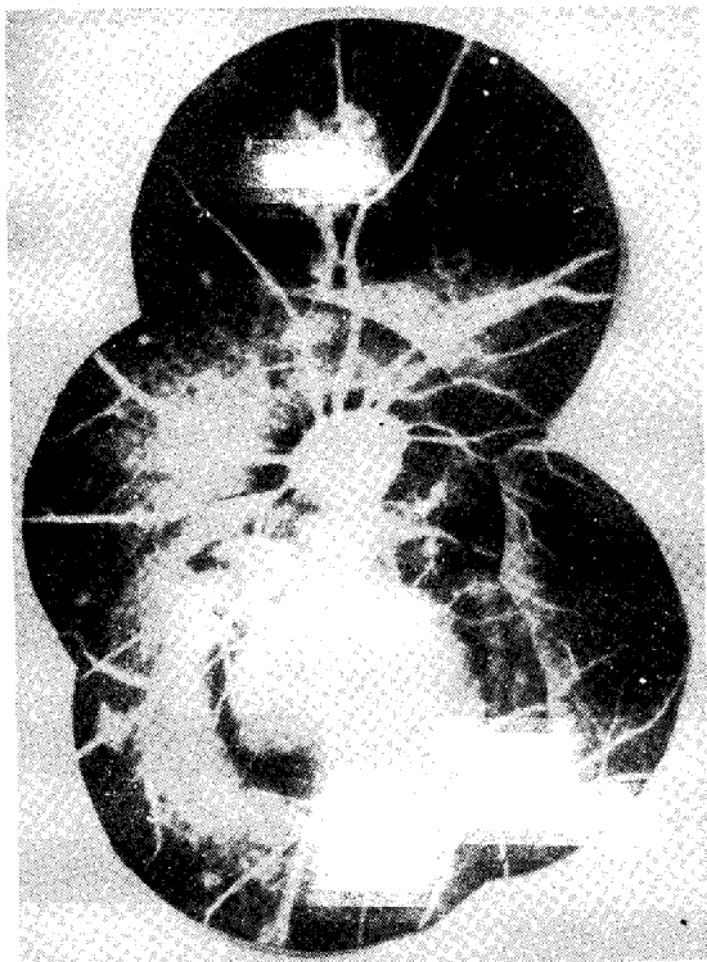


Fig. 1. Fundus fluorescein angiogram of the right eye during dye transit showing a large well defined 4 DD size transmission defect above the optic disc. A large patch of transmission defect surrounded by hypofluorescence corresponding to a pigmented halo and multiple small defects are seen below the optic disc.

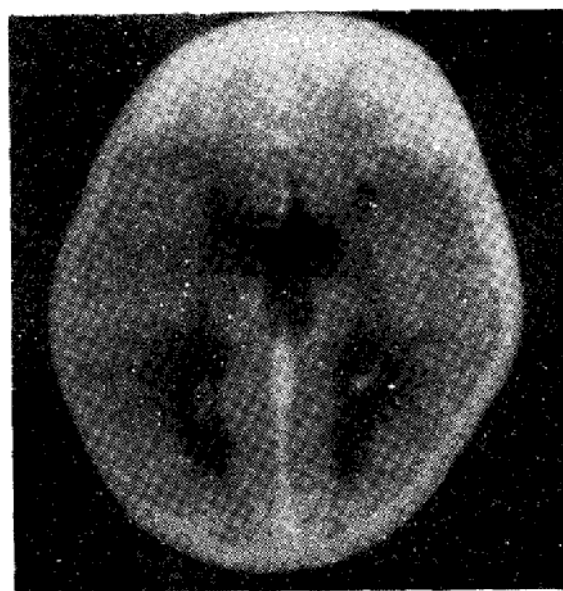


Fig. 3.

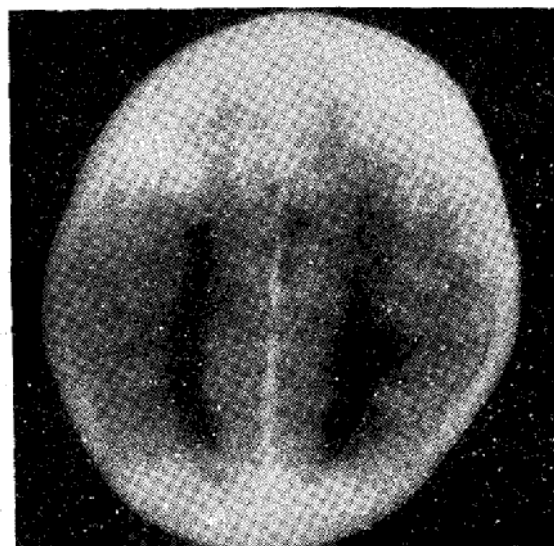


Fig. 4.

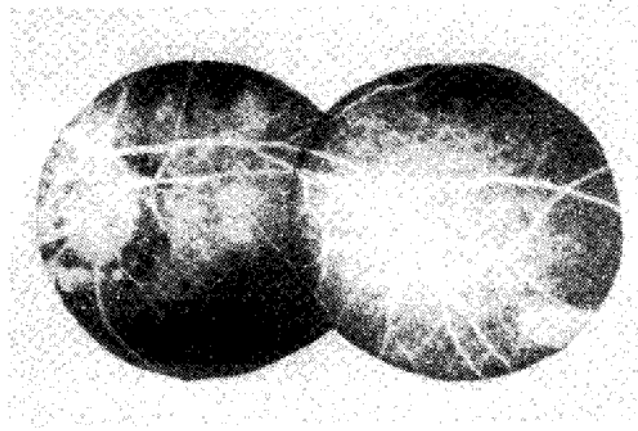


Fig. 2. Fundus fluorescein angiogram of the left eye during dye transit showing peripapillary halo of hyper and hypofluorescence and a transmission defect seen temporal to the macula.

Figs. 3 & 4. CT Scan of head showing large third ventricle with ascension of its roof and lateral displacement of lateral ventricles indicative of corpus callosum agenesis.

membrane. Findings in this case also showed transmission defect suggesting retinal pigment deficiency with choroid atrophy. The electro-retinogram has been reported as normal in some cases and abnormal in others. Abnormalities in VEP have also been reported. At least some degree of vision is preserved in most patients and blindness is distinctly unusual(3).

Skeletal abnormalities especially, fusion of vertebral bodies, fused ribs, hemivertebrae, scoliosis and spinal bifida are often found in these patients(4). This child did not have any such abnormalities.

The availability of CT Scan and MRI have made the diagnosis of AS much easier. Agenesis of the corpus callosum is one of the criteria that define AS. It is generally total but may be partial. Other associated brain malformations—asymmetry between the 2 hemispheres, cortical heterotopia, microgyria, porencephaly and arachnoid cysts are easily demonstrated by these modalities(6,7) when present.

All the cases of AS described have been females, one phenotypic male with 47 XXY, chromosomal pattern has been reported(9). Except for one case report of AS in two sisters(10), the syndrome has not been encountered in siblings or relatives of affected probands.

The precise causative factor for AS is unknown. The insult during embryogenesis probably is during the fourth and eighth week of intrauterine life(3). The condition probably is due to a newly mutated X-chromosomal dominant gene, lethal *in utero* for males(2).

The diagnosis of AS has important implications regarding both prognosis and genetic counselling. Individual mental and neurologic prognosis is extremely poor; most patients continue to have seizures, develop marked scoliosis and die early in

life. Risk of recurrence of AS in the case of further gestation is probably nil(3).

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