

## Refractory seizures with global developmental delay: A rare cause

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Aicardi syndrome is a genetic disorder characterized by the triad of infantile spasm in flexion, callosal agenesis and ocular abnormalities (chorioretinal lacunae, coloboma of optic disc). We report a typical case of Aicardi syndrome with all the classical features.

**Key words:** Callosal agenesis, chorioretinal lacunae, coloboma, infantile spasm

### Introduction

Aicardi syndrome is a rare genetic disorder characterized by the partial or complete absence of corpus callosum. Triad of spasm in flexion, ocular abnormalities and callosal agenesis were the components of this syndrome described initially by Aicardi *et al.*<sup>[1]</sup> Now, skeletal deformities like vertebral anomalies, cortical heterotopias in the eye, mental subnormality and electrophysiological and radiological abnormalities characteristic for this syndrome have been added.<sup>[2]</sup> We report a typical case of Aicardi syndrome with all the classical features.

### Case Report

A 1-year-old girl presented to us with refractory

seizures since the age of 2 months. She was born to second degree consanguineous parents by an uncomplicated normal vaginal delivery at term. There were no significant issues in the antenatal period. She was reported to have myoclonic jerks since the age of 2 months, and later developed to refractory generalized tonic clonic convulsions. She did not achieve any of the age-appropriate milestones, including social smile and head control yet. Her examination revealed microcephaly with marked hypotonia and bilateral extensor plantar response. Fundoscopy in the right disc showed coloboma and multiple areas of choroidal lacunae. Left disc showed retino choroidal coloboma (bridging type) and multiple areas of choroidal lacunae. X-ray of the spine showed kyphoscoliosis and multiple hemivertebrae in the lower thoracic region. X-ray chest and skull were normal. EEG showed burst suppression pattern suggestive of diffuse encephalopathic process. Agenesis of corpus callosum [Figure 1], pachygyria [Figure 2] and arachnoid cyst [Figure 3] were observed in the computed tomography scan of the brain. Karyotyping found the 46 XX pattern. Serological tests for intrauterine infections were negative. The child was commenced on anticonvulsants. Multiple anticonvulsants were needed to decrease the frequency of seizures. Developmental rehabilitation was initiated. Prognosis was explained to parents and need for regular follow-up was advised. However, the child was lost to follow-up.

### Discussion

Aicardi syndrome is a genetic disorder characterized

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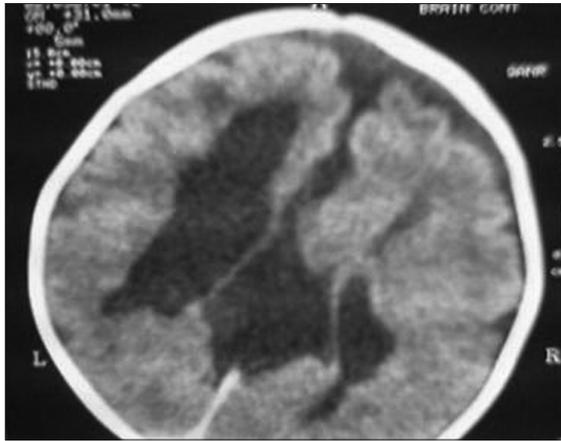
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**Figure 1: Computed tomography scan of the brain axial sections show parallel lateral ventricles, agenesis of corpus callosum and asymmetry of cerebral hemispheres**



**Figure 2: Computed tomography scan of the brain axial sections show agenesis of corpus callosum, asymmetry of cerebral hemispheres and pachygyria**



**Figure 3: Computed tomography scan of the brain axial sections show right arachnoid cyst**

by the triad of spasm in flexion, callosal agenesis and ocular abnormalities. Aicardi *et al.*, in 1965, first described eight cases with a triad of spasm in flexion, ocular abnormalities and callosal agenesis.<sup>[1]</sup> Our patient had all the three characteristic features. Now, skeletal deformities like vertebral anomalies, cortical heterotopias in the eye, mental subnormality, electrophysiological and radiological abnormalities characteristic for this syndrome have been added,<sup>[2]</sup> most of which are present in our case.

X-linked dominant inheritance with mutational event occurring during meiosis in one of the X chromosomes is suggested as a cause.<sup>[3]</sup> It is mostly lethal in males. The condition has been recognized only in individuals with two X chromosomes; only two were in boys, both with

an XXY chromosomal complement.<sup>[4]</sup> Aicardi syndrome is not a familial condition; only one familial instance is known involving two sisters.<sup>[5]</sup> The actual frequency of the condition is not known.

Neural tube over distension during embryonic life at 4–8 weeks of gestation is attributed to be the cause for this anomaly. It is often recognized during the neonatal period and infancy, but could be delayed from 11 to 234 weeks after the onset of seizures.<sup>[6]</sup> Although cases occur throughout the world, the exact incidence and prevalence is unknown.

Seizures in Aicardi syndrome usually start early in life and are mostly myoclonic in type, and other seizure types follow this. Mental retardation, hypotonia and variable pyramidal tracts signs have been observed. Lissencephaly, polygyria, microgyria and cortical heterotopias have been found on pathological examination of the brain.<sup>[6]</sup>

The most common skeletal abnormality described is fusion of the vertebral bodies. Other abnormalities include hemivertebra, butterfly vertebra, spina bifida occulta, scoliosis, abnormalities in costovertebral articulations, facial and skull asymmetry and increased interorbital distance.<sup>[7]</sup>

The ophthalmologic findings are usually bilateral, but both eyes are not always equally affected. Ophthalmologic findings include coloboma of the optic disc, chorio retinal lacunae, retinal dysplasia with total detachment, microphthalmia, persistent pupillary membrane, synechiae of

iris and colobomatous cyst.<sup>[8]</sup> This chorio retinal lacunae has to be differentiated from chorioretinitis of intrauterine infection, especially congenital toxoplasmosis.<sup>[9]</sup> Bilateral retino choroidal coloboma and choroidal lacunae were present in our child, and the TORCH titers were negative.

Agenesis of corpus collasum and cortical heterotopias are the hallmark of this syndrome. But, asymmetry of the cerebral hemispheres arachnoid cyst, Dandy Walker syndrome, colpocephaly, porencephalic cyst, pachygyria and parallel lateral ventricles have also been described.<sup>[10]</sup> Our patient had parallel lateral ventricles, arachnoid cyst and pachygyria in addition to collasal agenesis. Microscopic evaluation of the parenchyma commonly reveals disordered cellular organization and disruption of the normal layered appearance of the cortex.

EEG pattern is characteristic, which consists of multifocal epileptiform discharges occurring in the burst suppression pattern, showing complete asynchrony between the two hemispheres. Anatomical and electrophysiological disconnection between the two hemispheres is proposed to be the cause for this EEG abnormality.<sup>[11]</sup>

The course and outcome of Aicardi syndrome is extremely severe. The condition often leads to death in the first decade. Sudden, unexplained death can occur, but patients commonly die from pulmonary infections.

We report this case to alert pediatricians to suspect this syndrome when they come across girl children with seizures and developmental delay. Careful ophthalmologic examination and electrophysiological and radiological investigations are essential to diagnose this syndrome and to differentiate it from intrauterine infection.

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