AICARDI SYNDROME - A RARE NEURODEVELOPMENTAL DISORDER

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Abstract:
Aicardi syndrome is a rare neurodevelopmental disorder identified by the French Neurologist, Dr. Jean Aicardi in 1965. The diagnostic triad of Aicardi syndrome is composed of infantile spasms, agenesis of corpus callosum and chorioretinal lacunae. Cerebral malformations like microgyria, heterotopias, intraventricular cysts and choroid plexus papillomas coexist at times. The other occasional findings are abnormalities of ribs and spine, microphthalmia, optic nerve coloboma and asymmetry of cerebral hemispheres. A significant number of females with Aicardi syndrome are normal at birth and develop normally until three months of age when infantile seizures begin. It is a rare genetic disorder and from our country only a few case reports of Aicardi syndrome have been published so far. Complete evaluation is needed for a case of agenesis of corpus callosum as there are a wide range of associated syndromes. To predict the prognosis, it is necessary to differentiate between isolated agenesis of corpus callosum and syndromic agenesis of corpus callosum.

Case report - We present a case of Aicardi syndrome who had come to our hospital at 4 months of age with multiple episodes of seizures. She had been subjected to neurological evaluation and found to have agenesis of corpus callosum. Further evaluation done for other anomalies revealed the presence of chorioretinal lacunae in both eyes and coloboma of the left optic disc. The constellation of seizures, agenesis of corpus callosum and chorioretinal lacunae suggested the diagnosis of Aicardi syndrome.

Keyword: Aicardi syndrome, Corpus callosum, Seizures, Chorioretinal lacunae.

INTRODUCTION:
Aicardi syndrome is a rare genetic disorder identified by the French Neurologist, Dr. Jean Aicardi in 1965 (1). From India only a few case reports of Aicardi syndrome have been published so far (2), (3), (4), (5). Aicardi syndrome is due to X-linked dominant inheritance occurring sporadically. Skewing of X chromosome (6) is present in a much higher number of affected girls than what would be expected. Recurrences within the family is extremely uncommon.
The few males those have been identified with Aicardi syndrome have proved to have 47XXY chromosome pattern. Aicardi syndrome appears to be lethal in normal males who have only one X chromosome (7).

CASE REPORT

4 months old female baby 1st born of non consanguineous marriage brought for multiple episodes of seizures not associated with fever since 3 months of age. She was born by uncomplicated vaginal delivery at term. Antenatal and neonatal period was uneventful. The baby did not attain social smile and head control. Since 3 months of age the baby used to get tonic clonic seizures about 20 to 25 times per day. On examination there was no facial dysmorphism, external abnormalities or neurocutaneous markers. The baby had head lag and marked hypotonia with normal deep tendon reflexes and bilateral extensor plantar response. The blink reflex and auriculo palpebral reflex were absent. On fundus examination the right optic disc was normal and the left sided optic disc could not be visualized. Blood sugar, calcium, renal function tests and liver function tests were normal. Urine metabolic screening was negative. Serologic test for intrauterine infections was negative. Neuroimaging with Computed tomography revealed a complete agenesis of corpus callosum (fig.2), interhemispheric communicating cyst (fig.3), colpocephaly and asymmetry of lateral ventricles, diffuse cerebral atrophy (fig.4). MRI was done to confirm these findings.

Fig1.Normal corpus callosum.

Fig2.Showing absence of corpus callosum.

Fig3.Arrow showing interhemispheric communicating cyst.

Fig4.Showing dilated posterior horn of right lateral ventricle (colpocephaly) and asymmetry of lateral ventricles.
**DISCUSSION:**

Originally, Aicardi syndrome was characterized by three main features: absence of corpus callosum, complex seizures generally starting as infantile spasms and retinal lacunae. However, Aicardi syndrome is now known to have a much broader spectrum. Typical findings in the brain of girls with Aicardi syndrome include partial or complete absence of corpus callosum, heterotopias, polymicrogyria, or pachygyrias, arachnoid cyst, asymmetry of lateral ventricles, cerebellar abnormalities, rarely dandy walker syndrome (8). These are well appreciated in CT or MRI. Girls with Aicardi syndrome have varying degrees of mental retardation and developmental delay. In this case there is complete absence of corpus callosum, interhemispheric communicating cyst, colpocephaly and asymmetry of lateral ventricles.

The eye findings are constant and necessary for the diagnosis of Aicardi syndrome. The various ocular anomalies described include microphthalmia, chorioretinal lacunae, coloboma of optic disc, persistent pupillary membrane, synechiae of iris, retinal dysplasia with total detachment, colobomatous cyst, etc (9). The chorioretinal lacunae may vary in size from <1/10 to six times the disc diameter (8). These findings are usually bilateral, but not all eyes are equally affected. In this case chorioretinal lacunae present in both eyes and the left disc had coloboma. Good visual function in Aicardi syndrome patients do occur if the fovea is uninvolved with chorioretinal lacunae.
Seizures in Aicardi Syndrome generally start early in life usually within 5 months of life and its of myoclonic type. They may precede, accompany or followed by other seizure types. Electrophysiologically, disconnection between the two hemispheres is characteristic EEG pattern found in Aicardi syndrome. In this case the child had generalized tonic clonic seizures and the EEG revealed intermittent paroxysmal spike and wave discharges with complete asynchrony between the cerebral hemispheres. Some workers have concluded that the EEG pattern is pathognomonic of Aicardi syndrome while others have questioned it (10).

Skeletal abnormality described in association with Aicardi syndrome are fusion of the vertebral bodies, block vertebrae, hemivertebrae, butterfly vertebrae, spina bifida occulta, scoliosis, abnormalities in costovertebral articulations, facial and skull asymmetry and increased interorbital distance (11). Some people with Aicardi syndrome have unusual facial features including a narrow philtrum, a flat nose with an upturned tip, large ears, and sparse eyebrows. Small hands and hand malformations. They often have gastrointestinal problems such as constipation or diarrhea, gastroesophageal reflux, and feeding difficulty. This case did not have any of these abnormalities.

Treatment of Aicardi syndrome primarily involves management of seizures and early continuing intervention programs for developmental delays. Infantile spasms may be recalcitrant to therapy. Guidelines for the medical treatment of infantile spasms have been established by the American Academy of Neurology and the Child Neurology Society. Adrenocorticotropic hormone is effective for some patients and should be considered. Vigabatrin, a recently introduced in therapy for infantile spasm. Although concerns have been raised about possible ophthalmologic sequelae after using vigabatrin, it has been effective for infantile spasms without the serious life threatening adverse effects of ACTH. A recent report showed better results with vigabatrin and recommends this as the first-line drug in the treatment of seizure in Aicardi syndrome cases (12). Profound mental retardation, immobilization, seizures and scoliosis may contribute to cardiopulmonary dysfunction. Patients have a shortened life span and commonly die from pulmonary infections. Consultation with a neurologist is probably needed during the first year of life. A pediatric ophthalmologist is best able to confirm retinal lacunae.

Consultation with an orthopedician, pulmonologist or gastroenterologist is needed if complications arise from scoliosis, pulmonary function, feeding or aspiration difficulties. Complete evaluation is needed for a case of agenesis of corpus callosum as there are a wide range of associated syndromes. To predict the prognosis, it is necessary to differentiate between isolated agenesis of corpus callosum and syndromic agenesis of corpus callosum.

Fig 7. Aicardi syndrome baby - the head being supported by the mother.

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