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CASE REPORT

Aicardi Syndrome: A Case Report of a 7 Months Old Girl with Infantile Spasm, Ocular Abnormalities and Severe Psychomotor Retardation

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Abstract:

Aicardi syndrome a rare form of neurodegenerative encephalopathy affecting mostly woman as it follow X-linked recessive inheritance. It has a classical triad for diagnosis which is composed of agenesis of corpus callosum, infantile spasm and chorioretinal lacunae. Patients may have also the additional features of microcephaly, severe psychomotor retardation and spasticity. Male are embryonically lethal in early gestation so female are the only sufferer. Here we reporting a 7 months old girl who had history of recurrent spasm, global developmental delay and bilateral clouding of cornea, her MRI of brain have shown features of hypoplastic corpus callosum, prominent megacistern, cortical atrophy, eye findings have shown bilateral corneal haziness multifocal discharge on EEG findings. We have counseled the parents and treated the patients by anticonvulsants, anti spastic medication. We have also initiated rehabilitation by providing developmental therapy, and opthalmological consultation.

Key words: *Aicardi syndrome, corpus callosal agenesis, infantile spasm*

Introduction:

French neurologist Dr. Jean Dennis Aicardi first described 8 children with infantile spasm having variable corpus callosal agenesis with ocular abnormalities[1]. Same type of presentation also noticed at 1949 and concluded as an etiology of congenital infection. In 1969 and 1972 seven more patients were described having the same features, from where Dennis and Bower established the Aicardi syndrome designation[2].

Aicardi syndrome is a very rare syndrome to affect all ethnicities equally with incidence of 1 in 1, 05,000 in USA and 1 in 93000-99000 in European countries[3].

The gene causes Aicardi syndrome not known yet, it has been hypothesized that spontaneous mutation occurs in the Xp22 ch5omosomes[4]. A report described the changes in the genes TEAD1 and OCEL1 in two girls with Aicardi syndrome but not confirmed with large cohort of other girls with Aicardi syndrome[5]. Piras et al discussed recurrent hypomethylation in the KCNAB3 gene promoter and 5' areas in patients with Aicardi syndrome which may be responsible for neuronal hyperactivity and neurodevelopmental and neuroinflammation pathways[6]. Several observations support the hypothesis of de novo pathogenic variant in a gene on the X chromosome that is subject to X-Chromosome inactivation, so Aicardi syndrome is typically observed in females but has also been reported in males with 47 XXY karyotype and very rarely in 46 XY[7]. Most of the cases Aicardi syndrome represents as a single affected family member, there is no reports of parent to child transmission of Aicardi syndrome. Recurrence risk to sibs proband is reported less than 1%[8]. The mean survival age is about 16 years, but there is a report of maximum 49 years life expectancy with a mild form of the syndrome[3].

Clinical criteria are the mainstay to diagnose Aicardi syndrome. Modified diagnostic criteria have been proposed as

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- The presence of classic triad
- The presence of two of the classic triad plus at least two other major or supporting features is strongly suggestive of diagnosis of Aicardi syndrome.

Classical triad is agenesis of corpus callosum, chorioretinal lacunae and infantile spasm. Major features are, cortical malformations, periventricular and subcortical heterotopia, cyst around third ventricle, optic disc or nerve hypoplasia, supporting features are vertebral rib abnormalities, microphthalmia, split-brain EEG, gross cerebral hemispheric asymmetry, vascular malformations or vascular malignancy[9].

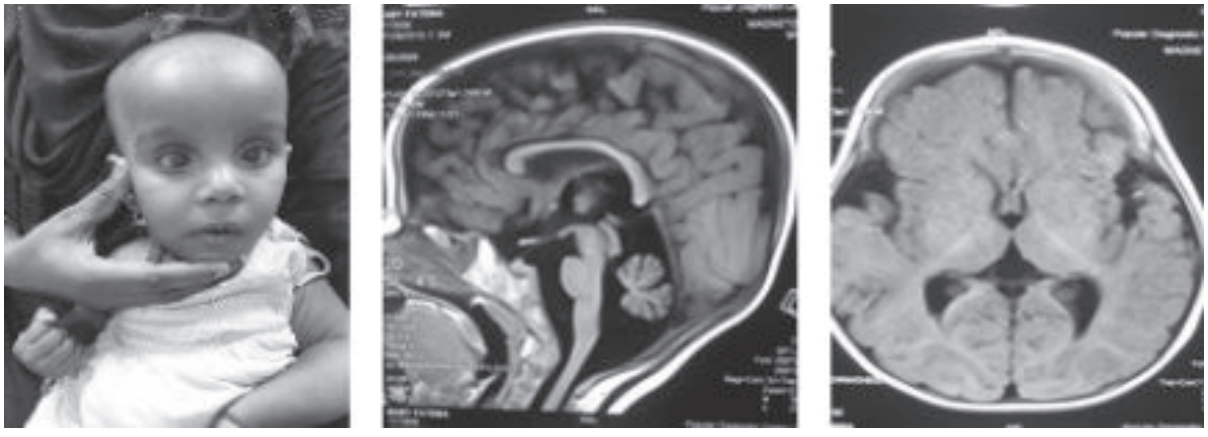
No curative treatment established here other than palliative and preventive measures about the onset of symptoms. Majority of patients began to develop spasm since 2-3 months of age which require anticonvulsants medication, like vigabatrin or ACTH and other antiepileptics like Na-valproate, levetiracetam, topiramate. A multidisciplinary team approach is essential to manage a child with Aicardi syndrome that includes a pediatric neurologist, ophthalmologist, occupational and speech therapist. Treatment of spasticity along with physiotherapy will improve motor problems. Genetic counseling is the important part of management which will provide the information about the nature, mode of inheritance and implications of genetic disorders to help them make medical and personal decisions. No prenatal testing is possible as the causative pathogenic variants yet not to identify[9].

Case:

A seven months old girl only issue of a consanguineous parents presented with recurrent seizures since 6 months of age in the form of sudden flexion of head and limbs towards trunk occurs in a cluster specially after awakening, each cluster have 8-10 spasms and occurs 6 to 10 times in a day. Mother also complained that she still unable to control her neck and her vision is low as there is opacity on both eyes; she stopped crying on mother voice. She was delivered at term with average birth weight by lower uterine caesarean section and cried immediately after birth. No other family member had same type of illness. All domain of development grossly delayed and motor age corresponds around 1 month of age, only vowel vocalization present, no fix and follow to object, no social smile, startle present on sound. On examination her OFC 41 cm, lies on 10th centile, bilateral corneal opacity present, but light reflex preserved, no other facial dysmorphism or neurocutaneous markers. Vitals were stable during examination. Antropometrical examination reveals her weight is 6 kg, weight for age lies just below 5th centile, supine length is 63 cm, length for age just on 25th centile. Hypertonia present on four limbs. Cortical thumb and constant fisting present on both hands. All deep tendon reflexes are exaggerated with presence of clonus.

Investigations:

TORCHS screening was negative, S.ammonia, Blood lactate, CBG, S electrolytes, ABG all reports



(A) (B) (C)

Fig.-1: *(A) Picture showing bilateral corneal haziness, (B) Severe hypoplastic corpus callosum with prominent cisterna megna-developmental with cerebellar atrophy, (C) Severe cortical atrophy with temporo-parietal atrophy*

were within normal levels, IMD panel was normal. EEG showed multifocal discharge with poverty of normal activity in background: suggestive of modified hypsarrhythmia. Hearing assessment refers to moderate hearing impairment. Eye evaluation reveals hazy cornea with non visualization of retina and fundus. MRI of brain reveals severely hypoplastic corpus callosum with gross cerebral and cerebellar atrophy with temporo-parietal predominance, prominent cistern megna-developmental.

This baby was treated with vigabatrin and spasm was controlled. Spasticity was treated with ant spastic drugs Tizinadine. Ophthalmological consultation was taken regarding eye problem. Developmental therapy, speech and language therapy, auditory stimulation, occupational therapy was continued simultaneously. Parents were counseled regarding her genetic pattern of disease with probable outcome.

Discussion:

Aicardi syndrome is one of the X-linked rare genetic disorders which estimated over 4000 cases worldwide[3]. Developmental delay and infantile spasm is one of the earliest and constant features of Aicardi syndrome which usually appears around second to third months of life and flexor pattern of spasm is found to be common here, children with Aicardi syndrome usually start with infantile spasm and then have generalized tonic clonic or focal or myoclonic types of seizure. Most of the time the seizure become refractory to medical treatment. Though the possibility of seizure remission is low however Banerjee et al acheived 100% seizures control on their two reported cases with vigabatrin[10]. Our patients also responded well with vigabatrin. Electroencephalography reports have shown dissociated burst-suppression or burst-suppression pattern asymmetrically in either cerebral hemisphere[11]. Multifocal or localized discharge may also be reported from some cases. The developmental delay is the second most common presenting features and the motor, language, cognitive domains are affected mostly. Chevrie et al observed 184 patients of Aicardi syndrome none of them had meaningful speech[12] though a significant number of girls with Aicardi syndrome normal at birth and normally developed up to 3 months of age especially before the development of spasm[13]. But higher functioning Aicardi syndrome individuals also exist which indicate larger spectrum of the disease[14].

Corpus callosal agenesis either complete or partial is a constant feature of Aicardi syndrome which present in all the diagnosed cases of Aicardi syndrome[10,15]. In our present cases there is severe hypoplastic corpus callosum, severe cortical and cerebellar atrphy and prominent mega cistern was the neuroimage findings. Cerebral heterotopias, interhemispheric cysts, polymicrogyria, intraventricular cysts, porencephalic cysts and choroid plexus papillomas may coexist at times[13].

The third features of diagnostic triad are chorioretinal lacunae presents among 50% of cases. In our reported cases ophthalmologist found bilateral hazy cornea with non visualization of retina and fundus, absence of this findings does not interfere with clinical diagnosis which is based on two classic characteristics hypoplastic corpus callosum and infantile spasms along with additional findings of muscular hypertonia, motor and cognitive delay[10,16]. Some studies considered eye findings as prognostic markers i.e patients having retinal lesions five times the size of the optic disc diameter show poorer cognitive outcome, patients with less eye change observed better prognosis[17,18]. Regarding radiological findings 75% of children with Aicardi syndrome have thoracic vertebral malformation in the form of congenital fusion, hemivertebrae and butterfly vertebrae[19] which is not evident in the studied case.

Though there are no typical facial dysmorphic features of Aicardi syndrome Americal researchers defined the facial features of the affected females as prominent maxilla, upturned nasal tip, decreased angle of the nasal bridge, sparse lateral eyebrows[20].

Female with Aicardi syndrome may develop vascular malfomations, pigmentary lesions in skin, GIT complications, hormonal imbalances like precocious puberty reported from some a case series [21] .

In the absence of reliable genetic or biochemical marker diagnosis of Aicardi syndrome based on clinical and neuroradiological grounds, so female child with recurrent seizure in early infancy especially with infantile spasm should be evaluated properly with neuroradiologically and ophthalmologically to exclude Aicardi syndrome. Most of the reports considered vigabatrin as the first line antiepileptic drugs for the treatment of infantile spasm. Multidisciplinary team approach for the management of Aicardi syndrome is very much essential for the patients care as well as to give the support to the parents.

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