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Aicardi Syndrome

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Abstract: *A female child aged 8 months presented with features of infantile spasms, partial corpus callosal agenesis and chorioretinal lacunae. She had early onset infantile spasms from 2 months of age. This patient responded well to vigabatrin used over 2 months at our center, after failure of many antiepileptic drugs. This case is reported for its rarity and the classic clinical, electrographic and radiological features particularly in Indian context.*
Keywords: *Aicardi syndrome, split-brain EEG, Infantile spasms, corpus callosal agenesis*

I. Introduction

Aicardi Syndrome (AS) is a clinical triad of infantile spasms, agenesis of the corpus callosum, and distinctive chorioretinal lacunae. These three features are also called classic features of AS. AS is an X linked dominant disorder commonly manifesting in female children, although hemizygous male (Klienfelter syndrome XXY) may also be affected [1,2]. All cases described till now were found to be nonfamilial and were due to sporadic mutations [3]. Till now only two boys were described with AS.

AS was first reported in 1965 by Jean Aicardi [4].

Other Major features are cortical malformations (mostly polymicrogyria), periventricular and subcortical heterotopias, cysts around cerebral third ventricle and/or choroid plexus, optic disc /nerve coloboma or hypoplasia [5].

Supporting features are vertebral and rib abnormalities, micropthalmia, split–brain electroencephalogram (EEG) in the form of dissociated burst suppression between two cerebral hemispheres, gross cerebral hemispheric asymmetry, vascular malformations or vascular malignancies. Presence of all classic features is diagnostic of AS. The existence of any two classic features plus two other major or supporting features is strongly suggestive of diagnosis of AS[5]. The index patient had infantile spasms, agenesis of the corpus callosum, and chorioretinal lacunae which are diagnostic of AS.

Most of these patients have global developmental delay and moderate to severe mental retardation [6]. Seizures are common initial manifestations within first 3 months of life, most frequently as infantile spasms. On-going medically refractory epilepsy with a variety of seizure types develops over time [5].

II. Case Report

This 8 months old female child came with history of episodes of sudden flexion of both upper limbs, neck and lower limbs since the age of 2 months associated with transient staring in upward direction. She used to have recurrent episodes around 4-5 times per day. Relatives noticed that there was a delay in milestones in the form of delayed development of social smile, difficulty in holding neck, rolling over in bed, and inability to sit.

Birth History: She was delivered by Caesarean section for breech presentation, baby cried immediately after birth. There was no cyanosis or jaundice after birth. No maternal infections (negative maternal toxoplasma and cytomegalovirus antibodies) or pregnancy induced hypertension or gestational diabetes.

Drug History: She was started on anti-epileptic (levetiracetam, phenobarbitone) drugs at the age of 2.5 months. Thereafter the frequency of spasms decreased to 4-5 episodes per week.

On examination

No dysmorphic features , vitals stable.

There was no microopthalmia or coloboma. On Fundus examination, chorioretinal 'lacunae' were observed by an ophthalmologist, even before she was brought to our hospital. Visual acuity and hearing were apparently normal; appropriate for the age, but the examination was limited and only gross changes could be noted.

Motor system examination showed normal tone with normal power as per the age, Moro`s reflex, placing reflex were present. Intermittent infantile spasms (Fig1) were present during examination. Child was unable to sit by herself, and when made to sit she tended to slip into the bed backwards.

No skull and spine abnormalities were detected.

Her EEG recorded at age of 4 months (Fig 2) showed high voltage sharp waves followed by burst suppression pattern (modified hypsarrhythmia), EEG at 8 months at our center (Fig 3) showed sharp waves and spikes from right and left hemispheres independently, and this activity was not synchronized. There was splitting of EEG between both hemispheres even in sleep spindles which were asynchronous.

Her magnetic resonance imaging (MRI) of brain showed partially developed corpus callosum (MRI 1,2,3) and high riding 3rd ventricle (MRI 4) as seen in Fig 4.

She was started on vigabatrin at 25 mg/Kg/day in two divided doses, later up-titrated to 50 mg/Kg/day after a few days. After starting the drug, her infantile spasms decreased in frequency significantly.

Diagnosis : Early onset infantile spasms with partial corpus callosal agenesis with EEG splitting (asynchrony between the two hemispheres), with chorioretinal lacunae - Aicardi Syndrome.

III. Discussion

Here we are reporting a case of AS emphasizing on the electrographic and imaging features of this syndrome.

EEG findings reported by Katsuhiro Kobayashi et al[(7)] in AS were hypsarrhythmia with bilateral bursts independently between left and right hemispheres which was also found in our patient. These EEG findings were described as 'Split-brain EEG'.

Donnenfeld found complete agenesis of the corpus callosum in 72% and partial agenesis in 28% of his patients [(2)]. Thin unlayered cortex with diffuse polymicrogyria, nodular heterotopia in periventricular region and in centrum semiovale, besides corpus callosal agenesis were also found in the brains of children with AS. In our patient's MRI we found complete agenesis of corpus callosum and high riding third ventricle, however there was no evidence of cortical or subcortical malformations.

Though AS is rarely reported from India, there are a few case reports of AS which described all classic features [(8)]. In a female child with infantile spasms with onset before 3 months of age one has to consider AS, especially when associated with corpus callosal agenesis and/or chorioretinal lacunae. In these patients MRI imaging of the brain should be performed to look for agenesis of corpus callosum and other malformations.

The most common ophthalmic findings in one study were chorioretinal lacunae, which are punched out lesions in the pigmented layer of retina, and which look like yellowish spots on fundus examination, in 66 (88%) of 75 eyes and optic nerve abnormalities in 61 (81%) of 75 eyes. Other less common findings included persistent pupillary membrane in 4 (5%) of 79 eyes and anterior synechiae in 1 of 79 eyes (1%) [(9)].

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Fig 1.

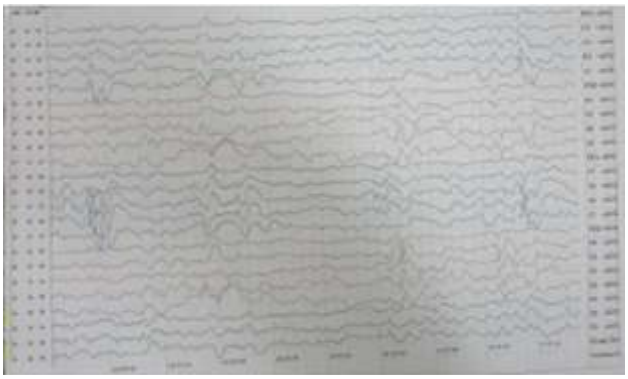

Fig 2

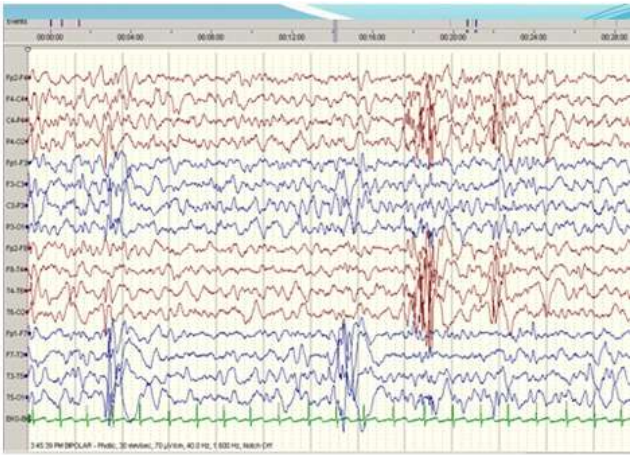

Fig 3

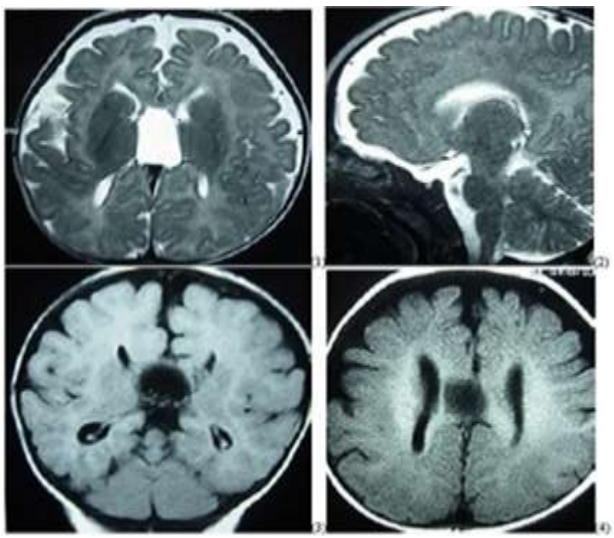

Fig 4

Legends

Fig 1 Eight months old index case
Fig 2 EEG done in another hospital at 4 months of age showing modified hypsarrhythmia pattern
Fig 3 EEG done at 8 months age showing Split-Brain EEG pattern
Fig 4 MRI brain at 8 months age

1. T2 WI axial section showing agenesis of corpus callosum
2. T2 WI sagittal section showing agenesis of corpus callosum
3. T1 WI axial section showing agenesis of corpus callosum
4. T1 WI axial section showing high riding cyst-like third ventricle