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ASD, Anophthalmia and Aicardi Syndrome

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Abstract:

Aicardi syndrome is a rare genetic disorder, X linked dominant; the syndrome is almost exclusively seen in females. It is characterized by classic triad of agenesis of corpus callosum, infantile spasm, and chorioretinal lacune. We report a case of this rare disorder, two and half month old female child who presented with frequent episodes of seizures and multiple congenital anomalies. Examination revealed microcephaly, anophthalmia, cleft lip and palate and atrial septal defect (ASD). MRI revealed agenesis of corpus callosum and dilated ventricular system. In this paper we present a case of Aicardi Syndrome associated with anophthalmia and ASD which were not reported before. She was put on clonazepam and was having a good seizure control.

Key word: Aicardi Syndrome-ASD-Anophthalmia.

Introduction:

In 1965, a French neurologist, Dr.Jean Dennis Aicardi, described 8 children with spasm in-flexion, total or partial agenesis of corpus callosum and variable ocular abnormalities⁽¹⁾. And additional seven patients were described in 1969, and in 1972, Dennis and Bower established the Aicardi Syndrome designation.⁽²⁾

Aicardi Syndrome is typically characterized by the triad of feature: 1- Partial or complete absence of corpus callosum in the brain (agenesis corpus callosum); 2- Eye abnormality and 3- Infantile spasm. However one of the classic features being missing, does not preclude a diagnosis of Aicardi syndrome, if other supporting features are present⁽³⁾. Other types of defects of the brain such as microcephaly, porencephalic cyst and enlarged cerebral ventricles due to hydrocephalus are also common in Aicardi syndrome.⁽³⁾ Craniofacial features include hemi facial asymmetry, microphthalmia and cleft lip and palate also occur with increased frequency. Vertebral body abnormalities and abnormalities of neuronal migration are additional characteristics of Aicardi syndrome.⁽⁴⁾

The absolute restriction of the syndrome to the female sex was ascribed by Aicardi to the presence of single dominant gene on the X chromosome which is produced by spontaneous mutation and is lethal to the male.⁽¹⁾

Concerning imaging studies neuroimaging can delineate the degree of CNS dysgenesis and help evaluate other potential etiologies of intractable epilepsy and developmental delay⁽⁵⁾. EEG studies may reveal hypsarrhythmia which is characteristics of the spasm of Aicardi syndrome⁽⁶⁾. MRI pictures of the patient revealed the presence of genu associated with agenesis of the rest of corpus callosum⁽⁶⁾. Prenatal sonography may be used to reliably diagnose corpus callosum anomalies⁽⁷⁾. Fundoscopic examination revealed Chorioretinal lacunae.⁽⁶⁾

Case report:

A two and half-month-old female child was admitted to Ribat University hospital for evaluation of her multiple congenital anomalies. There was a history of frequent episodes of seizures since one month of age.

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Each episode recurred nearly two to three times per day. She was the fourth child to a consanguineous marriage. She was an outcome of full term pregnancy and normal delivery at hospital. There was no history of jaundice, fever or convulsion in the immediate neonatal period.

On examination the head circumference was 33 cm (below 3rd centile), micro cephalic, length 45cm (below 3rd centile) and her weight also below 3rd centile (2.3 kg) (Figure 1). Ophthalmic examination revealed bilateral anophthalmia, confirmed by eye U/S (Figure 2). On cardiovascular examination there is fixed splitting of the second heart sound and ejection systolic murmur at the upper to middle area of the left sternal border.

Echocardiography revealed ASD. As the child had seizures, electroencephalography (EEG) was done. It showed hypsarrhythmia pattern (infantile spasm). MRI of the child revealed agenesis corpus callosum, dilated ventricular system. This patient diagnosed as Aicardi syndrome: based on: Agenesis of corpus callosum, infantile spasm, anophthalmia, dilated ventricles system, cleft lip and palate, microcephaly (Figures 3 A & B).

She was put on anti-epileptic medication clonazepam and showed a good seizure control.



Figure (1): Show the desmorphic features of the child

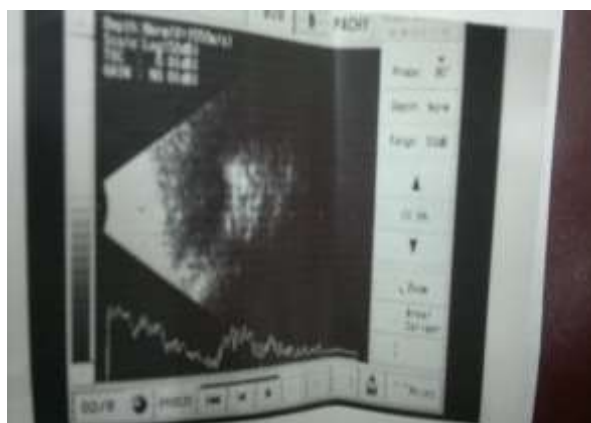
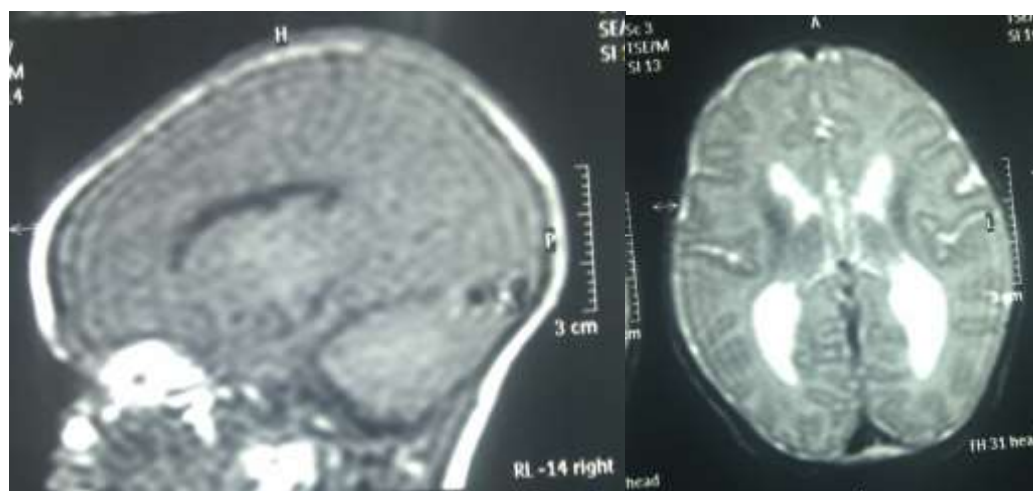


Figure (2) Eye ultra-sound

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Discussion:

The diagnosis of Aicardi syndrome is mainly based upon the elastic triad of infantile spasm, agenesis of corpus collosum and chorioretinal lacune ⁽¹⁾. MRI pictures of the patients revealed the presence of genu associated with agenesis of the rest of corpus collosum and dilated ventricular system ⁽⁶⁾, which was seen in our case.



3-a

3-b

Figure (3) A & B: MRI of the child

Infantile spasm typically starts in early childhood, dissociated burst suppression or burst suppression pattern appearing asymmetrically in cerebral hemisphere is a characteristic EEG finding in this syndrome. This reveals a pattern characteristic of the spasm of Aicardi syndrome called hypsarrhythmia ⁽⁶⁾, which was seen in our case. Chorioretinal lacune are well defined, multifocal pale areas with minimally pigmented borders and they are usually clustered around the optic disc, which was not seen in our case, because this case presented with anophthalmia which was not reported before as one of the associations of Aicardi syndrome. Other ocular abnormalities reported are optic nerve hypoplasia, optic disc pigmentation, microphthalmos, retrobulbar cyst, retinal detachment, macular scars, cataract, iris colobom⁽⁹⁾. Reported skeletal abnormalities were costovertebral malformation such as hemivertebrae, fusion of vertebrae, kyphoscoliosis, absent or malformed ribs ⁽⁶⁾. However, none of these findings were detected in our case. Occasionally cleft lip and palate may also be associated with Aicardi syndrome ⁽⁶⁾, and these findings were detected in our case.

Cardiovascular examination and echocardiography were done in our case and revealed ASD, which also was not reported before as one of association of Aicardi syndrome. Most of Aicardi syndrome cases die at an early age due to aspiration pneumonitis, but some do live up to adolescent years and even into their twenties⁽¹⁰⁾. ACTH, prednisone, valproic acid and clonazepam have been used as antiepileptic medication with variable success⁽¹¹⁾. In our case we used clonazepam which showed good seizure control.

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In conclusion, Aicardi syndrome should be put in mind while investigating female child with recurrent seizures in early childhood. The case presented here is apparently the first one to report child with Aicardi syndrome associated with ASD and anophthalmia.

Acknowledgement

Authors would like to thank Dr. Ahmed Fahmi, Dr. Ahmed Obed, Dr. Mona Awad, Dr. Hwida Almaki, Dr. Walaa Mohamed and Dr. Mazin Mohamed for their help to diagnose this patient.

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