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Aicardi syndrome

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ABSTRACT Aicardi syndrome is a rare neurodevelopmental disease characterised by congenital chorioretinal lacunae, corpus callosum dysgenesis, seizures, polymicrogyria, cerebral callosum, chorioretinopathy and electroencephalogram abnormality. We present a case of Aicardi syndrome with callosal hypogenesis in a 4.5-month-old baby who presented with infantile spasms. Ophthalmoscopy revealed chorioretinal lacunae. The clinical and magnetic resonance imaging features were diagnostic of Aicardi syndrome.

Keywords: Aicardi, callosal dysgenesis, chorioretinal lacunae, infantile spasms
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INTRODUCTION

Aicardi syndrome is defined by the triad of infantile spasms, agenesis of the corpus callosum and chorioretinal lacunae. Central nervous system (CNS) abnormalities are the key components of the phenotype, and these include callosal dysgenesis, polymicrogyria, cerebral heterotopias, intracranial cysts and occasionally, cerebellar abnormalities. This syndrome has been described only in females and 47, XXY males.[1] We present a case of Aicardi syndrome in a 4.5-month-old female infant, along with a brief review of this rare syndrome.

CASE REPORT

A 4.5-month-old baby girl presented to our outpatient child neurology clinic with a ten-day history of flexion spasms of the body. She used to have a cluster of 10–15 spasms soon after waking up from sleep. The spasms lasted for a brief period of time and were associated with brief upturning of the eyes and crying. After the spasms ceased, the child would remain irritable for about one hour. She was the second child born to non-consanguineous parents by Caesarean section after full-term pregnancy. She suffered no perinatal asphyxia or other problems. Developmental history revealed social smile at three months and head control at four months. Family history was positive for epilepsy in an aunt.

On examination, the infant was awake and alert. She had poor eye contact but appeared to follow things. Physical examination was normal and no neurocutaneous markers were noted. There was no organomegaly. Neurological examination revealed hypotonia with retained deep tendon reflexes. Ophthalmic examination revealed the presence of multiple small discrete depigmented chorioretinal lesions in both eyes, with the largest one in the left eye superior to the optic disc, which was suggestive of chorioretinal lacunae. Electroencephalogram (EEG) revealed poorly organised background with large-amplitude slow waves and multifocal spikes suggestive of hypsarrhythmia.

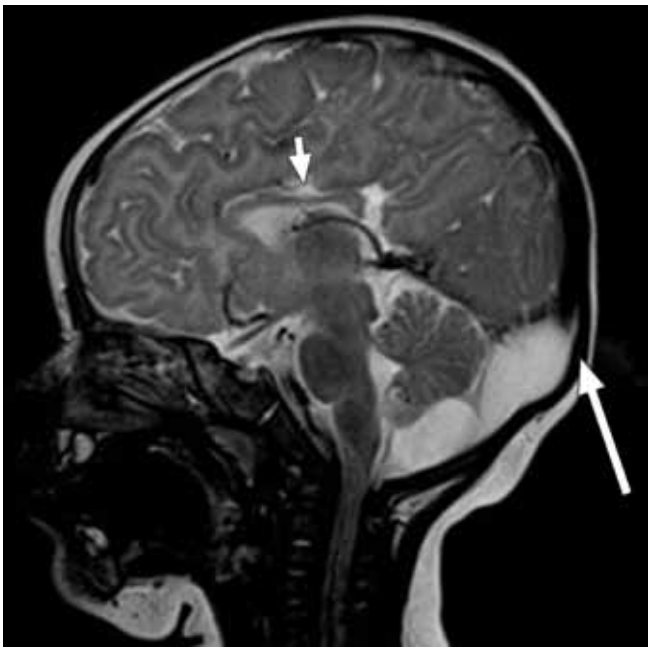

Fig. 1 Sagittal T2-W MR image shows hypogenesis of the corpus callosum (arrowhead), especially in the region of the body with extra-axial cysts (arrow) in the posterior fossa.

Magnetic resonance (MR) imaging of the brain was performed (Figs. 1–4).

Sagittal T2-weighted MR image revealed hypogenesis of the corpus callosum, more so in the region of the body with extra-axial cysts seen in the posterior fossa (Fig. 1). Axial inversion recovery MR images indicated the possibility of multiple small gyri (polymicrogyria) in the bilateral frontal lobes (Fig. 2), as well as widely separated bodies of lateral ventricles with an interhemispheric cyst and periventricular nodular subependymal grey matter heterotopia along the body of the left lateral ventricle (Fig. 3). Multiple extra-axial cysts were also seen on the sagittal T2-weighted MR image, with one of them abutting the body (arrow) of corpus callosum (Fig. 4). Clinical and MR imaging findings were diagnostic of Aicardi syndrome. The patient was started on antiepileptic drugs, including oral

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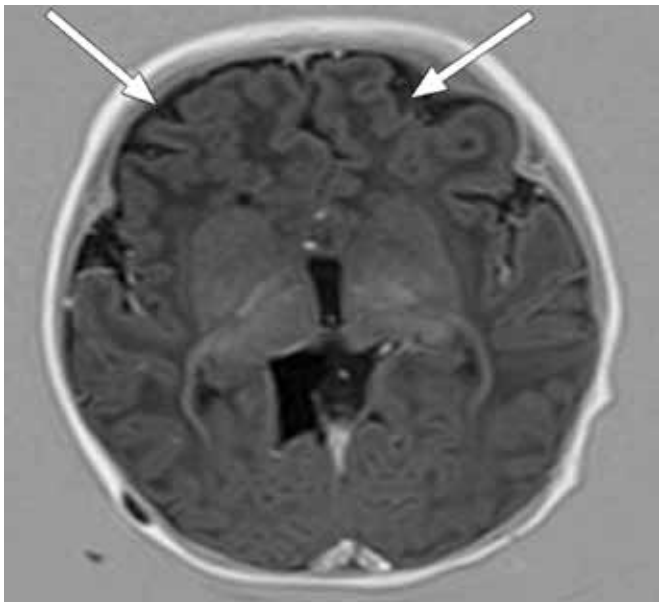

Fig. 2 Axial inversion recovery MR image shows multiple small gyri (polymicrogyria) in the bilateral frontal lobes (arrows).

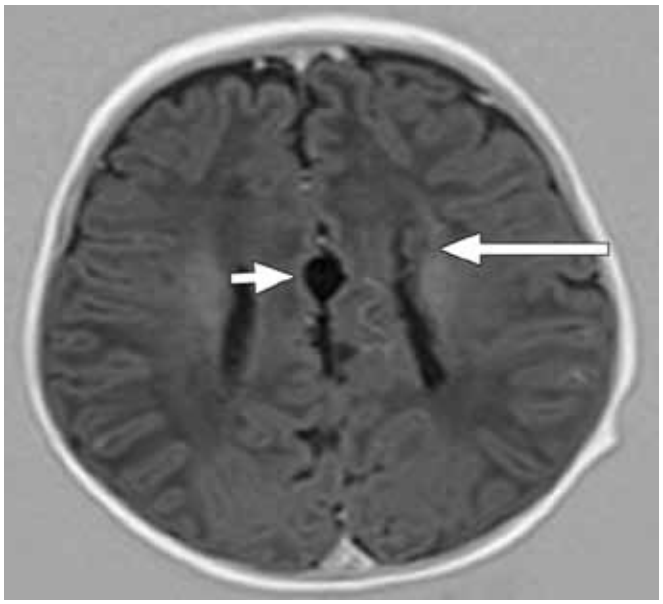

Fig. 3 Axial inversion recovery MR image shows widely separated bodies of lateral ventricles with an interhemispheric cyst (arrowhead) and periventricular nodular subependymal grey matter heterotopia (arrow) along the body of the left lateral ventricle.

corticosteroids. Follow-up four weeks later showed a marked reduction in spasms. Spine radiographs were advised, as scoliosis and segmentation abnormalities of the vertebrae and ribs might be associated with this condition. The patient was on regular follow-up with the paediatric neurologist at the time of this writing.

DISCUSSION

The presence of the classical triad of infantile spasms, dysgenesis of the corpus callosum and chorioretinal lacunae is diagnostic of Aicardi syndrome. The presence of two classic features plus at least two other major or supporting features is highly indicative of the diagnosis. Major features include polymicrogyria or pachygyria, intracranial cysts, heterotopias (periventricular and subcortical) and optic disc, retinal or choroidal coloboma. Vertebral and rib anomalies, 'split brain' EEG and microphthalmia are included in the supporting features.[1-3] Our patient did not have complete agenesis of the corpus callosum, which may not be present in all the cases, but had two other classical and three major features, thus confirming the diagnosis. This syndrome is assumed to be caused by a dominant mutation in an X-linked gene, as it is seen only in females and 47, XXY males, with lethality in 46, XY males.[1]

Neurological abnormalities include microcephaly, developmental delay, mental retardation, intractable (medically refractory) epilepsy, axial hypotonia and limb hypertonia with spasticity.[1,4] Classical craniofacial features that have been described include a small philtrum with upturned nasal tip and decreased angle of the nasal bridge, big ears, prominent premaxilla and sparse eyebrows on lateral aspects, but these were not present in our case.[3] Skeletal anomalies such as fused vertebrae, hemi-vertebrae, blocked vertebrae and absent ribs could be present, which may lead to scoliosis.[5] Undersized hands have also been reported.[3] An increased incidence

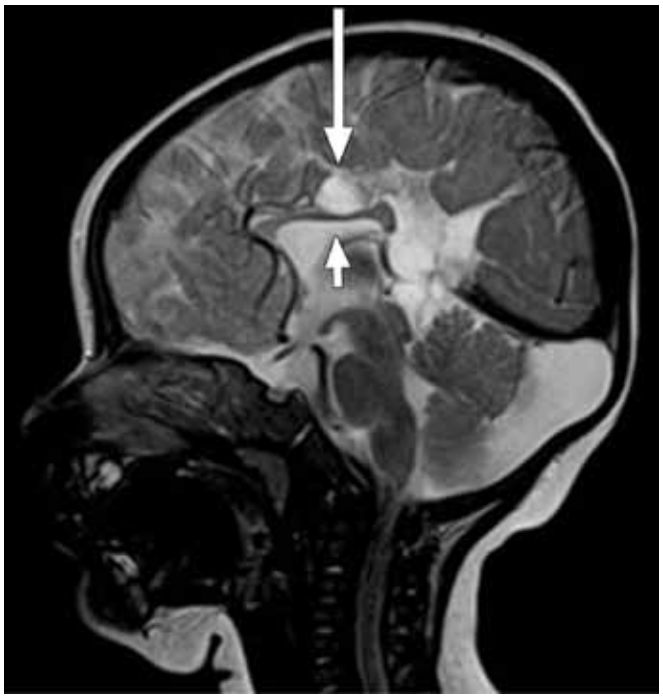

Fig. 4 Sagittal T2-W MR image shows multiple extra-axial cysts, with one abutting the body (arrow) of the corpus callosum (arrowhead).

of dermatologic vascular malformations and pigmentary lesions, intracranial tumours like choroid plexus papillomas, gastrointestinal complications and hormonal imbalance leading to precocious puberty or delayed puberty have also been reported.[3,6,7]

CNS abnormalities are the most important constituent of this syndrome. Hopkins et al[8] performed a comprehensive categorisation of abnormalities identified on MR neuroimaging studies from 23 girls with Aicardi syndrome and found that all patients had polymicrogyria (predominantly frontal and

perisylvian), periventricular nodular heterotopias and intracranial cysts.[8] All these features were also present in our case. Although underdevelopment of the operculum, cerebral asymmetry and ventriculomegaly are also frequently present, they were not seen in our case. Posterior fossa abnormalities include unilateral hypoplasia or dysplasia of the cerebellar hemispheres with associated large cisterna magna, hypoplastic cerebellar vermis, cerebellar heterotopias, cerebellar intraparenchymal and extra-axial cysts and tectal enlargement. Tectum can be measured in the mid-sagittal plane. Cutoff values for tectal enlargement are length > 15 mm and width > 5 mm.[8] Out of the posterior fossa abnormalities described above, only mega cisterna magna and extra-axial cysts were present in our case. The occurrence of cyst wall contrast enhancement in most intracranial cysts mimics the contrast enhancement seen in the choroid plexus, which can also contain papillomas in Aicardi syndrome, possibly suggestive of a common origin of these findings.[8] Since mildly affected patients who have partial callosal agenesis and a patient with normal corpus callosum with Aicardi syndrome have been reported, this suggests that callosal agenesis may not be present in all cases, as was seen in the present case.[4,9]

In conclusion, agenesis of the corpus callosum in association with cysts that do not communicate with the ventricles and the existence of heterotopias, polymicrogyria and chorioretinal lacunae are quite specific, with the latter regarded as virtually pathognomonic for Aicardi syndrome, even in the absence of callosal agenesis.[10,11] However, callosal agenesis, polymicrogyria and heterotopias may occur as isolated malformations or associated with other syndromes or chromosomal abnormalities.[1] Aicardi syndrome carries a bad prognosis due to its association with medically intractable seizures and mental retardation.[12]

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