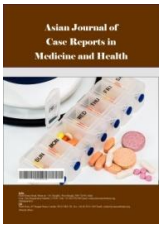

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The Aicardi Syndrome: Case Report about a 3-month-old Infant

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Authors' contributions

This work was carried out in collaboration among all authors. Authors OB and AR designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors OB and AR managed the analyses of the study. Author OB managed the literature searches. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Aicardi syndrome, exclusively occurring female patient, was originally characterized by triad: agenesis of the corpus callosum, distinctive chorioretinal lacunae, and infantile spasms. Besides the triad, several other findings are present in patients with this condition. We here shortly report the case of a 3-month-old female infant with Aicardi syndrome, who had non-consanguineous parents. Triad was seen: infantile spasm with abnormal EEG, agenesis of corpus callosum revealed by MRI, and chorioretinal lacunae of the posterior pole. We diagnosed this condition as Aicardi syndrome. After treatment with vigabatrin and psychomotor sessions at the age of 3 months, it is noted that the attacks were reduced and psychomotor development was normal at the age of 5 months. We summarized the clinical characteristics of this syndrome based on the literature survey.

Keywords: Agenesis of the corpus callosum; chorioretinal lacunae; spasms.

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1. INTRODUCTION

Aicardi syndrome (AS) is characterized by a triad: agenesis of the corpus callosum, distinctive chorioretinal lacunae, and infantile spasms. The etiology of Aicardi syndrome is unknown; however, the disorder is almost always seen in females and is thought to be a de novo mutation on the X-chromosome with hemizygous lethality in males [1]. There are reports of males affected with Klinefelter syndrome (XXY genotype) [2] and an isolated case of a XY genotype with Aicardi syndrome [3]: these patients show atypical findings. The syndrome is rare with age-adjusted prevalence of 0.63 in 100,000 female births [4,5]. There are no identified maternal risk factors. We here briefly report a case of this syndrome. We summarized the clinical characteristics of this syndrome, which may be useful for care-givers dealing with patients having this syndrome.

2. CASE REPORT

We report the case of a 3-month old girl from non-consanguineous parents. The patient was born through a normal delivery, and the physical examination was normal at birth. The patient was asymptomatic during the first 2 months of life. there was no family history of childhood epileptic disorder, having presented flexion spasms and abnormal eye movements 15 days ago. Antiepileptic agents have been shown to be ineffective in controlling seizures. On physical examination, the head circumference was 39 cm and cognitive studies showed normal psychomotor development. Examination of the fundus revealed a chorioretinal gap in the left posterior pole respecting the fovea, measuring ¼ of the papillary diameter. The EEG showed asymmetric background activity, theta on the right and slow on the left with an aspect of SPLIT BRAIN. Cerebral MRI showing a separation of the lateral ventricles with colpocephaly in connection with agenesis of the corpus callosum (Fig. 1). Skeletal radiography and abdominal ultrasound were normal.

After treatment with vigabatrin and psychomotor sessions at the age of 3 months, it is noted that the attacks were reduced and psychomotor development was normal at the age of 5 months.

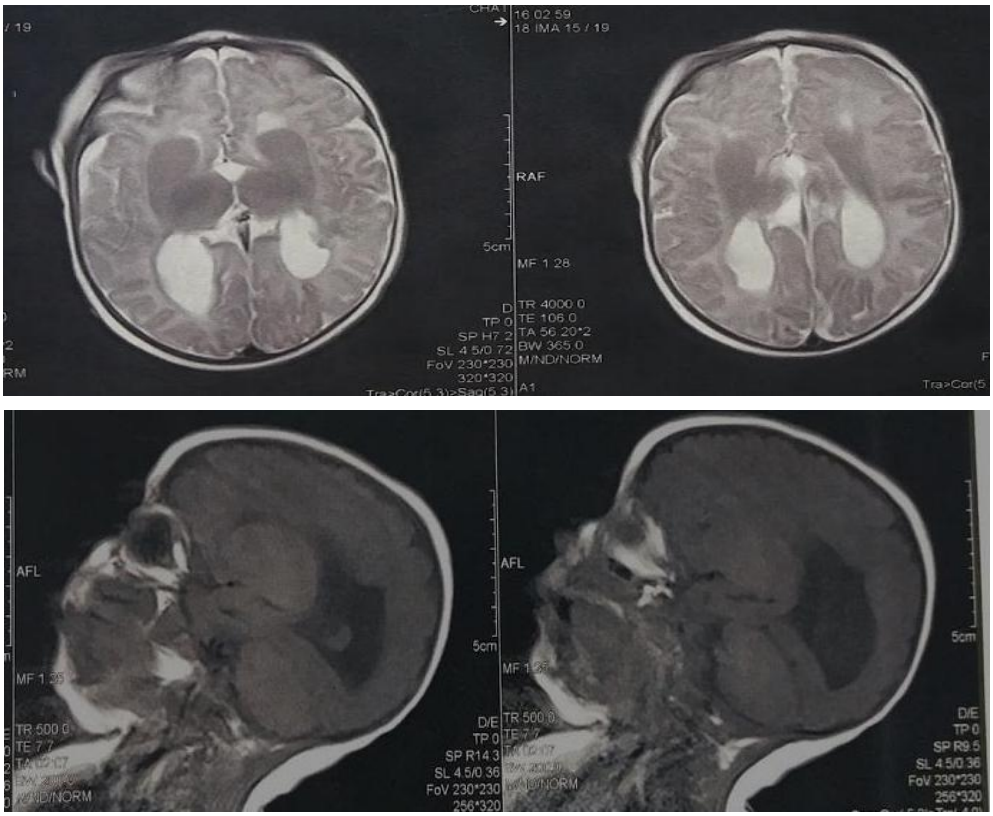

Fig. 1. Cerebral MRI showing a separation of the lateral ventricles with colpocephaly in connection with agenesis of the corpus callosum

3. DISCUSSION

Aicardi syndrome, first described by Aicardi et al. [6], is a neuro developmental disorder that mainly affects women [1,7,8]. Initially, it was characterized by a typical triad of agenesis of the corpus callosum, typical chorioretinal gaps and infantile spasms [6,9]. However, as more and more cases have been reported, it has become clear that other neurological and systemic defects are common. Indeed, not all affected girls have the three characteristics of the classic triad.

Neurological examination can reveal microcephaly, axial hypotonia and appendicular hypertonia with spasticity often affecting one side and deep and rapid tendon reflexes as well as hemiparesis, which is not the case in our patient [1]. Moderate to severe developmental delay and intellectual disability are expected, but people with only mild or no learning disabilities or developmental delay have been reported [10-15].

Many girls with Aicardi syndrome develop seizures before the age of three months, and most before the age of one year. Infantile spasms are observed early, but medically refractory epilepsy continues with a variety of types of seizures develops over time. Common EEG results include asynchronous multifocal epileptiform abnormalities with suppression of bursts and dissociation between the two hemispheres.

The MRI reveals a dysgenesis of the corpus callosum, which is most often complete, but can be partial, which is observed in our case [7,16]. Polymicrogyria or pachygyria, which are mainly frontal and perisylvian and associated with under-sealing, are typical. Periventricular and intracortical heterotopia of gray matter is very common. Macroscopic cerebral asymmetry, papillomas of the choroid plexus, ventriculomegaly and intracerebral cysts, often in the third ventricle and in the choroid plexus, are frequently present [1,17]. Recently, posterior fossae and cerebellar abnormalities are increasingly recognized as important components of the phenotype [17,18].

The pathognomonic chorioretinal gaps of Aicardi syndrome are white or yellow-white, well circumscribed, round and depigmented areas of the retinal pigment epithelium and the underlying choroid with variable pigmentation at their borders [16,19,20] which can be grouped in the posterior pole of the globe around the optic nerve, this is the case of our patient. The sensory retina covering the gaps is generally intact but can be disorganized or completely absent.

Donnenfeld et al. interviewed ophthalmologists to determine the incidence of various ophthalmologic findings in Aicardi syndrome [16]. Although these figures may be useful, clinicians should be aware that these data come from several ophthalmologists and that, historically, chorioretinal gaps have been the sine qua non condition for the diagnosis of Aicardi syndrome, even in the absence of dysgenesis. of the corpus callosum [19-21]. The reported incidences of ophthalmological results in 18 patients:

- Perforated chorioretinal gaps, 100% (18/18)
- Unilateral microphthalmia, 33% (6/18)
- Coloboma of the optic nerve, 17% (3/18). Colobomas usually involve the optic nerve, choroid and / or retina, but almost never the iris.
- Nystagmus, 6% (1/18)
- Detached retina, 6% (1/18)

Other eye discoveries include severe optic nerve dysplasia, optic nerve hypoplasia, and persistent fetal vascularization (formerly known as persistent hyperplastic primary vitreous). All ocular findings can be unilateral or bilateral and asymmetrical.

Characteristic facial features reported in Aicardi syndrome include a short philtrum, a prominent premaxilla with the resulting inverted nasal tip and a narrowed angle of the nasal bridge, large ears and sparse lateral eyebrows [22]. Plagiocephaly and facial asymmetry, occasionally with cleft lip and palate (3%), have been reported. The Pierre-Robin sequence has been reported in only one case [23]. None of these Characteristics were reported in our case.

Costovertebral defects, such as hemivertebrae, blocked vertebrae, fused vertebrae and missing ribs, are common and can lead to marked scoliosis in up to a third of those affected [16]. Hip dysplasia has been reported. none of thesedefects were found in the squellet radiography of our case.

Constipation, gastroesophageal reflux, reflux, diarrhea and feeding difficulties are perceived by parents as the second most difficult problem to manage after seizures [24]. None of these symptoms were reported in our case.

Small hands, as well as an increased incidence of hand deformities, have been reported [22]. An increased incidence of vascular malformations and pigmented lesions has been observed [22]. none of these disorders were found in our case.

The incidence of tumors may be increased. The most common tumors are papillomas of the choroid plexus [25,26]; however, lipomas, angiosarcomas, hepatoblastomas, intestinal polyposis and embryonic carcinomas have also been described [22,27]. Large cell medulloblastoma has been reported in only one case [28].

Average height and weight of girls with Aicardi syndrome closely follows that of the general population up to the age of seven and nine, respectively, after which the growth rate for height and weight is lower. The growth charts for Aicardi syndrome based on data from the parent survey have been published. The weight / height ratio remains similar to that of the general population [24].

An investigation has not documented microcephaly, but objective measurements at one point suggest that microcephaly is occurring [24].

Early puberty or delayed puberty may be present [24].

Survival from Aicardi syndrome is very variable and probably depends on the severity of the attacks. In an investigation by Glasmacher et al [24], the average age at death was 8.3 years, although the median age at death was 18.5 years. The ages of death were distributed before the age of one year to over 23 years. The oldest surviving individual reported in this survey was 32 years old. Another article also reported that survival is longer than previously reported, particularly in those with less severe disease, with the highest risk of death at 16 and a probability of survival at 27 of 0,62 [29]. A 49-year-old woman with a mild form of the syndrome has been reported.

For the differential diagnosis, convulsive disorder may be significant and may appear to be associated with Dandy-Walker syndrome, corpus callosum agenesis, neuronal migration disorders, Lennox-Gastaut syndrome (LGS), lissencephaly, West syndrome and cyclin-dependent kinase type 5 (CDKL5). Small gaps or gaps may appear in ocular toxoplasmosis or chorioretinopathy seen in microcephaly with or without chorioretinopathy, lymphedema or mental retardation (MCLMR). Chorioretinal deficiencies have been described in orofaciodigital type IX syndrome (OFD 9), but this syndrome is different from AS clinically. In the case of microphthalmia, microphthalmia with linear skin defect syndrome (MLS) can be considered.

Regarding patient management, a pediatric neurologist specializing in the management of infantile spasms and medically refractory epilepsy is essential for the long-term management of seizures.

People with Aicardi syndrome usually need multiple antiepileptics (AEDs) for adequate seizure control. An improvement in results with vigabatrin [11] and vagus nerve stimulators has been reported, which is the case for our patient. however, these treatments do not work for everyone [8,22].

Physical therapy, occupational therapy, speech therapy, and vision therapy should begin at diagnosis stage to ensure the best functionality and developmental outcome possible. An individualized therapy plan should be developed and implemented by the therapists and caregivers.

Resection of large choroid plexus papillomas has been reported for management of hydrocephalus [25]. Improvement of seizures was also noted in the individual reported. Whether this improvement was related to resolution of the hydrocephalus or whether the choroid plexus papillomas may have been epileptogenic is not clear.

Spasticity could be resulted in contractures or limited range of motion affectingnot only the mobility but as wellhygiene care. Patient benefit from evaluation by physicians specializing in physical medicine and rehabilitation as well as physical, occupational, and speech therapists [30]. Costovertebral defects can lead to scoliosis. Appropriate musculoskeletal support and treatment for prevention of scoliosis-related complications is indicated.

Table 1. Disorders can be associated with aicardi syndrome

Disorder	Type
Characteristic facial features	Short philtrum, Prominent premaxilla,the resulting inverted nasal tip,a narrowed angle of the nasal bridge,Large earsSparse lateral eyebrows Plagiocephaly and facial asymmetry, Cleft lip and palate.
Costovertebral defects	Such as hemivertebrae,Blocked vertebrae, Fused vertebrae and missing ribs, Scoliosis,Hip dysplasia,Small hands, hand deformities
Gastroenterology	Constipation,Gastroesophageal reflux, Diarrhea and feeding difficulties
Tumors	Papillomas of the choroid plexus,Lipomas,Angiosarcomas, Hepatoblastomas,Intestinal polyposis Embryonic carcinomas, Medulloblastoma,

Constipation and gastrointestinal problems are frequent and require ongoing management at regular physician visits.

For Surveillance, The following are appropriate:

- Routine dermatologic evaluation to monitor for vascular and other malignancies.
- Monitoring for and treatment of gastrointestinal complications at regular physician visits.
- Regular monitoring of the spine to assess the degree of scoliosis.

4. CONCLUSION

Aicardi syndrome is a dominant X-linked genetic disorder. The diagnosis is based on clinical signs, brain MRI, and skeleton X-ray. Physiotherapy, occupational therapy, re-education of language and vision must start early. Appropriate restraint and preventive treatment of costovertebral complications are recommended.

CONSENT

As per international standard, parental written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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