Aicardi’s Syndrome: A Case Report

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Aicardi’s syndrome consists of infantile spasms, defects of the corpus callosum, dorsal vertebral anomalies, and chorioretinal lacunar defects. The etiology is, as yet, unknown. The most likely cause, however, is an X-linked mutational event that is lethal in males. This paper presents a girl 3 years 8 months old with Aicardi’s syndrome who received corticotropin therapy for intractable seizures. Brain magnetic resonance imaging (MRI) of this girl revealed typical findings of dysgenesis of the corpus callosum, hypoplasia of the inferior vermis, and obvious heterotopic nodular gray matter over the lateral wall of the left lateral ventricle. The above findings associated with the ophthalmic finding of chorioretinal lacunar defect, a clinical history of mental subnormality, and electroencephalographic pattern could be well correlated with a confident diagnosis of Aicardi’s syndrome. Thus, we suggest that MRI is essential in establishing this diagnosis. In addition, while corticotropin therapy reversed the EEG abnormality, it has had no immediate effect within short-term (1-month) follow up.

Key words: Aicardi’s syndrome; Magnetic resonance imaging, corticotropin

In 1965, Aicardi described a syndrome consisting of infantile spasms, chorioretinopathy, agenesis of the corpus callosum, costovertebral anomalies, and mental subnormality [1, 2]. By 1979, more than 100 cases had been reported in the medical literature [3, 4]. All the described patients were females. In this report, we highlight the MRI impact on the differential diagnosis and our experience with corticotropin treatment.

CASE REPORT

A 3-year-8-month-old girl was admitted for evaluation of intractable seizures. The girl was born after a normal pregnancy and delivery to a 25-year-old mother with no alcohol ingestion or previous miscarriages. The father was 30 years of age, and there was no consanguinity. Birth weight was 2900 g. The family history was non-contributory.

At 2 months of age, the infant began to have abrupt episodes of flexion spasms after a vaccination (diphtheria, pertussis, tetanus) that recurred frequently throughout the day. Seizures were described as generalized with uprolling eyes and spasmodic flexion of the legs. She was studied at another hospital using brain MRI; the report noted hypogenesis of the corpus callosum and left retinal lacunae on ophthalmic examination. Aicardi’s syndrome was diagnosed. Control of the seizures was not achieved with daily 500 mg Valproic acid, 1 g Vigabatrin, 300 mg Lamotrigine, and 200 mg Topiramate. The seizure frequency remained 5 times a day.

The patient had severe psychomotor retardation with speechlessness and even marked mental regression after frequent seizure attacks. She had a severe delayed milestone as she began to stand as late as 3 years 2 months of age. Her body weight was 14 kg at the age of 3 years 8 months.

Results of the patient’s ophthalmic
examination were as follows. Her extraocular movements were full. Mild ptosis of the left lid was noted. Both pupils were 3 mm and equally reactive. A direct fundus examination revealed left optic nerve colobomas with surrounding multiple, discrete chorioretinal lacunae extending out to the periphery.

Dysgenesis of the corpus callosum and hypoplasia of the inferior vermis, a condition referred to as a Dandy-Walker variant, were demonstrated by sagittal view on T1-weighted MRI (TR/TE: 400/25) of the girl's head (Fig. 1). There were cerebral cortical dysplasia and heterotopia seen on T2-weighted MRI (TR/TE: 4000/40), especially in the left frontal region and obvious heterotopic nodular gray matter over the lateral wall of the left lateral ventricle (Fig. 2). Also seen was hypo-opercularization of the bilateral sylvian region. Proton density-weighted (TR/TE: 2800/40) image revealed colpocephaly which is characterized by selective much-greater dilatation of the occipital horns than of the frontal or temporal horns of the lateral ventricles due to loss of surrounding tissue, particularly white matter. In addition, MR images of the orbit demonstrated a seemingly enlarged left retrobulbar optic nerve which could be detected by a partial volume effect with the surrounding fat. There was an additional finding of an abnormal curvilinear line of a T1WI high signal along the posterior pole of the left eyeball which may have been due to subdural effusion or hemorrhage. There was no MRI evidence of coloboma-like retinal defect in this patient despite the ophthalmologist having declared its existence. CSF flow artifacts were also found at the aqueduct of Sylvian and third ventricle which indicated the pulsatile CSF flow (Fig. 2). An interictal electroencephalogram demonstrated right frontal epileptic-form discharge and nonsustained theta wave background. Her blood test results were within normal limits. Her ECG demonstrated sinus arrhythmia, and results of valproic acid drug serum level were within the therapeutic range.

The above observations, including the child's gender, suggested the possibility of Aicardi's syndrome. We did not complete the work-up with a skeletal survey. Chest X-ray was normal. Treatment with corticotropin was begun with daily intramuscular injections of 0.017 mg/kg for 28 days followed by daily oral 10 mg prednisone. Other antiepileptic agents were maintained. Adverse effects such as increased appetite and mild motor weakness in chewing and hand gripping were described 2 days after corticotropin therapy. Fluctuating emotional irritability was noted. Interictal electroencephalogram 24 days after the first dose of corticotropin demonstrated no epileptiform discharge during a short (15-minute) recording period, but it was associated with diffuse low-amplitude beta activity. The frequency of seizures was not reduced at 1-month's follow up.

Figure 1. Sagittal view of cerebral T1-weighted image (TR/TE: 400/25) showing dysgenesis of the corpus callosum in the absence of splenium (black arrow) and hypoplasia of the inferior cerebellar vermis (black arrowhead), a condition referred to as a Dandy-Walker variant. 

Figure 2. Axial view of cerebral T2-weighted image (TR/TE:3196/96) showing diffuse cortical dysplasia, hypo-opercularization of the bilateral cortical dysplasia, heterotopia of the left frontal region, left periventricular nodular heterotopia (white arrow), and colpocephaly with a CSF artifact at the third ventricle (arrows).
DISCUSSION

In 1965, Aicardi described a combination of agenesis of the corpus callosum and infantile spasms with ocular abnormalities which comprises the syndrome that now bears his name [1]. Following that description, Aicardi reviewed 117 cases of infantile spasms and immediately found 8 new cases of the syndrome [4].

Since the first description, more than 100 additional cases have been added [2, 3]. The main pitfall in the diagnostic procedure is the eye examination, since the chorioretinal lacunae may be confused with findings in cases of intrauterine infection, especially in children/infants[5] with congenital toxoplasmosis or cytomegalic inclusion disease. The features of chorioretinal lacunae are considered pathognomonic for Aicardi’s syndrome which can easily be seen in a fundus examination [2, 3]. Nowadays, application of MRI can readily detect dysgenesis of the corpus callosum, hypoplasia of the inferior vermis, cortical dysplasia, and heterotopic gray matter. These MRI findings can easily differentiate the diagnosis of Aicardi’s syndrome from congenital toxoplasmosis or cytomegalic inclusion disease. The defective gene and transcription product have been identified as double cortin [8]. There is no reported linkage between Aicardi’s syndrome and double cortin to date despite its genetic mimicry [9].

On the other hand, colpocephaly was also noted, which is selective, much-greater dilatation of the occipital horn than the frontal or temporal horns of the lateral ventricle due to loss of surrounding tissue, particularly white matter. Colpocephaly may result from a primary malformation like Aicardi’s syndrome which is histologically associated with subcortical heterotopia and defective ependymal lining[9] of the occipital horn. Colpocephaly is also common in many cases of agenesis of the corpus callosum because of absence of the splenium [8]. Colpocephaly has its usual clinical findings of moderate vision loss due to bilateral occipital lobe lesions. But it does not always cause complete blindness. Impaired vision in colpocephaly can be coded as cerebral blindness due to its retrogenticulate location. Occipital lesions of colpocephaly are not accompanied by clinical impairment of pupillary reactivity or optic atrophy [10]. The MRI finding of colpocephaly in Aicardi’s syndrome patients may impact the prognosis of these patients suggesting a major risk of vision loss [9] which will produce great burdens to caregivers. However, we failed to detect visual impairment of this girl, and her speechlessness made clinical assessment impossible; thus more-sensitive tools such as electrophysiological visual evoked potential (VEP) studies may be required.

The convulsive disorder of this patient was consistent with infantile spasms. An EEG done at 3 years 8 months old did not show the typical pattern of hypsarhythmia replaced by right frontal epileptic-form discharge with a theta wave background. Various EEG patterns have been reported in infantile spasms including a burst suppression pattern arising independently from the 2 hemispheres, hypsarhythmia, diffuse lateralized or bilateral shifting and paroxysmal discharges, and diffuse lateralized slowing of intrinsic activity [11]. Thus her interictal EEG finding was not contrary to a diagnosis of infantile spasms. Although corticotropin therapy did reverse this EEG abnormality on the 24th day, it had little effect on seizure control, while the frequency of her seizures remained the same.

With regard to the long-term prognosis, patients with Aicardi’s syndrome-related infantile spasms have only about a 5% to 10% chance of achieving normal or near-normal intelligence while more than 66% have severe disabilities [10]. T2WI-illustrated hypo-opercularization of the bilateral sylvian regions are compatible with clinical observations of developmental delay. Hypo-opercularization as its anatomical implication may have been relevant to her speechlessness and developmental delay such as starting to walk as late as 3 years 2 months of age, while her cortical dysplasia and heterotopia will most likely lead to major learning deficits. Although corticotropin therapy as given to the girl usually controls spasms and reverses EEG abnormalities, it has little effect on the long-term prognosis [10].

A CSF flow artifact was found in her lateral
and third ventricle which indicates a significant CSF flow velocity fluctuation [12]. CSF flow artifacts may reflect the dynamic magnitude of the CSF flow which can be seen in most pediatric patients in this age range [12]. Of course, the dilated third ventricle was due to the dysgenetic corpus callosum. The pulsatile CSF in the enlarged third ventricle is neither specific for this disease, nor contributory to a correct diagnosis.

In conclusion, brain MRI is capable of detecting the broad spectrum of cerebral manifestations in Aicardi’s syndrome. Thus brain MRI is suggested to be essential in establishing this diagnosis. Corticotropin therapy can reverse the EEG abnormalities but has no immediate effect on seizure control, while the frequency of seizures remained the same during 28 days of follow up.

REFERENCES

Aicardi氏症候群：壹病例報告

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Aicardi氏症候群包含了胎兒癲癇，胼胝體缺損，脊椎體畸形以及視網膜嵌板形缺損。其病因為至今未明。然而，X性染色體突變是最常被觀察到的致病因。在此提出一個三歲八個月大的女性病例，其因發癲癇住院接受皮質酮刺激素治療我們在此病患之腦部磁振造影中可找到典型的病兆包括胼胝體缺損，小腦蚓部缺損及多發性大腦皮質移行不良。根據這些影像發現再佐以眼底檢查所見之視網膜嵌板形缺損以及臨床之智能障礙及腦波異常發現將可有效診斷此一症候群。據此，我們認為腦部磁振造影對此疾病診斷是必要的。此外，我們所給予的皮質酮刺激素治療雖然減少了腦波上的異常，但是在後續28天的追蹤中卻不見癲癇頻率有效的降低。

關鍵詞：Aicardi氏症候群，腦部磁振造影，皮質酮刺激素