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Choroid Plexus Papilloma Expansion Over 7 Years in Aicardi Syndrome

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Abstract

Choroid plexus papillomas have been reported in Aicardi syndrome. Management of these tumors is controversial because their natural progression in Aicardi syndrome has only been rarely documented. This report describes the progression of such a tumor over 7 years in a girl with Aicardi syndrome. A magnetic resonance imaging study at 2 months of age demonstrated a right ventricular mass that was consistent with a unilateral choroid plexus papilloma. The mass enlarged over the next 7 years without causing any clinically apparent symptoms, ventricular enlargement, hydrocephalus, or mass effect. The tumor was removed without change in behavior or development. The known cases of Aicardi syndrome associated with choroid plexus papillomas are reviewed. The heterogeneous nature of this lesion is highlighted.

Keywords

Aicardi syndrome; choroid plexus papilloma

Aicardi syndrome (AS) is an X-linked dominant syndrome, almost exclusively affecting females. It is primarily defined by the triad of infantile spasms, corpus callosum agenesis, and pathognomonic chorioretinal abnormalities (lacunes). Choroid plexus papillomas have been reported in 14 cases of Aicardi syndrome (including this report). As choroid plexus papilloma is a rare tumor, the natural progression is not well characterized in Aicardi syndrome. The case presented below documents the growth of this lesion over a 7-year period. This case is contrasted with previous cases.

Case Report

The child was the nonconsanguineous product of a 23-year-old primigravida. She was born at term by normal spontaneous vaginal delivery with a birth weight of 7 pounds, 11 ounces. The gestation, delivery, and neonatal periods were without complications. The child's development was normal until her first seizure at 2 months of age. At that time, the patient developed right arm and leg rhythmic clonic-tonic activity followed by flexor spasms of the trunk. This seizure

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activity continued for approximately 2 hours until it was controlled with diazepam at a local emergency department.

The child was admitted to the hospital for further evaluation. Physical examination was unremarkable except for a glabella hemangioma, and neurological examination was significant for right upper extremity weakness. An electroencephalogram (EEG) demonstrated abnormalities in the left frontal-central region, including spindle reduction during sleep, paroxysmal sharp waves, and bursts of high-voltage theta. Magnetic resonance imaging (MRI) of the brain demonstrated nearly complete agenesis of corpus callosum, a 1.5-cm midline inter-hemispheric cyst located near the remnant of the corpus callosum, a dysplastic left cerebellar hemisphere associated with a prominent cisterna magna, and a choroid plexus mass adjacent to the trigone of the right lateral ventricle (Figure 1A, B). Funduscopic examination identified punched-out retinal lesions with macula sparing consistent with chorioretinal lacunae.

Phenobarbital was initiated, but occasional persistent seizures continued. Seizures consisted of clonic right limb activity lasting up to 10 minutes usually associated with sleep-wake transitions. By the end of the first year of life, her seizures were controlled with carbamazepine monotherapy. Right hemiparesis improved only after adequate seizure control.

The patient manifested mild developmental delay. She rolled over at 7 months, sat unsupported at 9 months, and walked unaided at 18 months. She demonstrated a delay in acquisition of single words and received speech therapy until 3 years of age. At approximately 6 years of age, the patient developed prominent impulsivity and spontaneous behavioral outbursts. A trial of stimulant medication was unsuccessful. She attended a regular kindergarten class at 6 years of age with a one-on-one assistant and continued into a regular first-grade classroom with assistance. Family history was unremarkable.

At 7 years of age, the patient developed sleep disturbance consistent with night terrors and occasionally complained that her “brain hurt.” An ambulatory EEG revealed bifrontal spike and sharp waves and periodic slowing. However, these abnormalities did not correlate with behavioral outbursts, headaches, or sleep disturbance. A follow-up brain MRI at 7 years of age demonstrated that the choroid plexus papilloma lesion had enlarged. The choroid plexus papilloma had expanded the trigone of the right lateral ventricle but was not associated with hydrocephalus (Figure 1C-F). Dysplastic changes within the left cerebellum were more obvious on this second MRI. Due to the growth of the tumor and the child’s complaints of headache, a craniotomy was performed to remove the choroid plexus papilloma. The surgery was performed without complications, but the child’s behavior and sleep issues remained unchanged.

Discussion

Since Dr Jean Aicardi originally described the triad of infantile spasms, corpus callosum agenesis, and chorioretinal lacunes in 1965,¹ more than 400 cases of Aicardi syndrome have been published. Magnetic resonance imaging studies have identified new features since the original description. Such features include cortical malformation, gray matter heterotopias, choroid plexus cysts, and choroid plexus papilloma.²

The prognosis for children with Aicardi syndrome is generally poor, with intractable seizures and severe developmental delay.³ This report describes one of the few children with a mild form of Aicardi syndrome. The patient manifested only mild developmental delay, performed reasonably well in a regular classroom, and eventually remained with good seizure control. The choroid plexus papilloma was first noted at 2 months of age and demonstrated a rather benign course over the 7-year follow-up period without causing any clearly significant clinical symptoms.

Although choroid plexus papillomas have been previously described in 13 patients with Aicardi syndrome,^{4–15} this is the first case reported in the literature that documents the growth of a choroid plexus papilloma over an extended time in a child with Aicardi syndrome. This report is consistent with the notion that choroid plexus papillomas develop very early in life, possibly congenitally, and progress slowly over many years. This case also emphasizes that choroid plexus papillomas can remain asymptomatic despite growth to a significant size.

Table 1 outlines all of the known cases of choroid plexus papillomas in Aicardi syndrome. All cases listed in Table 1 were reported to have chorioretinal lacunae, agenesis of the corpus callosum, severe developmental delay, and at least 1 choroid plexus papilloma—except for the current report, in which the child only had mild developmental delay, and the case reported by Hopkins,¹² which had normal development and an intact corpus callosum. Dysmorphology and neurological abnormalities are indicated as documented in previous case reports. Keys for the abbreviation are outlined below the table, and each abbreviation is supplemented by an indication whether the abnormalities are lateralized to the left (l), right (r), or bilateral (b). Age of diagnosis is also included and is supplemented with whether the diagnosis was made by autopsy (a), computed tomography scan (c), or MRI scan (m). The outcome column indicates changes that may have occurred after choroid plexus papilloma resection or, in some cases, changes detected by follow-up neuroimaging.

In most cases of Aicardi syndrome, the choroid plexus papilloma lesion is located in only 1 lateral ventricle. Four cases of bilateral choroid plexus papilloma lesions have been reported. Of the 4 cases with bilateral choroid plexus papilloma lesions, only 1 case did not also have the choroid plexus papilloma located in the third ventricle.¹² In this case, no ventricular enlargement was reported; furthermore, the choroid plexus papilloma and ventricle size remained stable over a 2-year period.¹² In the other 3 cases that demonstrated bilateral choroid plexus papilloma lesions, the tumor was large and extended into the third ventricle. All such cases have been associated with at least some form of ventricular enlargement. In the case that only manifested unilateral ventricular enlargement, repeat neuroimaging demonstrated a stable size of the choroid plexus papilloma and the ventricles over a 6-month period.⁹ Bilateral ventricular enlargement was present in the other 2 cases. However, in both cases, staged resection did not improve the ventricular dilatation, and placement of a ventriculoperitoneal shunt was necessary.^{14,15} Although it is not known whether the ventricular dilatation could have been successfully treated without tumor resection, in 1 case, the choroid plexus papilloma lesion quickly increased in size on repeated neuroimaging, requiring urgent treatment.¹⁴

This report documents the association between Aicardi syndrome and choroid plexus papilloma and demonstrates the potential slow, insidious growth of this lesion. This case emphasizes 2 important points. First, this lesion can continue to grow over an extended time span, suggesting that interval neuroimaging should continue for nonresected lesions. Second, this lesion may not necessarily be symptomatic, even when it has enlarged to a significant size. Clearly, the presentation and progression of choroid plexus papillomas in Aicardi syndrome is heterogeneous and is most likely best managed expectantly.

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Figure 1.

The brain magnetic resonance imaging (MRI) at 2 months of age (A, B) depicts the nearly complete corpus callosum agenesis, inter-hemispheric neuroepithelial cyst, and choroid plexus papilloma. The follow-up MRI brain images at 7 years old (C–F) document the slow growth of the choroids plexus papilloma. The lobulated enhancing intraventricular mass is isointense relative to gray matter on T1- and T2-weighted sequences (C, D, and F). The mass expands the trigone of the right lateral ventricle without associated hydrocephalus. Dysplastic changes are also seen within the left cerebellar hemisphere (E).

Reported Cases of Aicardi Syndrome With a Choroid Plexus Papilloma

Table 1

Reference	Dysmorphology	Neurological Abnormalities	Ventricle Location	Diagnosed (months)	Resection	Outcome
Rosser et al ³	MO-r, ONC-l, CRL-l	EP, CD	Not reported	55m-a	No	
de Jong et al ⁴	MC, ONC-b, CRL-b PG-r, MG-r	IS, CD, CH, LS-l,	Left	14m-a	No	
Tachibana et al ⁵	VA	IS	Right and third ventricle	1m-c	2m	Improved seizures
Robinow et al ⁶	CLP, MO-b, mC, PC, VA, ONC	IS, GMH, LVD-b	Left	4m	6m	No change Improved seizures
Nishimura et al ⁷			Third ventricle	2m	2m	No change on computed tomography at 6 and 8 mo
Donnenfeld et al ⁸	PC, EM, VA	IS, CH, LVD-r, GMH, MG	Left, right, and third ventricle	2m-m	Yes No	No choroid plexus papilloma at 6 and 12 mo No change at 2 y HP worse
Hamano et al ⁹						No change in IS Ventriculoperitoneal shunt placed at 14 mo
Trifiletti et al ¹⁰		GMH, CA	Left	54m-m	No	Ventriculoperitoneal shunt placed at 21 mo No change
Aguiar et al ¹¹	MO	IS	Left	5m-m	No	
Hopkins ¹²	ONH-r	IS	Left and right	5m-m	No	
Uchiyama et al ¹³	ONC-l, ONH-r	IS, HP-r	Left	3m-m	Yes	
Taggard et al ¹⁴	ONC-r, ONH-r	EP, VM or LVD-b	All	3m-m	At 3m, 5m, and 11m	
Pianetti et al ¹⁵	Strabismus Colobomas	IS, MC, HC	All	15m-m	16m, 17m, 19m	
Frye	Strabismus, CRL-b	EP, CD	Right	2m-m	7 y	

Dysmorphology key: EM, ear malformations; CLP, cleft lip and palate; ONC, optic nerve coloboma; ONH, optic nerve hypoplasia; MO, microphthalmia; PC, plagiocephaly. Neurology key: MC, macrocephaly; mC, microcephaly; IS, infantile spasms; EP, epilepsy; HC, hydrocephalus; HP, hemiplegia. Brain malformations key: CD, cerebellum disturbances; CH, congenital hydrocephalus; LS, lissencephalia; PG, polygyria; MG, microgyria; CA, cerebral asymmetry; LVD, lateral ventricle dilatation; VM, ventriculomegaly; GMH, germinal matrix hemorrhage; CRL, chorioretinal lacunes