Case 1922

Aicardi syndrome
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Section: Paediatric radiology
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Case Type: Clinical Cases
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Patient: 6 months, female

Clinical History:
Intractable seizures, right anophthalmia, left retrobulbar cyst, optic disc coloboma and chorioretinal lacunae with multiple CNS anomalies including callosal agenesis, choroid plexus cysts and papillomata, polymicrogyria, grey matter heterotopia, and Dandy-Walker malformation.

Imaging Findings:
The patient was referred for evaluation of epilepsy. She was born at 32 weeks gestation. Polyhydramnios was present during the pregnancy. Amniocentesis confirmed a normal female karyotype, thus excluding Patau, Edwards’ and Down syndromes. The neonatal history was uncomplicated. Tonic seizures with back arching started 6 weeks after birth, increased to 8-10 times daily with a duration of 3-12 minutes and worsened despite various medications. On examination right anophthalmia and left proptosis was noted. The patient was below the 3rd percentile for weight, height and occipito-frontal circumference and was hypotonic. She had plagiocephaly and frontal bossing. Fundoscopy revealed a left optic disk coloboma, partial retinal detachment and extensive chorioretinal lacunar defects. In addition, she had a cleft soft palate and a type 1 laryngeal cleft. The electroencephalogram was severely abnormal with an asymmetric burst suppression pattern.

An unenhanced CT of the head was performed at 3 days of age for dysmorphic features and an MRI at 6.5 months for persistence of intractable seizures. Both were reviewed. They showed agenesis of the corpus callosum (Figs 1,2a,b), dilated ventricles with colpocephaly (Figs 2a,3a,4a), lateral and third ventricular choroid plexus papillomata with multiple cysts (Figs 2a,b), an interhemispheric cyst (Figs 3a,b), grey matter heterotopia and polymicrogyria (Figs 4a,b) as well as a Dandy-Walker malformation (Figs 1,2b,4b,5). Right anophthalmia was noted together with a cystic lesion in the left retrobulbar space, which did not communicate with the subarachnoid space (Fig. 5).

Discussion:
This patient presented with multiple CNS anomalies, causing severe psychomotor and mental retardation and intractable seizures as well as major ophthalmological malformations and ENT anomalies. The triad of infantile spasms, callosal agenesis and chorioretinal lacunae (Fig. 6) was described first by Aicardi in 1969 [1]. Associated conditions include Arnold-Chiari malformation, septo-optic dysplasia, ventriculomegaly, gyral anomalies with schizencephaly and grey matter heterotopia as well as delayed and asymmetric myelination. Choroid plexus cysts and papillomata, porencephaly, interhemispheric cysts, midline lipoma, aqueduct stenosis, absent pineal gland, craniosynostosis, scalp lipomas, microphthalmia, optic disc coloboma, retrobulbar encephalocele as well as
vertebral and rib anomalies are also described [1]. Around 200 cases of Aicardi syndrome in children have been reported to date. A broad spectrum of manifestations has been described ranging from relatively indolent cases to very severe presentations [2]. This patient is at the more severe end of this spectrum in view of the extensive nervous system and ophthalmological anomalies.

Aicardi syndrome is a congenital X-linked dominant disorder with heterozygous male lethality, thus it affects girls only [1]. The only male presentation occurred in a boy with an XXY chromosomal karyotype [3]. The chromosomal anomaly is situated on chromosome Xp22 with a breaking point between p22.2 and p22.3. The occurrence is due to a new spontaneous mutation without genetic transmission [4]. No specific test, antenatal or postnatal, exists to date for Aicardi syndrome. Age of onset is in the first few months of life, usually from 3 to 5 months [1]. A more indolent form of this syndrome has been described in a 49-year-old woman with well-controlled epilepsy and mild mental disablement only [2]. The insult occurs between the 12th and 17th week of gestation due to an injury to the commissural plate. Most of the described malformations in Aicardi syndrome originate from this early embryonic period, such as agenesis of the corpus callosum, which is complete in 72% and partial in 28% of patients [4].

The patient in this case was diagnosed with Aicardi syndrome at the age of 6.5 months. This was based mainly on the MRI findings and to a lesser extent on retrospective review of the neonatal CT. The simultaneous presence of major CNS and ophthalmological anomalies led to the correct radiological diagnosis. She also had a cleft soft palate and a laryngeal type 1 cleft.

Interhemispheric cysts have been previously described in Aicardi syndrome [1]. Barkovich et al. established a classification of interhemispheric cysts [5]. They distinguish cysts extending from the ventricular system (type 1) from separately loculated cysts (type 2). Whereas type 2a cysts are not associated with any malformations other than callosal agenesis/hypogenesis, type 2b cysts are associated with deficiencies of the falx cerebrum, grey matter heterotopia and polymicrogyria. These type 2b cysts are specifically identified with Aicardi syndrome [5].

Plagiocephaly was present in this patient but without evidence of craniosynostosis. Vertebral and rib anomalies have been reported in 39% of Aicardi syndrome patients [4], but neither was present in this patient.

In summary, the diagnosis of Aicardi syndrome, even though rare, is important for genetic counselling. The diagnosis is made clinically and based on the presence of seizures (usually infantile spasms), severe mental retardation, callosal agenesis and chorioretinal lacunar defects.

**Differential Diagnosis List:** Aicardi Syndrome

**Final Diagnosis:** Aicardi Syndrome

**References:**

Description: Midsagittal contrast-enhanced T1-weighted image shows agenesis of corpus callosum with high-riding third ventricle. Bulky enhancing choroid plexus is present in the roof of the third ventricle containing papillomata. More posteriorly there is a rim-enhancing cystic structure representing a choroid plexus cyst extending into a left parasagittal midline cyst. The posterior fossa is characterised by a typical Dandy-Walker malformation consisting of a high-riding torcula, free communication between the fourth ventricle and a large supra- and retrocerebellar CSF cyst as well as absence of the inferior vermis. Origin:
Description: Axial post-contrast T1-weighted image at the level of the roof of the high-riding third ventricle confirms agenesis of the corpus callosum and dilated ventricles with colpocephaly. Markedly enhancing choroid plexus containing papillomata is present in the third and right lateral ventricle. Multiple rim-enhancing cysts are present in the left lateral ventricle and the midline region. Posteriorly, there is a high-riding torcula. Origin:
Description: Axial contrast-enhanced T1-weighted image at the level of the mid third ventricle displays again choroid plexus papillomata and cysts in both atria and the third ventricle. A large CSF supracerebellar cyst making part of the extensive Dandy-Walker malformation is continuing the third ventricle posteriorly. Origin:
Description: Axial post-contrast T1-weighted MRI at the level of straight sinus displays a left parasagittal midline cyst containing a choroid plexus cyst. This parasagittal cyst has markedly decreased in size from previous CT. (Fig. 3b) Origin:
**Description:** Axial enhanced CT image at similar table position to corresponding MR image (Fig. 3a) shows large left parasagittal midline cyst as present in the neonatal period. **Origin:**

**c**

**Description:** Axial enhanced CT scan displays the same, but larger interhemispheric cyst in the neonatal period. **Origin:**
Description: Axial T2-weighted imaging allows optimal assessment of the grey matter, which displays immature development. Thickened poorly folded cortical grey matter represents polymicrogyria, best demonstrated around the perisylvian fissures and occipital lobes bilaterally as well as the right frontal lobe. In addition, multiple heterotopic low signal nodules are bordering the lateral ventricles and thus creating a wavy appearance of their margin. The choroid plexus and papillomata are less well outlined on T2-weighted imaging. They are of decreased signal. Two of the previously described cysts are of slightly higher density than the adjacent CSF due to a difference in protein concentration. Origin:
Description: Axial T2-weighted image at the level of the cerebral peduncles displays again extensive polymicrogyria, best observed in the right temporal region. Posteriorly is a further demonstration of the Dandy-Walker malformation with free communication between the fourth ventricle and a large retrocerebellar CSF cyst due to agenesis of the inferior vermis. Origin:
Figure 5

Description: Axial T1-weighted image demonstrates right anophthalmia and left proptosis due to a retrobulbar CSF density cystic structure situated at the medial aspect of the optic nerve. This collection does not communicate with the CSF spaces, though being of CSF density, it represents a retro-ocular cyst or dural ectasia. Dandy-Walker malformation is again noted in the posterior fossa. Origin:
Description: Fundoscopy reveals several well-defined large patchy pale areas surrounding the optic disk. They represent chorioretinal lacunar defects, characteristic of Aicardi syndrome. Origin: