ABSTRACT

Objective: Three cases of Aicardi Syndrome were diagnosed in our hospital. This syndrome is a rare, female-restricted genetic disease, characterized by agenesis of the corpus callosum, other central nervous system malformations, and chorioretinal lacunae. We have compared these cases with other cases of Aicardi Syndrome described in the world literature.

Methods: We have reported the three cases of Aicardi Syndrome and detailed the important heterogeneity of phenotypic features and clinical severity.

Results: The most benign case (case number 1) was characterized by mild ocular morbidity, absence of both migration abnormalities and epilepsy, and normal psychomotor development. Case number 2 achieved long-term survival with mild ocular alterations, but had severe retardation in psychomotor development. Case number 3 had the most severe ocular abnormalities which evolved rapidly and resulted in early death.

Conclusions: Aicardi Syndrome can be phenotypically heterogeneous, presenting with substantial variability in the severity of clinical features such as psychomotor development and survival. Our study
The Aicardi syndrome is a generally very severe congenital disease, typically characterized by agenesis of the corpus callosum, infantile spasms and chorioretinal lacunae in the eye fundus. Said complex malformations of the central nervous system can include neuronal migration defects as well as cystic malformations which can give rise to convulsions and severe mental retardation.

The Aicardi syndrome comprises ocular expressions which include colobomae at the papillary level and chorioretinal lacunae. Other systemic expressions may arise in the Aicardi syndrome such as vertebral anomalies and renal displasia.

The negative prognosis typically associated to the Aicardi syndrome seems to comprise an increasing number of symptoms and exceptions, with a small proportion of girls who exhibit only slight or moderate mental retard (1). However, to this date it is not clear which characteristics of the syndrome are related to a good prognosis in terms of psychomotor development and survival. This article describes three cases of Aicardi syndrome, each one with different clinical and phenotypical expressions. Our observations point out some phenotypical characteristics which could form a basis for a more precise prognosis for patients with the Aicardi syndrome.

**SUBJECTS, MATERIAL AND METHODS**

**Case 1**

A girl aged 3 years and 18 months. Gestational diabetes and mother Rh – grade A, 38-233k gestation and normal birth. Female chariotype 46 XX normal.

**Key words:** Aicardi Syndrome, chorioretinal lacunae, cortical migration abnormalities, epilepsy, coloboma, psychomotor development.

indicates that cortical migration abnormalities and retinal lesions may be useful prognostic factors (Arch Soc Esp Oftalmol 2008; 83: 29-36).

**INTRODUCTION**

The prenatal echography diagnostic of this girl exhibited agenesis of the corpus callosum and multicystic displasic right kidney. The central nervous system exhibited a choroidal plexus cyst and a cyst in the deep inter-hemispheric region. The NMR scan did not reveal abnormalities of neuronal migration (fig. 1). EEG records gave normal results. Cognitive studies showed a normal rate of psychomotor development.

The eye fundus exploration revealed a virtually normal appearance of the right eye fundus with normal optical papilla, 2 small underpigmented chorioretinal lacunae and absence of macular involvement. However, the left eye fundus showed a colobomatous malformation of the optic nerve and a greater number of chorioretinal lacunae without macular involvement (fig. 2).

**Case 2**

A girl, 11 years and 10 months old, normal female chariotype and normal gestation and birth. A brain NMR revealed agenesis of corpus callosum together with broad anomalies of neuronal migration (fig. 3). This patient exhibited epilepsy in early childhood, with the first seizures occurring at 2 years of age. The EEG recordings showed asymmetric hypsarrhythmia. The funduscopic examination shows a complete papilla in the right eye, peripapillary pigment and areas of peripapillary underpigmented chorioretinal lacunae which extend towards the retinal vascular arches. However, there is no macular involvement. The left eye fundus exhibited a colobomatous optic disc and small and chorioretinal underpigmented areas. No other kidney or spinal malformations appeared. The patient is characterized by long survival, with actual age of 11 years and 10 months albeit with severe psychomotor retard.

**Palabras clave:** Síndrome de Aicardi, lagunas corioretinianas, anomalías de la migración neuronal, epilepsia, coloboma, desarrollo psicomotor.

**Key words:** Síndrome de Aicardi, lagunas corioretinianas, anomalías de la migración neuronal, epilepsia, coloboma, desarrollo psicomotor.

**SUBJECTS, MATERIAL AND METHODS**

**Case 1**

A girl aged 3 years and 18 months. Gestational diabetes and mother Rh – grade A, 38-233k gestation and normal birth. Female chariotype 46 XX normal.

**Key words:** Aicardi Syndrome, chorioretinal lacunae, cortical migration abnormalities, epilepsy, coloboma, psychomotor development.

indicates that cortical migration abnormalities and retinal lesions may be useful prognostic factors (Arch Soc Esp Oftalmol 2008; 83: 29-36).

**INTRODUCTION**

The prenatal echography diagnostic of this girl exhibited agenesis of the corpus callosum and multicystic displasic right kidney. The central nervous system exhibited a choroidal plexus cyst and a cyst in the deep inter-hemispheric region. The NMR scan did not reveal abnormalities of neuronal migration (fig. 1). EEG records gave normal results. Cognitive studies showed a normal rate of psychomotor development.

The eye fundus exploration revealed a virtually normal appearance of the right eye fundus with normal optical papilla, 2 small underpigmented chorioretinal lacunae and absence of macular involvement. However, the left eye fundus showed a colobomatous malformation of the optic nerve and a greater number of chorioretinal lacunae without macular involvement (fig. 2).

**Case 2**

A girl, 11 years and 10 months old, normal female chariotype and normal gestation and birth. A brain NMR revealed agenesis of corpus callosum together with broad anomalies of neuronal migration (fig. 3). This patient exhibited epilepsy in early childhood, with the first seizures occurring at 2 years of age. The EEG recordings showed asymmetric hypsarrhythmia. The funduscopic examination shows a complete papilla in the right eye, peripapillary pigment and areas of peripapillary underpigmented chorioretinal lacunae which extend towards the retinal vascular arches. However, there is no macular involvement. The left eye fundus exhibited a colobomatous optic disc and small and chorioretinal underpigmented areas. No other kidney or spinal malformations appeared. The patient is characterized by long survival, with actual age of 11 years and 10 months albeit with severe psychomotor retard.

**Palabras clave:** Síndrome de Aicardi, lagunas corioretinianas, anomalías de la migración neuronal, epilepsia, coloboma, desarrollo psicomotor.

**Key words:** Síndrome de Aicardi, lagunas corioretinianas, anomalías de la migración neuronal, epilepsia, coloboma, desarrollo psicomotor.
Case 3

The third patient exhibited the most severe phenotype of our Aicardi syndrome series. Normal gestation, birth and female chariotype.

The brain NMR was carried out 4 days after birth, revealing a complex malformation with agenesis of the corpus callosum, displastic left front lobe with subcortical nodular heterotopias, arachnoid cyst in posterior fossa and coloboma in the left

Fig. 1: Brain NMR of patient 1 with Aicardi syndrome. (A) Corona section in T1 showing corpus callosum agenesis (arrow). (B) Sagittal section in T1 shows sub-arachnoid cyst (arrow) in deep inter-hemisphere region. (C) Axial section in T1 illustrating choroidal plexus cyst (arrow). (D) Axial section in T2 showing macroscopic absence of brain malformations compatible with neuronal migration anomalies.
ocular globe (fig. 4). The patient exhibited at important involvement of psychomotor development. The EEG showed a highly disorganized asymmetric hypsarrhythmia, clinically exhibiting convulsive seizures impervious to treatment.

The left eye exhibited an important microphthalmia. The right eye fundus exploration showed a colobomatous right optic disc of the Morning Glory type with chorioretinal lacunae in the central retina, involving the macular area. The left eye fundus included a colobomatous papilla of the Morning Glory type with surrounding chorioretinal lacunae. At the age of 9 months, the patient exhibited an inferior bullous retinal detachment in the left eye. The visual evoked potentials (VEP) were delayed in the right eye and absent in the left one. The patient also exhibited left kidney agenesis, hemi vertebrae and severe scoliosis. The patient died at 18 months of age.

RESULTS (TABLE I)

The first case is the most benign one, exhibiting at 3 years and 8 months of age absence of seizures,
good visual development and normal psychomotor developments. The central nervous system is characterized by the absence of cortical and neuronal migration anomalies. The eye exhibited small lacunar islets in the eye fundus with respect for the macular area and small unilateral optic nerve coloboma. The patient did not exhibit complications like retina detachments and remained in orthophoria with good visual development.

The second patient exhibited severe psychomotor retardation and severe epilepsy with poor clinical control. However, she exhibited long survival (current age: 11 years and 10 months). The central nervous system exhibited cortical alterations of neuronal migration. The ocular clinical symptoms are benign, with small chorioretinal lesions, respect for the macula and small unilateral optic nerve coloboma. She did not exhibit either associated ocular complications and remains in orthophoria with good visual development. No other kidney or vertebral malformations are associated.

The third patient is the most severe, with untreatable epilepsy and deep psychomotor retardation. She died at 18 months of age. The cortex exhibited important neuronal migration anomalies. The ocular alterations are severe with pathological VEP and large chorioretinal lacunae in the eye fundus involving the macular area, large bilateral optic nerve coloboma, microphthalmic left eye and evolution to retinal detachment. In addition, she exhibited severe systemic malformations with kidney agenesis and multiple vertebral alterations.

**DISCUSSION**

The Aicardi syndrome can be heterogeneous at the phenotype level, exhibiting substantial variations in the severity of its clinical expressions, in psychomotor development and survival (1-4). The longest series published in the last twenty years comprises 77 cases corresponding to members of the Aicardi Foundation from all over the world. Information was obtained from questionnaires filled in by relatives, who referred the presence of significant mental retard in all cases and convulsions in 92% of cases (5). A recent publication analyzed the responses of care givers of 69 patients with the Aicardi syndrome, which contributed new data about the mean survival age which is estimated at 18.5 years. This estimate is more favorable than previously published data (6). Very few studies have examined the clinical characteristics which may predict clinical evolution (7,8).

In this study we present three Aicardi syndrome cases corresponding to a phenotypical clinical ran-
ge from slight to severe and their evolutionary prognosis. We have found an association of some specific encephalic and ocular characteristics with a better clinical prognosis, supporting previous articles about the potential prognosis value of specific clinical characteristics (7,8) which, when detected, could contribute to a more precise prognosis for patients affected by this syndrome.

In the brain, the absence of cortical neuronal migration anomalies is a positive prognosis factor as regards psychomotor development and survival (case 1, a patient without epilepsy and normal psychomotor development).

In the eye, unilateral involvement of the optic nerve coloboma and the presence of predominantly small chorioretinal lacunae which respect the central retina and the macula are also related to an improved prognosis in what concerns psychomotor development (case 1) and survival (cases 1 and 2) as well as good visual development (cases 1 and 2). This had already been considered as a positive prognosis factor in terms of psychomotor and language development, as well as a good development of the visual function (8).

Patient 1 seems to be the most benign Aicardi syndrome case of those described to date in literature (3,4). It is surprising to notice that the low ocular morbidity (unilateral coloboma, predominantly small chorioretinal lacunae with respect for the macular area) is related to a good psychomotor development and good general condition (absence of epilepsy) even though the central nervous system exhibits important malformations.

Similarly, we also observed that the presence of a unilateral coloboma, together with macular respect of the chorioretinal lacunae are clinical characteristics which also appear in case 2 and are related to a good survival in the presence of complex brain malformations, together with epilepsy and severe psychomotor retard (actual age, 11 years and 10 months).

On the contrary, we found negative survival prognosis and greater clinical severity factors such as the magnitude and bilateral nature of colobomatous optic disc lesions as well as optic disc fossae which could give rise to serous retinal detachments and larger size of chorioretinal lacunae, with involvement of the central and macular retina (patient 3 who exhibited a large clinical morbidity, large psychomotor retard and severe epilepsy, with a survival of eighteen months).

A careful and detailed eye fundus examination can have not only a diagnostic value for the Aicardi syndrome but also prognostic significance. On the basis of the above observations, we consider that a careful ophthalmological control is necessary for these patients. Finally, we believe that a longer series of cases are required to validate the results we have obtained. We have analyzed our statistical data, which is highly suggestive.

**REFERENCES**


