PROGRESSIVE GEOGRAPHIC CHORIORETINOPATHY ASSOCIATED WITH ALAGILLE SYNDROME

ABSTRACT

Case report: We report the case of a patient with the genetic diagnosis of Alagille Syndrome, who has attended our hospital since 1992, and has shown a progressive bilateral chorioretinopathy with severe deterioration in visual acuity.

Discussion: Ocular abnormalities associated with Alagille Syndrome are variable and can affect most ocular structures. Although severe visual threat or progressive ocular disease associated with Alagille syndrome have not yet been described, our patient has shown a marked decrease in visual acuity and a clear progression of the chorioretinal atrophy (Arch Soc Esp Oftalmol 2007; 82: 513-516).

Key words: Alagille Syndrome, Jagged 1 gene, chorioretinopathy, serpiginous choroiditis, posterior embriotoxon.

INTRODUCTION

The Alagille Syndrome (AS) is a dominant autosomal family hereditary disease with variable penetrance and expressivity, clinically characterized by neonatal cholestatic jaundice and hypoplasia of the intrahepatic bile ducts (1). Mutations have been detected in the Jagged 1 gene, which codifies a ligand of the transmembrane notch receptor (2).

The ophthalmologic manifestations associated to this syndrome vary, although the posterior embriotoxon is the main criterion to diagnose this syndrome and is the most frequent manifestation of all (3). The diffuse hypopigmentation of the retinal

RESUMEN

Caso clínico: Paciente diagnosticada genéticamente de Síndrome de Alagille, vista en el servicio de oftalmología desde 1992 por atrofia coriorretiniana progresiva que ha dado lugar a una pérdida severa de agudeza visual bilateral.

Discusión: Las manifestaciones oftalmológicas asociadas al síndrome de Alagille son variables, pudiendo afectarse la práctica totalidad de las estructuras oculares. A pesar de que hasta el momento no se han descrito alteraciones severas de la agudeza visual ni progresión de las lesiones oculares asociadas al síndrome de Alagille, nuestra paciente ha presentado una marcada disminución de su agudeza visual así como una clara progresión de las lesiones coriorretinianas.

Palabras clave: Síndrome de Alagille, gen Jagged 1, coriorretinopatía, coroiditis serpiginosa, embriotoxon posterior.
pigment epithelium (RPE) is the most constant retinal alteration among these patients.

CASE REPORT

A female patient checked in the ophthalmology unit for the first time in our hospital in the year 1992 (at the age of 33) reporting a reduction in visual acuity of the right eye. Initial ophthalmologic examination revealed a 0.2 visual acuity (VA) in the right eye (RE) and 0.6 in the left eye (LE), with −5.0 and −4.0 spherical diopters, respectively. The biomicroscopic examination of the anterior pole revealed a marked posterior embriotoxon (fig. 1) and 12 mmHg intraocular pressure in both eyes. The patient’s eye fundus showed the following traits (fig. 2) RE: RPE’s circumpapillary geographic atrophy and choroids with precise limits covering the whole macular area and allowing for visualization of the underlying choroidal vessels. LE: Diffuse injuries with traits similar to those found in the RE, with half-moon shaped atrophy partially involving the macular area. In view of this condition, a fluorescein angiography (FAGAFG) was performed, revealing the already described RPE and choriocapillary atrophy, without clear signs of activity. Faced with the possibility of a serpiginous choroiditis, treatment with immunosuppressants was prescribed with corticoids and Cyclosporine, in addition to vitamin supplements to address a potential nutritional deficit; no favorable response was observed. Subsequently, and due to the unfavorable progression, immunosuppressants were administered once again with Azathioprine and Methotrexate; to date, no improvement could be confirmed.

In the year 2003, and based on her family history (two nephews genetically diagnosed with Alagille Syndrome without associated ophthalmologic manifestations), a genetic study of the patient was performed which revealed a 2785+3 mutation of the AAGT in intron 19 in the Jagged 1 gene, thus confirming the suspected Alagille Syndrome.

Today, after a 14-year-long follow-up, the patient exhibits visual acuity of light perception in the RE and 0.1 with eccentric fixation in the LE. The eye fundus revealed the growth of chorioretinal atrophic injuries fully covering the macular area, without presenting any evidence of angiographic signs of activity during the regular checkups performed during follow-up in our unit (fig. 3).

DISCUSSION

In the existing literature, there are 11 series and at least 57 patients with ophthalmologic manifestations associated with Alagille Syndrome (3-5). Asides from the almost universal presence of a posterior embriotoxon, the main criterion for the diagnosis of this syndrome, ophthalmologic manifestations involve almost every ocular structure and vary considerably from one series to the next. In most of the series of patients with ophthalmologic manifesta-
tations associated with Alagille Syndrome, Hingorani et al (3) detected anomalies in the eye fundus in 90 percent of patients, of which 57 percent show RPE diffuse hypopigmentation, the most constant manifestation of all. However, and despite the large number and variability of ophthalmologic manifestations, different authors stress the absence of a significant decrease in visual acuity and the progression of these injuries (3).

Initially, our patient exhibited bilateral chorioretinal atrophic injuries which suggested a serpiginous choroiditis as the first and foremost diagnostic option. In spite of the immunosuppressants prescribed, injuries progressed without showing any signs of angiographic activity at any time, giving way to a gradual structural and functional deterioration and marked decrease in visual acuity. This lack of response to treatment, together with the absence of inflammatory activity in subsequent angiographic checkups in view of worsening symptoms, led to new diagnostic efforts. Today, the first diagnostic option is a peripapillary chorioretinal dystrophy casually associated with Alagille Syndrome, although it could also be blamed on a serpiginous choroiditis with a more indolent progression. Peripapillary chorioretinal dystrophies are defined by the presence of changes limited to the choriocapillary, as opposed to those patients suffering from Alagille Syndrome whose choroids remains intact (5). During progression, these patients develop pigmented scars with RPE and choriocapillary atrophy which, as in the case of this patient, may be associated with adjacent secondary sources in the posterior pole.

Finally, it is worth mentioning the existence of this association not described so far, together with the concurrence of a pathology involving severe visual deterioration in the patient suffering from Alagille Syndrome.

REFERENCES