Short communication

X linked retinoschisis, unusual presentation: Strabismus

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ABSTRACT

Case report: X linked retinoschisis is a recessively inherited degenerative retinopathy. We report two cases that debuted with an unusual presentation (strabismus) in early childhood (months). Both of them presented with vitreous veins in the retinal periphery. Mutation in the XLRS1 gene was detected in both cases.

Discussion: X linked retinoschisis is one of the leading causes of macular degeneration in male children. Clinical features include a stellate foveal schisis, with or without peripheral retinoschisis. Clinical diagnosis is often difficult because of a high degree of phenotype variability. Furthermore, ERG and OCT may be normal in early stages of the disease. In our opinion, the XLRS1 gene mutation screening provides a powerful clinical tool for evaluating clinically ambiguous cases of X linked retinoschisis.

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Retinosquisis ligada al cromosoma X, presentación inusual: estrabismo

RESUMEN

Caso clínico: La retinosquisis ligada al cromosoma X es una retinopatía degenerativa de carácter recesivo. Presentamos dos casos clínicos que debutaron con una presentación atípica (estrabismo) en la infancia precoz (lactancia). Ambos niños presentaban velos vitreos en retina periférica. Se encontró una mutación en el gen XLRS1 en ambos casos.

Discusión: La retinosquisis ligada al cromosoma X es una de las causas principales de degeneración macular en niños varones. Se caracteriza por una esquisis foveal estrellada, asociada o no a retinosquisis periférica. El diagnóstico clínico puede ser difícil por la alta variabilidad fenotípica del cuadro. Además, el ERG y la OCT pueden ser normales en fases precoces de la enfermedad y de difícil realización en niños pequeños. Consideramos que el cribado para la mutación del gen XLRS1 es útil para evaluar casos con presentación...


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Introduction

Retinoschisis linked to chromosome X, described by Hass in 1898 as an early visual loss associated to bilateral foveal schisis, is the most frequent cause of macular degeneration in children.

The prevalence of the disease is low: 1/120,000 (except Finland: 1/20,000 due to mutations of the population which founded the country). As this disease is recessive inheritance linked to chromosome X, it expresses almost exclusively in males even though the literature describes cases of affected women due to consanguinity.

The most frequent form of presentation is diminished visual acuity. The typical debut involves difficulty in reading at school (5–10 years of age). Bilateral foveal squisis is the most frequent clinical finding (68–100% of cases). Half of patients exhibit peripheral schisis, typically in the inferotemporal retina. Said schisis can be very noticeable in childhood when it can cause nystagmus or strabismus due to its large size. It can even affect the visual field. Typically, schisis remits spontaneously leaving a marking line.

Clinic cases

Case 1

Lactating infant, aged 6 months (affected) and in heterozygosis in the mother, who was treated in our practice due to diverging strabismus with lack of fixation in the left eye.

Pregnancy and delivery had taken place without complications. The infant’s personal history includes a traffic accident one month earlier.

Upon exploration, the anterior pole was normal in both eyes.

The left ocular fundus showed an inferior retina detachment associated to a vitreous veil with retinal traction up to the papilla (Fig. 1).

The right ocular fundus did not reveal retinal alterations.

Retinoscopy showed a neutral point of +3.00 –2.00 at 10’ in the right eye and +3.50 +0.50 a 7’ in the left eye.

Due to the traffic accident history a traumatic origin was attributed to the retinal detachment in the left eye.

Regular controls were carried out. The retina detachment evolved to complete reabsorption with the appearance of a marking line in the temporal retina. The macula adapted and exhibited an alteration at the retina pigment epithelium level (Fig. 2).

A few months later, vitreous flanges were observed in the inferior temporal arch of the right eye. This led us to consider the likelihood of peripheral retinoschisis as the cause of the retina detachment in the left eye.

Macular OCT and ERG were made without meaningful results due to the poor cooperation of the infant. It was then decided to carry out a DNA study on the basis of peripheral blood sample. This found a mutation (Q154R) in exon 5 of gene XLRS which accounts for the X-linked retinoschisis. The mutation expressed in hemizygosis in the affected patient and in heterozygosis in the mother (carrier).

At the age of 6, visual acuity was of 20/20 in the right eye and 20/400 in the left eye, regardless of extended treatment with hourly occlusions of the right eye.

The exploration revealed an inferior temporal vitreous condensation in the right eye and peripheral retinoschisis in the left one, associated to residual fibrosis of the inferior temporal arch (Fig. 3).

The absence of foveal schisis in OCT in both eyes was worthy of note.

Fig. 1 – Retinal traction up to the papilla in the left eye.

Fig. 2 – Temporal peripheral schisis together with marking line in the right eye.
Case 2

Male, 11 months old, treated in our practice for converging strabismus study with the lack of focus in the right eye.

The exploration exhibited a neutral point of +5.50 −1.00 a 10° in the right eye and +8.00 −1.00 a 10° in the left eye. A +10° endotropia, LE dominance.

The anterior pole did not exhibit alterations in both eyes.

The right ocular fundus did not reveal significant alterations with the exception of an inferior temporal peripheral vitreous veil (Fig. 4).

The ocular fundus in the left eye was normal.

Treatment was established with occlusion of 4 h/day in the left eye. In regular checkups vitreous condensation was observed at the inferior temporal level, without tractions or retina detachment in the right eye.

Due to the lack of response to the occlusion treatments ERG and VEP were performed with results within normality.

During evolution, peripheral retinal schisis was appreciated under the vitreous condensation in the right eye (Fig. 5).

Genetic study was performed on the basis of a peripheral blood sample, which yielded a mutation in exon 5 of gene RS1 located in chromosome Xp22.2-p22.1.

The patient was diagnosed with X-linked retinoschisis, with his mother being the carrier.

At the age of 5 years the patient exhibited a visual acuity of 20/125 in the right eye and 20/40 in the left eye, despite the occlusion treatment.

The ocular fundus exhibited an inferior temporal retinal schisis in the right eye, reaching the posterior pole, without macular involvement and temporal peripheral schisis in the left eye.

OCT in both eyes did not reveal macular alterations (Fig. 6).

Discussion

The clinical diagnostic of the X-linked retinoschisis could be difficult due to the high degree of phenotype variability.3

Typically, the diagnostic was based in the hereditary nature linked to chromosome X and the negativity of binocular wave in the scotopic ERG. At present, OCT is a useful method to study foveal cysts.5 The Oxford Eye Hospital has developed a method to carry out OCT even of a peripheral retina in new-borns under general anesthesia.4

ERG could be normal in the early stages of the disease or could be altered by the presence of retina alterations.3,5

The genetic confirmation is the final diagnostic in cases with atypical clinic and absence of affected relatives.3

The X-linked retinoschisis gene (XLS1) is found in the short distal arm of chromosome X(Xp22).2 This gene encodes the retinoschisin protein secreted by photoreceptors and bipolar cells. This protein is involved in early retinal differentiation as well as in intercellular adhesiveness and signaling. Secondly, the Müller cells become altered due to the accumulation of said mutated retinoschisin. This would explain the findings in studies with OCT4,5 showing the initial schisis at the level of the internal nuclear layer (bodies of Müller cells and bipolar cells). On the other hand, the fact that the Müller cells
cells that are in charge of controlling the extracellular K are
damaged would explain the typical alteration found in ERG.
The visual prognosis of X-linked retinoschisis is controver-
sial. It is considered that visual acuity remains stable after
a marked worsening during the schooling age, with a new
worsening as of age 40–50 due to macular atrophy.
In what concerns treatment, it is focused on controlling
possible complications (RD, vitreous hemorrhage, ambliopy,
etc.). Prophylactic laser treatment around the peripheral
cyst cavities is not indicated due to the possibility of
complications.\(^2\)

Recent studies propose vitrectomy because vitreous trac-
tion could play a crucial role in retinoschisis (due to the
lack of coexisting cellular adhesion). Accordingly, eliminat-
ing the vitreous would avoid complications such as the cheers
hemorrhage, macular atrophy and retina detachment among
others.\(^5\)

This short paper presents 2 cases in which the disease
debuts with strabismus in the lactation period with the com-
mon characteristic of a vitreous veil. In these cases, in which
generally supplementary tests are unreliable, we believe that
genetic diagnosis is essential.
In case 2, genetic studies of the patient relatives gave rise
to the diagnosis of the same disease in a brother even though
he did not exhibit signs of the disease. The case is inheri-
tance linked to chromosome X, with complete penetration of
the mutation and highly variable expressiveness, even within
members of the same family, so that the mutation can be
found in males even when they do not exhibit signs of the
disease.

**Conflict of interests**
The authors have no conflict of interests to declare.

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