Short communication

Ophthalmic manifestations in Mexican patients with Fabry disease

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ABSTRACT

Fabry disease (FD) is a rare X-linked genetic lysosomal storage disease caused by a deficiency of the enzyme α-galactosidase A that produces accumulation of globotriaosylceramide. There is a multisystemic involvement, including renal, cardiac, eye, and nervous system manifestations.

Aim: To perform a descriptive analysis of the ophthalmological manifestations in Mexican patients with FD.

Material and methods: We studied 13 patients with clinical and biochemical diagnostic of FD.

Results: Cornea verticillata was found in 57% of men and 33% carriers.

Conclusion: Cornea verticillata was the most common ocular manifestation in males and carriers of FD in Mexico.

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Manifestaciones oftalmológicas en pacientes mexicanos con enfermedad de Fabry

RESUMEN

La enfermedad de Fabry (EF) es una patología genética rara ligada al cromosoma X, de depósito lisosomal, por la deficiencia de la enzima α-galactosidasa A, que produce la acumulación de globotriaosilceramida, ocasionando afectación renal, cardiaca, oftalmológica y del sistema nervioso.

Objetivo: Realizar un análisis descriptivo de las manifestaciones oftalmológicas en pacientes mexicanos con EF.

Material y métodos: Se incluyeron 13 pacientes con diagnóstico clínico y bioquímico de EF.

Resultados: La córnea verticillata se encontró en el 57% de varones y en el 33% de portadoras.


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Conclusion: La córnea verticilata es la manifestación oftalmológica más frecuente en varones afectados y portadoras de EF en México.

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Introduction

Fabry disease (FD) (OMIM 301500) is an innate error of the catabolism of glycosphingolipids linked to chromosome X. It is caused by a deficiency in the α-galactosidase A enzyme which produces progressive accumulation of the globotriaosylceramide glycosphingolipid (Gb3) in liposomes, mainly in the vascular endothelium and in podocytes, affecting the nervous, cardiac, renal and ophthalmological systems.

The prevalence of FD in men is one for every 117,000 live births, with a variation between one for every 20,000 up to one for every 4,000,000. The accumulation of Gb3 at the ocular level causes a typical but not pathognomonic FD lesion called Cornea verticilata, and opacity in the cornea with an irradiating pattern which does not affect vision and can only be seen with slit lamp. However, it can also be observed in Tangier’s disease, in striated melanokeratosis, in the Melkersson–Rosenthal syndrome and secondary to drugs (chlorokine, kinacrine, amyodarone, idometacine and chlorpromazine). Cornea verticilata is present in nearly all male FD patients and in 70–90% of FD carriers. In addition, vascular abnormalities can be found in the conjunctiva, in posterior cataracts (Fabry cataracts), anterior cataracts, tortuosity of retinal vessels, papilledema, periortitary edema, optic atrophy and nystagmus.

In 1925, Weicksel reported for the first time ophthalmological findings in FD, and since then ocular findings are considered as one of the early and characteristic clinical expressions of FD. Several studies at the world level have reported the frequency of ophthalmological expressions in FD patients and carriers. However, to date there is no report covering the Mexican population. The purpose of this paper is to report the frequency of ophthalmological expressions in a group of FD patients in Mexico.

Materials and methods

This study included 13 individuals with a clinical and biochemical diagnostic of FD. They all agreed to participate in the study and signed an informed consent. Full clinical history and ophthalmological exploration was made for each participant using a slit lamp SL 120 (Carl Zeiss, Jena, Germany), Topcon air tonometer, Topcon indirect ophthalmoscope and 20 DP Volk lens.

Results

Of the 13 assessed patients, 7 (53.8%) were male and 6 (46.1%) female. The age range of patients was of 16–50 years, with an overall mean age of 39.9 years. In the male group, the mean age was 36.2 years (range, 21–50 years) and in females was 37.6 years (range, 16–48 years). During the assessment it was seen that 12 of the 13 patients had never received ophthalmological attention and none referred diminished visual acuity. Table 1 illustrates the frequency of observed alterations, where it can be seen that 69% (9/13) of the group exhibited at least one ophthalmological alteration.

The most frequent alteration among male patients and carriers in Mexico was Cornea verticilata (6/13). Retinal vessel tortuosity was not found in any of the assessed patients. In what concerns carriers, posterior cataracts and anomalies in conjunctival vessels exhibited the same frequency (16.7%), whereas anterior cataracts were not present in this group. No statistically significant differences were found (p = 0.97) when comparing affected and carrier males.

Discussion

Cornea verticilata is the most frequent ophthalmological alteration with early onset in FD, and is characterized by the deposit of glycosphingolipids between the corneal epithelium basal membrane and Bowman’s membrane. This is the most frequent expression in affected and carrier males in Mexico, which matches the findings of world literature. However, the frequency of Cornea verticilata varies among the various populations of the study. For example, in Spain 75% has been reported, in France 90%, in Italy 100%, in the United States 100% and 73.1% in patients throughout the European Union. When comparing the Cornea verticilata frequency found in our study (males 57% and carriers 33%) with those mentioned above, utilizing χ² with the Yates correction, no significant differences were found between the Mexican patients vis-à-vis Spanish, French or Italian patients (p = 0.95, p = 0.32 and p = 0.54 respectively). However, when comparing the Mexican population with the USA and European Union carriers, statistically significant differences were found (p = 0.01 and p = 0.05 respectively). This could be explained by the differences in the age at which the patients were assessed and in the sample sizes (number of recruited patients and families).

Conclusion

Despite differences in distribution of Cornea verticilata frequencies, this sign remains constant between patients and carriers.

Table 1 – Frequency of ophthalmological expressions of Fabry disease in Mexico.

<table>
<thead>
<tr>
<th></th>
<th>Males, n = 7 (%)</th>
<th>Carriers, n = 6 (%)</th>
<th>Total, n = 13 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cornea verticilata</td>
<td>4 (57.1)</td>
<td>2 (33.3)</td>
<td>6 (46.2)</td>
</tr>
<tr>
<td>Vascular abnormalities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>in conjunctiva</td>
<td>2 (28.6)</td>
<td>1 (16.7)</td>
<td>3 (23.1)</td>
</tr>
<tr>
<td>Posterior cataracts</td>
<td>1 (14.3)</td>
<td>1 (16.7)</td>
<td>2 (15.4)</td>
</tr>
<tr>
<td>Anterior cataracts</td>
<td>1 (14.3)</td>
<td></td>
<td>1 (7.7)</td>
</tr>
<tr>
<td>Retinal vessel tortuosity</td>
<td>–</td>
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</tbody>
</table>
Therefore ophthalmological assessments are crucial for an early detection of FD patients and for an early prevention of the complications which can be averted with adequate treatment.

Conflict of interest

No conflict of interest has been declared by the authors.

REFERENCES