OPHTHALMOLOGICAL MANIFESTATIONS IN FABRY'S DISEASE. FOUR CLINICAL CASES SHOWING DEFICIENT ALPHA-GALACTOSIDASE-A ACTIVITY

MANIFESTACIONES OFTALMOLÓGICAS EN LA ENFERMEDAD DE FABRY. A PROPÓSITO DE 4 CASOS CON ACTIVIDAD DEFICIENTE DE a-GALACTOSIDASA A

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ABSTRACT

Case report: Fabry’s disease is an illness produced by an alteration in the catabolism of the glycosphingolipids. We report ophthalmologic findings in 4 people, detected after 113 patient evaluations from an analytical, cardiological and genetic point of view.

Discussion: Fabry’s disease is uncommon and shows variable ophthalmologic affectation. Some patients with Fabry’s disease do not present ocular affectation, while, on the other hand, healthy carriers with important ocular alterations have been described. The deposit of glycosphingolipids produces affection at the corneal, crystalline, vascular and retinal levels. The vascular alterations affect not only the veins but also the arteries, as we report in our patients (Arch Soc Esp Oftalmol 2008; 83: 713-718).

Key words: Fabry’s Disease, alpha-galactosidase-A, vasculopathy.

RESUMEN

Caso clínico: La enfermedad de Fabry es una enfermedad producida por una alteración en el catabolismo de los glucoesfingolípidos. Se muestran las alteraciones oftalmológicas de cuatro pacientes detectados tras evaluar desde el punto de vista analítico, cardiológico y genético a 113 enfermos.

Discusión: La enfermedad de Fabry es una enfermedad infrecuente con afectación oftalmológica inconstante existiendo enfermos con Fabry sin afectación ocular y portadores sanos, con importantes alteraciones oculares. El depósito de glucoesfingolípidos produce afectación a nivel corneal, cristalino, vascular y retiniano. Las alteraciones vasculares afectan no sólo a las venas sino también a las arterias como mostramos en nuestros pacientes.

Palabras clave: Enfermedad de Fabry, alfa-galactosidasa A, vasculopatía.
INTRODUCTION

Fabry’s disease is a rare recessive systemic disease linked to X, produced by an alteration in the catabolism of glycosphingolipids due to a deficient activity of the lysosomal α-galactosidase A enzyme (AaGA; fig. 1). With a prevalence of 1/117000 cases, it produces alterations in different organs, mainly the kidney and at the neurological, cardiological, dermatological and ophthalmological level (1).

This short communication presents the ophthalmological expressions in four patients (three affected by Fabry’s disease and one carrier) that were detected after cardiological studies in 113 patients affected by hypertrophic myocardopathy (HMC) by the Cardiology Service of the Virgen de la Arrixaca Hospital. For the diagnosis, levels of AaGA <30% for males and <50% for females were taken as pathological. In addition, a genetic study of the Xq22 chromosome region was performed for each patient.

CASE REPORTS

The Ophthalmological Service of the Virgen de la Arrixaca University Hospital assessed 4 patients (three affected by Fabry’s disease and one carrier). Patient 1 (p1) exhibited a detection in exon 7 (1072-74 of GAG) and three patients (p2, p3, p4) exhibited an alteration in exon 6 (Asp313Tyr).

Case 1

A 52 year-old male affected by Fabry’s disease who is a member of family H171 (graph 1). He exhibits a corrected visual acuity (CVA) of 0.9 in both eyes (BE), bilateral nasal pterigion, dilatation of conjunctival vessels (fig. 2), Cornea verticillata (fig. 3), pigmented mobilization at the level of the posterior pole with increased pigmentation above the papilla and increase of arterial and venous and vascular tortuosity confirmed by FAG AFG (fig. 4). The remainder of the ophthalmological exploration was normal.

Fig. 1: Scheme of the catabolism of Globotriosylceramide (GL₃) to Lactosylceramide by means of the α-Galactosidase A enzyme.

Diagram 1: Showing the family tree of family H171.

Fig. 2: Conjunctival vascular alterations, with irregular width and vascular ectasiae in patient 1.
Case 2

An 81 year-old male diagnosed with EPOC, Fabry’s disease and HMC. The patient is a heart pacer user and is a member of family H202. CVA is of 0.3 RE. Amaurosis in LE secondary to traumatism. No signs of Fabry’s disease were detected.

Case 3

A 45 year-old healthy male, carrier of the alpha-galactosidase mutation, member of family H90 (graph 2). The ophthalmological assessment shows a CVA of 0.8 in RE and 0.9 in LE, dilatation of conjunctival vessels (fig. 5), lackluster cornea with

Diagram 2: Showing the family tree of family H90.
reduced transparency and crystal-like dotted opacities in the equator, pigmentary mobilization at the level of the posterior pole and equatorial, with alterations of the retinal pigmentary epithelium.

Case 4

A 56 year-old male, affected by Fabry’s disease and HMC, member of family H90 (graph 2). The ophthalmological exploration revealed a CVA of 1 in both eyes, slight bilateral phakosclerosis, ectasiae in conjunctival vessels, cornea verticillata and pigmentary alterations at the level of the posterior pole in the eye fundus and FAG (fig. 6).

Fig. 5: conjunctival vascular alterations of patient 3.

Fig. 6: Retinographies and FAG of patient showing pigmentary epithelium alterations at the macular level in both eyes. Note the normal width and regularity of the vessels.
DISCUSSION

Fabry’s disease is an infrequent disease that causes multiple pathologies at the systemic and ophthalmological level. The patients described above exhibited cardiological alterations undistinguishable from patients affected by hypertrophic cardiomyopathy with normal AaGA, for which reason the existence of ophthalmological alterations compatible with Fabry’s disease supports the diagnostic. Ophthalmological involvement is not constant. Some Fabry’s disease patients may not have eye disorders (patient 2) while healthy patients who carry Fabry’s disease may have characteristic ophthalmological expressions (patient 3).

The ophthalmological pathologies described in literature comprise vascular alterations, periorbital edema, Cornea Verticillata, cataracts, peripheral retinal pigmentations, papilledema, occlusion of the central retinal artery, optical atrophy, dischromatopsia, nistagmus and internuclear ophthalmoplegia (1-2,4).

Corneal involvement is most frequent, with the deposit of glycosphingolipids between the basal membrane of the corneal epithelium and Bowman’s membrane being characteristic, producing the corneal involvement in the form of Cornea Verticillata, which is also observed in patients affected by Tangier disease, striated melanokeratosis, Melkersson-Rosenthal syndrome and secondary to medications such as Amiodarona or Chlorokine. As patient 1 was in chronic treatment with Amiodarona, he was called in for an ophthalmological checkup six months after discontinuing the treatment, where the exploration exhibited Cornea Verticillata in the stage referred above. This suggests that said deposits could be secondary to Fabry’s disease.

The characteristic lens involvement consists in opacification of lens sutures at the posterior level, producing Fabry’s disease cataracts. There are other lens alterations such as phakosclerosis and nonspecific lens deposits and opacities.

Vascular conjunctival and retinal lesions are part of the systemic involvement of small vessels in Fabry’s disease (3,5) and is secondary to intra-cytoplasmic deposits in the vascular endothelium. Aneurismatic dilatations, angulations and segmentation of conjunctival vessels occurred in 60% of Fabry’s disease patients, but have not been referred in carriers of the disease or affecting the retinal arteries as in the above patients.

Fabry’s disease is an infrequent disease. However, detecting the ophthalmological involvement caused by this disease facilitates the early diagnosis thereof and allows early treatment, thus avoiding irreversible damages caused by the GL-3 deposits.

REFERENCES