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Ophthalmologic findings in Gaucher's disease type III: case report

Achados oftalmológicos na doença de Gaucher tipo III: caso clínico.

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Abstract

We report a case of a patient with Guacher's disease type III, with mutation in Exon9, 1246G> A and 1251G> C, seeking to investigate the suspected glaucoma, to describe the ophthalmological findings, as glycolipid accumulation in the pre-retinal region and to investigate The possible correlation with the decrease of the layer of nerve fibers.

Keywords: *Gaucher disease; Glaucoma; Eye manifestations; Case reports*

Resumo

Relata-se um caso de uma paciente com doença de Guacher tipo III, com mutação no Exon9, 1246G>A e 1251G>C, buscando investigar a suspeita de glaucoma, descrever os achados oftalmológicos, como acumulo de glicolipideo em região pré- retiniana e investigar a possível correlação com a diminuição da camada de fibras nervosas.

Descritores: Doença de Gaucher; Glaucoma; Manifestações oculares; Relatos de casos

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Introduction

Gaucher's disease (GD) is an autosomal recessive genetic disorder caused by mutations located in the arm 1q21 responsible for encoding the acidic β-glucosidase enzyme, also called glucocerebrosidase (GC).[1]

GC is a lysosomal enzyme that in macrophages helps to metabolize the glucocerebroside called glycosylceramide, a glycolipid originated from the decomposition of the membrane of red blood cells and leukocytes.[1]

GC deficiency causes glucocerebroside accumulation in macrophages, also called Gaucher's cells, and the main implications are in the spleen, liver, bone marrow, bones and lungs. The most common symptoms are hepatosplenomegaly, anemia, thrombocytopenia, and bone pain.[2]

Diagnosis can be made by detecting Gaucher's cells in tissues, or by measuring the activities of GC in leukocytes or in fibroblasts culture, or by molecular analysis.[1,2,3]

Ocular manifestations include oculomotor apraxia and supranuclear abnormalities, mainly type II and III. Intraocular manifestations include corneal opacification and pinguecula, cherry macula, and retinal lesions typical of the pre-retinal accumulation of glycolipid.[4,5] The incidence of vitreous opacities is approximately 3% in a series of 80 cases of Gaucher's type I.[6]

Tabuleiro do Norte (TN), located in eastern Ceará, has the highest prevalence of GD in Brazil (1:4,000 inhabitants).[7] It is speculated that this may be due to the low rate of migration, the high level of inbreeding over many generations, and the possible influence of the Jewish origin of some local families who came from Portugal to the Northeast Region of Brazil due to the wars against the Dutch in the second half of the seventeenth century.[8]

Case Report

GKMA, 29, female, from Tabuleiro do Norte - Ceará, Gaucher's disease type III patient with mutation in Exon9, 1246G>A and 1251G>C and enzymatic beta-glucosidase and chitotriosidase positive assays for Gaucher's, in use of Miglustat®, Depakot® and phenobarbital. She denies trauma, ophthalmologic surgeries, or chronic use of corticosteroids.

She reported frequent seizures during childhood. She was referred to evaluate suspected glaucoma presenting corrected visual acuity in the right eye 20/25 (2.25 -1.50 at 100º) and in the left eye 20/25 (-3.00 -0.50 at 5º). Eye movement had no restrictions or changes. No significant corneal or conjunctival changes were identified in biomicroscopy. Aplanation tonometry at 9:30 of 14 mmHg in both eyes. Pachymetry was normal, close to 530 microns, and open angle gonioscopy had normal pigmentation in both eyes.

In funduscopy there was a significant increase of excavations in the right eye 0.8H x 0.9V (Figure 1) and in the left eye 0.8H x 0.8V (Figure 2), and both eyes showed white point deposits in the perimacular region and on average retinal periphery. Such deposits in the analysis of optical coherence tomography were shown in pre-retinal location (Figure 3), and the nerve fiber layer was densely diminished in both eyes (Figure 4), characterizing glaucomatous neuropathy.

As a result of frequent myoclonic movements, the patient was not able to make the campimetry exam.

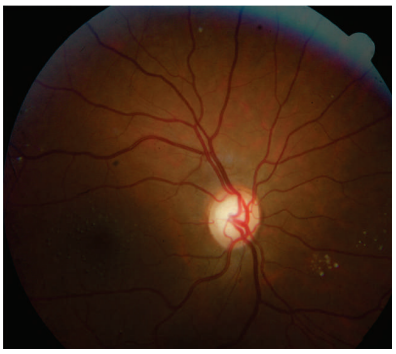

Figure 1: Retinography of the right eye

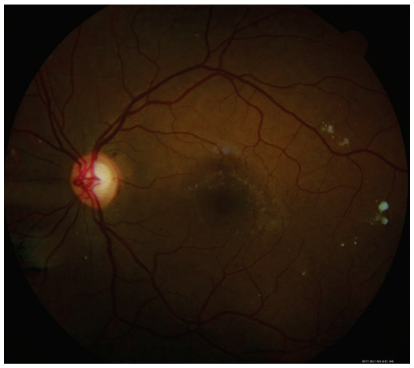

Figure 2: Retinography of the left eye

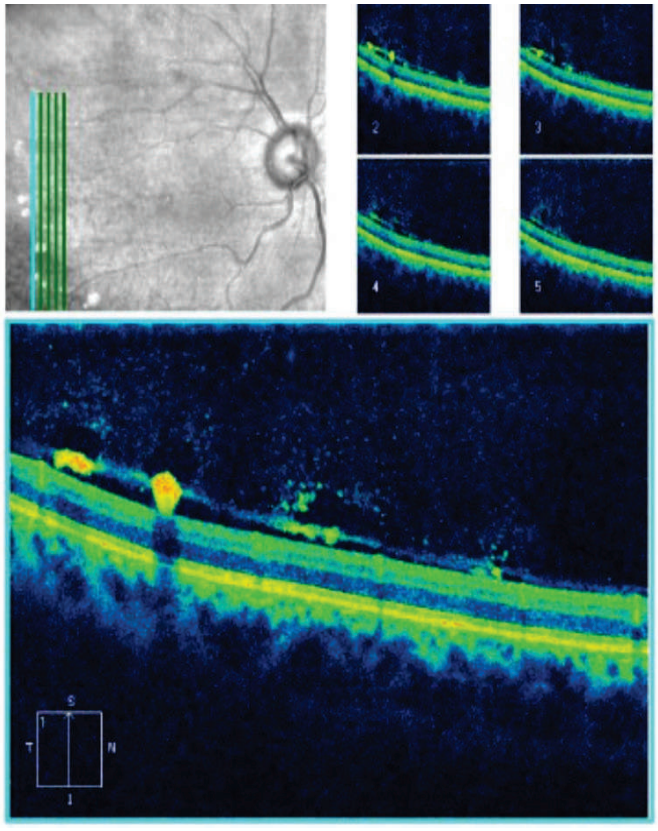

Figure 3: Optic coherence tomography showing deposition in the pre-retinal region

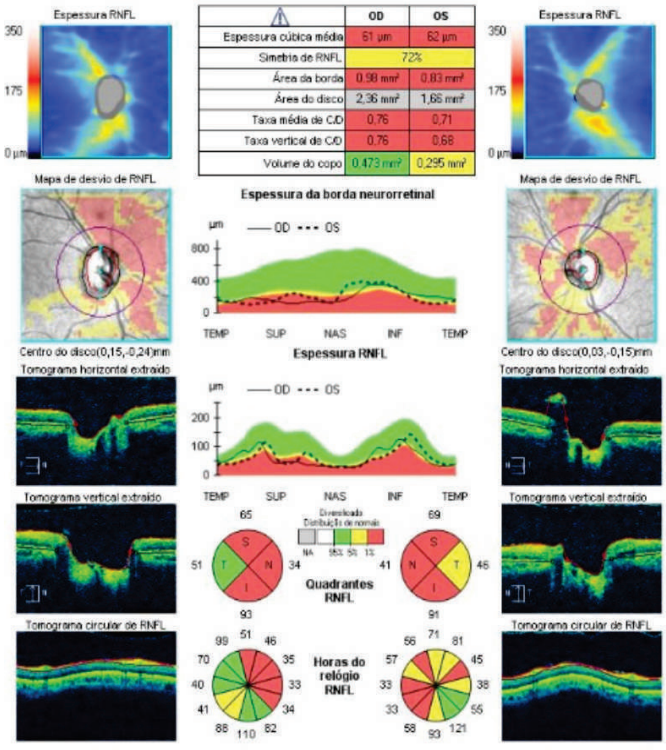

Figure 4: Optical coherence tomography demonstrating a decrease in the layer of nerve fibers in both eyes

Discussion

Gaucher's disease is autosomal recessive due to the deficiency of the beta glucosidase enzyme by mutation in the gene 1q21, promoting the accumulation of glucosylceramide in the cells of the reticuloendothelial system, with type III being characterized by neuropathic affection and myoclonic epilepsy.

Ophthalmologically, it is characterized by cherry macula and accumulation of points of typical preretinal white matter, by probable accumulation of higher levels of glucosilceramide, presented by the patient studied.

Glaucoma is not a finding described in the literature in Gaucher's disease. Some authors suggest that thinning of the nerve fiber layer of the retina is due to loss of the enzymatic activity of glucocerebrosidase associated to oxidative stress and mitochondrial dysfunction.[9] Gaucher's disease has also been correlated to the increased risk for Parkinson's, corroborating with the disease's influence on nerve cells.[10]

The correlation between glaucoma and Gaucher's disease was considered by Orwin in his dissertation by the mutation in the myocillin gene altering the protein conformation, as well as the β-glucosidase in DG.[11]

In the present case, the patient with Gaucher's disease type III had pre-retinal lesions from the deposit, and a marked decrease in the retinal fiber layer and increased excavations. However, she didn't present high intraocular pressure, which could lead to a diagnosis of glaucoma of normal pressure or a nervous degeneration not related to intraocular pressure, without the need for hypotensive treatment.

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