Exfoliation syndrome associated with LOXL1 gene polymorphisms in a Black patient from Latin America: a case report

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ABSTRACT | A 89-year-old Black female with a 6-year history of advanced open-angle glaucoma was referred to the Glaucoma Service of the Ophthalmology Department - Federal University of São Paulo (UNIFESP). Best-corrected visual acuity was 20/400 in the right eye and 20/60 in the left eye. Pseudoexfoliation material was observed at the iris border, angle, and the anterior lens surface. Anterior biomicroscopy revealed exfoliation material forming an evident peripheral zone and a central disc separated by a clear intermediate zone on the anterior lens surface OU. Gonioscopy showed an open-angle Sampaolesi's line and whitish material deposits OU. Fundus examination revealed a cup-to-disc ratio of 1.0 OU with peripapillary atrophy. Genetic analysis for single nucleotide polymorphisms of the lysyl oxidase-like 1 gene linked to exfoliation syndrome identified two such single nucleotide polymorphisms, rs1048661 and rs216524.

Keywords: Exfoliation syndrome; African continental ancestry group; Exfoliation syndrome; Lysyl oxidase-like 1 gene; Brazil

INTRODUCTION

Exfoliation syndrome (XFS) is the most identifiable cause of open-angle glaucoma1,10 and its prevalence has been studied in many different countries around the world. However, there are no large population studies on XFS incidence or etiology in South America.

The syndrome is often regarded as predominant in Caucasians due to high prevalence in Scandinavia2. There is strong evidence for a genetic predisposition to XFS based on associations with three single nucleotide polymorphisms (SNPs) of the lysyl oxidase-like 1 (LOXL-1) gene (15q24): rs1048661 (c.422G>T; p.Arg141Leu), rs3825942 (c.458G>A; p.Gly153Asp), and rs2165241 (c.1102 + 1976T>C). The LOXL-1 enzyme promotes cross-linking of collagen and elastin in the extracellular matrix, but its exact role in XFS pathogenesis has not been established.

While strongly linked to Caucasian ancestry, recent studies have demonstrated XFS in Black populations, such as South Africans4. Exfoliative syndrome and resulting exfoliative glaucoma (XFG) diagnosis may be under-diagnosed in the Black population because of low suspicion. This report describes the case of a 89-year-old Black female with advanced glaucoma, clear signs of pseudoexfoliation syndrome, and two specific LOXL1 gene polymorphisms.
doexfoliative material, and XFS-linked SNPs of LOXL-1, thus confirming the presence of XFS in the South American Black population.

CASE REPORT

A 89-year-old Black female patient was admitted with a 6-year history of advanced open-angle glaucoma with progressive vision loss OU. She also had a history of trabeculectomy OS 2 years before her first consultation at our service. Best-corrected visual acuity was 20/400 OD and 20/60 OS. Intraocular pressure (IOP) was 16 OU (4 p.m.) under topical therapy (Timolol maleate 0.5% BID, Brimonidine tartrate 0.2% BID, and Travaprost 0.004% QD).

Anterior biomicroscopy revealed pseudoexfoliative material forming three zones on the anterior lens capsule OU (Figure 1). The patient also had 2+ nuclear cataracts OU. Gonioscopy revealed an open-angle Sampaolesi’s line and whitish material deposits (Figure 2) OU. Fundus examination showed a cup-to-disc ratio of 1.0 OU with peripapillary atrophy (Figure 3). Left eye achromatic automated perimetry demonstrated advanced visual field damage.

Given these typical findings of XFS, genetic molecular testing was conducted to evaluate the presence of three LOXL-1 SNPs linked to XFS. The test revealed the presence of rs1048661 and rs216524 in heterozygosis and absence of rs3825942 (Figure 4).

DISCUSSION

Exfoliation syndrome is a frequent cause of open-angle glaucoma, and has important implications for clinical
that confers higher risk in one population can be protective in another. Environmental and behavioral factors also appear important for the genesis of XFS\(^{(7-10)}\), such as higher altitude, caffeine consumption, low folate, and excessive sun exposure (i.e., outdoor activities and more numerous sunny days and longer daylight hours)\(^{(9-10)}\).

Exfoliation material may be found in different visceral organs of patients with XFS\(^{(8)}\), and XFS has been associated with cardiovascular and cerebrovascular diseases, elevated homocysteine levels\(^{(7)}\), and deafness\(^{(8)}\). Therefore, early diagnosis and management of both ocular and systemic conditions is critical. This makes the XFS a very complex disease associated with genetic and environmental factors contributing to the disease appearance and severity.

The current case patient was positive for two of the three SNPs previously linked to XFS, rs1048661 and rs216524 (Figure 4). She also presented with the typical findings of XFS. While originally described in Scandinavians, XFS and XFG have worldwide distribution, and recent studies have revealed considerable prevalence among Blacks. To our knowledge, however, this is the first case described in a Black patient from South America.

Diagnosis of XFS relies on careful examination and a high level of clinical suspicion. The possibility of XFS should be considered when examining older patients with glaucoma regardless of ethnicity.

**REFERENCES**


**Figure 4.** LOXL1 gene sequencing for the polymorphisms (from top to the bottom) rs1048661 (present), rs3825942 (absent), and rs2165241 (present).