

Diagnostic and Therapeutic Challenges in Schnyder's Crystalline Dystrophy: A Family Report

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RESUMO

Introdução: A distrofia cristalina corneana de Schnyder (SCCD) é uma doença autossómica dominante rara caracterizada por depósitos de colesterol e fosfolípidos na córnea com *glare* e baixa desproporcional da acuidade visual (AV) em condições fotópicas.

Métodos: Os autores apresentam dois casos de SCCD da mesma família portuguesa.

Resultados: O primeiro caso é um homem de 60 anos com baixa da AV progressiva, bilateral e indolor ao longo de mais de 30 anos. Foi realizado o diagnóstico clínico de SCCD e confirmado histologicamente após queratoplastia penetrante. O segundo caso é uma mulher de 41 anos, filha do primeiro doente, com uma forma mais ligeira da doença, por vezes mais difícil de diagnosticar.

Conclusões: Os dois casos reportados confirmam o facto de que os doentes com mais idade com SCCD apresentam opacificação mais grave corneana e por esse motivo pior AV. A forma mais grave da doença do primeiro doente associada à presença de cristais tornou o diagnóstico mais fácil. No entanto, a segunda doente poderia ter sido erradamente diagnosticada, o que confirma a importância da observação dos familiares.

Palavras-chave

Distrofia de Schnyder, distrofia corneana.

ABSTRACT

Introduction: Schnyder's crystalline corneal dystrophy (SCCD) is a rare autosomal dominant condition characterized by abnormally increased deposition of cholesterol and phospholipids in the cornea leading to glare and disproportionate loss of photopic vision.

Methods: The authors present two cases of SCCD, from the same portuguese family.

Results: The first case is a 60-year-old man with progressive, bilateral and painless loss of visual acuity over more than 30 years. He was clinically diagnosed with SCCD and confirmed histologically after penetrating keratoplasty. The second patient is a 41-year-old woman, daughter of the first patient, with a milder form of the disease, often more difficult to diagnose.

Conclusions: The two cases reported confirm the fact that the more elderly patients with SCCD present with increasing opacification and therefore poorer vision. The more severe form of the disease of the first patient associated with the presence of crystals makes the clinical diagnosis easier. However, the second patient could have been easily misdiagnosed. This confirms the importance of other family members examination.

Keywords

Schnyder dystrophy, corneal dystrophy.

INTRODUCTION

Schnyder's crystalline corneal dystrophy (SCCD), also known as Schnyder's crystalline dystrophy sine crystals, hereditary crystalline stromal dystrophy of Schnyder, crystalline stromal dystrophy, central stromal crystalline corneal dystrophy or corneal crystalline dystrophy of Schnyder, is a rare autosomal dominant condition with 115 affected individuals from 34 families reported in literature.^{1,2} It is inherited as an autosomal dominant trait with high penetrance, has been mapped to the *UBIAD1* gene on chromosome 1p36.3 and is characterized by abnormally increased deposition of cholesterol and phospholipids in the cornea leading to glare and disproportionate loss of photopic vision.^{3,4,5}

This is a rare stromal dystrophy first described in three generations of a single family by Van Went and Wibaut, and the characteristics were further clarified by Schnyder. SCCD has previously been reported to be non progressive after childhood, but recent reports have documented significant progression. No regression of lesions has been reported.¹

A variety of symmetric, bilateral, corneal lesions are seen in this dystrophy.^{5,6,7} Bilateral gray, disclike opacities are seen, primarily in the anterior stroma. These opacities are often central and also may include fine polychromatic cholesterol crystals in the anterior stroma, which are more prominent in the earlier phases of the disease.¹ Because only 50% of affected patients have corneal crystals, diagnosis of affected individuals without crystalline deposits is often delayed and these individuals are frequently misdiagnosed.^{3,8} Arcus lipoides or senilis is often a finding in the peripheral cornea in patients over the age of 23 with this dystrophy.¹ The epithelium, endothelium and Descemet's membrane remain largely uninvolved, and patients rarely demonstrate epithelial erosions.¹ The clinical variations of the corneal opacities have been divided into five types, any of which may be present in the same family: 1) a central discoid lesion without crystals; 2) a crystalline discoid central lesion with a garland-like margin; 3) a crystalline discoid central lesion with a poorly defined edge; 4) a crystalline annular opacity with a clear center; 5) an annular opacity with crystal collections and a clear center.¹

SCCD is strongly associated with hypercholesterolemia (2/3 of patients) with or without hypertriglyceridemia and less commonly with genu valgum, which may be inherited as a separate trait.^{1,3} The serum lipid levels do not correlate with the density of the corneal opacities. The disease likely represents a localized defect in

cholesterol metabolism, which may be exacerbated by systemic hyperlipidemia.¹

Although the diagnosis is mainly clinical, histopathology may be important in questionable cases and for confirmation after penetrating keratoplasty. Lipid, neutral globular fat and cholesterol deposition have been identified at all levels of the corneal stroma. Cholesterol has been identified as birefringent crystals, noncrystalline cholesterol and cholesterol esters.¹

Few patients in the early phases of the disease have visual impairment significant enough to warrant a penetrating keratoplasty. Both visual acuity and corneal sensation, however, may deteriorate as the disease progresses, necessitating surgical intervention.¹ Recurrence of cholesterol crystals may occur in both lamellar or penetrating grafts. Increasing symptoms of glare in younger patients can be problematic, and some patients may undergo photorefractive keratectomy (PTK) in order to remove the more superficial stromal crystals.⁶ Anterior segment optical coherence tomography (AS-OCT) enables precise depth localisation of the opacity. While PTK may be appropriate for younger patients with more superficial lesion, it is ineffective for lesions deeper than 150 μ m and may be associated with significant haze and a hyperopic shift, following excimer laser treatment.⁶ Even though corneal dystrophies are likely to recur eventually after PTK, successful retreatment with PTK is possible.⁹

CASE PRESENTATION

The authors present two cases of SCCD, from the same family, after obtaining informed consent from both patients.

Patient One

The first case is a 60-year-old man, with previous history of acute myocardial infarction seven years before, hypercholesterolemia and arterial hypertension both medically treated with simvastatin 20mg/day, olmesartan/hydrochlorothiazide 20mg+12,5mg/day, furosemide 40mg/day and carvedilol 17,5mg/day. Patient's older sister had a history of bilateral and progressive visual acuity impairment and underwent bilateral penetrating keratoplasty ten years before in a different hospital. He had 4 more siblings who have never had any ocular symptoms or known ocular diseases. His parents died at young age and information about their ophthalmological clinical status wasn't possible to obtain.

Patient referred progressive, bilateral and painless loss

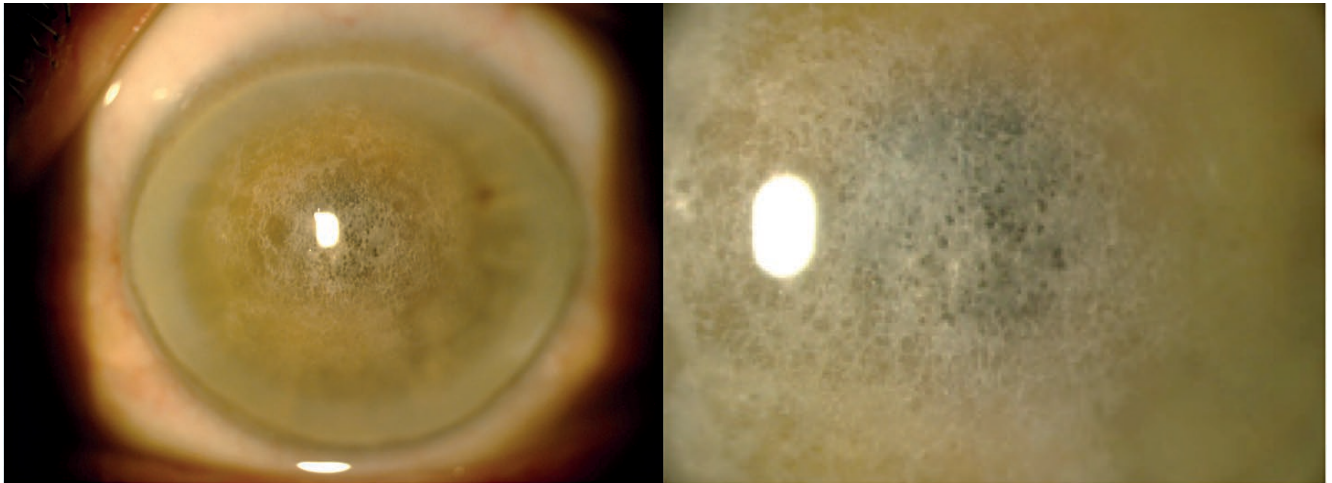


Fig. 1 | Anterior central disciform deposition associated with dense arcus.

of visual acuity over more than 30 years. Ophthalmological examination showed visual acuity of counting-fingers bilaterally, normal ocular tonus, bilateral decreased corneal sensation; on biomicroscopy we found bilateral central anterior stroma opacities with poorly defined edge and fine crystals deposited in a disciform pattern, dense arcus

in the peripheral cornea with diffuse haze in the intervening stroma (Fig. 1). The epithelium and Descemet's membrane showed no apparent changes. Fundoscopy was not possible to perform even with mydriasis.

Anterior segment optical coherence tomography (AS-OCT) revealed highly reflective opacity on the anterior central stroma, decreasing towards the periphery, as showed in Fig. 2.

Systemic evaluation revealed normal hemogram, elevated fasting LDL-cholesterol, normal triglycerides and normal serum protein electrophoresis.

Patient underwent penetrating keratoplasty on his right eye and the histopathological examination confirmed the diagnosis of SCCD. The stroma demonstrated focal round empty spaces which were likely to be the site of neutral fat deposits that were dissolved with tissue processing. Fundoscopy was unremarkable. Two months after surgery, best corrected visual acuity of the right eye was 20/80, graft was transparent without recurrence of the disease, as shown in Fig. 3.

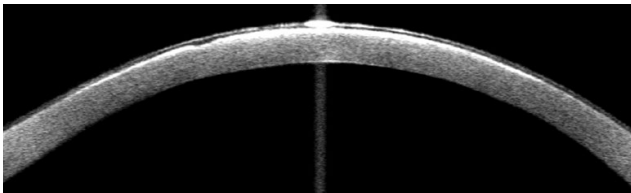


Fig. 2 | Visante AS-OCT showing hyperreflective opacity on the central anterior stroma.

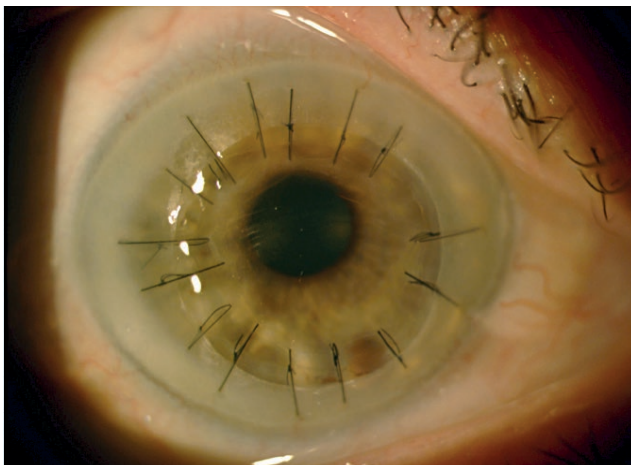


Fig. 3 | Anterior segment of the right eye of the first patient two months after penetrating keratoplasty.

Patient Two

The second patient is a 41-year-old woman, daughter of the first patient. She complained of progressive, bilateral and painless impairment of visual acuity for the past 15 years. Ophthalmological examination revealed visual acuity of 20/40 on both eyes, intraocular pressure (IOP) of 12 and 14 mmHg respectively on the right and left eyes, preserved corneal sensation, and biomicroscopy showed bilateral anterior stroma central disciform opacity without crystals, with poorly defined edge and dense arcus in the peripheral cornea with clear intervening stroma (Fig. 4).

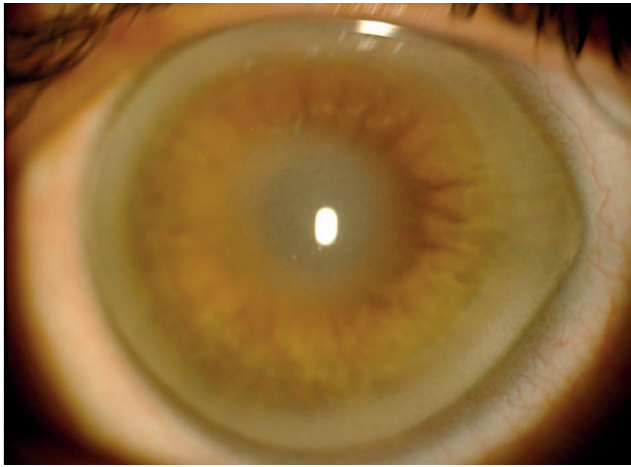


Fig. 4 | Anterior central opacity associated with dense arcus.

Systemic evaluation revealed normal cholesterol and triglycerides levels. AS-OCT confirmed bilateral highly reflective opacity on the anterior central stroma. Patient refused surgical intervention.

DISCUSSION

SCCD is a rare corneal dystrophy and the majority of published reports come from patients with European ancestry having Swedish-Finn origins. Reports in Asian patients are rare and there are very few reports in Chinese patients.^{6,10} To the best of our knowledge, this is the first report of the SCCD in a family in our country.

The two cases reported confirm the fact that the more elderly members present with increasing opacification and therefore poorer vision. The more severe form of the disease of the first patient associated with the presence of crystals makes the clinical diagnosis easier. However, the second patient could have been easily misdiagnosed. This confirms the importance of other family members examination.

Regarding surgical treatment, although the majority of patients do not require surgical intervention, there is an age-related increased incidence of penetrating keratoplasty (PK).⁶ The first patient presented was older, had a lower visual acuity, a more diffuse and dense corneal opacity and therefore underwent PK. On the other hand, the second patient could potentially be a candidate for PTK.

Studies have shown that newer surgical techniques, for example two-stage automated lamellar therapeutic keratoplasty (ALTK) and total stromal replacement with maximum depth deep anterior lamellar keratoplasty (DALK), offer viable alternatives to PK, allowing good visual

results without the risk of endothelial allograft rejection.⁶ However, ultrastructural changes have been demonstrated in the posterior stroma with lipid deposition in the entire stroma and the corneal endothelium.^{11,12,13} Given the fact that this is a rare disease, studies comparing different surgical approaches are not available and the ideal surgical treatment is still unknown. Considering this results and the larger experience in PK in our department, authors chose to perform it in the first patient, although anterior lamellar corneal transplantation would have been a plausible option as well.

CONCLUSION

We report a new family diagnosed with SCCD, the first described in our country. Two patients from two generations showed different severity manifestations of the disease and therefore careful observation of both was critical for a correct and precise diagnosis. Younger patients with an early form of SCCD, specially when crystals are not present can be easily misdiagnosed. The older patient underwent PK with good visual results and no evidence of recurrence after two months follow-up, showing that this is a valid surgical option.

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Os autores não têm conflitos de interesse a declarar.

Trabalho não publicado cedendo os direitos de autor à Sociedade Portuguesa de Oftalmologia.

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