

# In vivo confocal microscopy as a diagnostic tool in Schnyder Corneal Dystrophy's case

## *Microscopia confocal no auxílio diagnóstico de Distrofia Corneana de Schnyder*

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Débora Biazim<sup>1</sup> <https://orcid.org/0000-0002-2153-0364>  
Diego Casagrande<sup>1</sup> <https://orcid.org/0000-0001-5158-5457>  
Paula Kataguirí<sup>2</sup> <https://orcid.org/0000-0002-7972-548X>

### ABSTRACT

*Schnyder's corneal dystrophy (SCD) is a rare corneal condition characterized by cholesterol and phospholipids deposition in the stroma and Bowman's layer. We present a case report of a patient who had a progressive corneal stromal haze in both eyes since he was 15 years old. Etiological diagnosis of SCD was well established by In Vivo Confocal Microscopy (IVCM).*

**Keywords:** *Corneal dystrophies, hereditary/diagnosis; Microscopy, confocal; Corneal stroma*

### RESUMO

Neste relato, descrevemos um caso de Distrofia corneana de Schnyder que apresentou o desfecho de seu diagnóstico baseado em achados característicos na microscopia confocal, ferramenta que se aponta em destaque no universo oftalmológico.

**Descritores:** Distrofias hereditárias da córnea/diagnóstico; Microscopia confocal; Estroma corneano.

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<sup>1</sup> Third year resident at Centro de Oftalmologia Tadeu Cvintal, São Paulo, SP, Brazil.

<sup>2</sup> Department of Ophthalmology, Faculdade de Medicina do ABC, Santo André, SP, Brazil; Confocal Microscopy Service, Centro de Oftalmologia Tadeu Cvintal, São Paulo, SP, Brazil.

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## INTRODUCTION

Schnyder's corneal dystrophy (SCCD) is a rare autosomal dominant disorder characterized by the appearance of disc-shaped corneal opacity, which begins in the first decade of life and has a gradual progression of its intensity. Histopathologically, there are lipid deposits in the anterior stroma, especially in the central region.<sup>(1)</sup> Corneal crystals are present in 50% of patients, so the International Committee for Corneal Dystrophies Classification modified the original name of Schnyder's corneanacristalinian dystrophy for Schnyder's corneal dystrophy in 2008.<sup>(2,3)</sup>

As for other corneal dystrophies, complementary examinations are necessary to diagnose this disorder. Among these, we highlight confocal microscopy, a method that is being used more frequently in the ophthalmologic universe, allows images of corneal structures in high resolution<sup>(4-6)</sup> and which provided us with characteristic and sufficient data for the conclusion of our case.

## CASE REPORT

A 55-year-old male, a trader, born in São Paulo, was admitted to our service with complaint of opacification of both eyes (BE) for 20 years, with progressive worsening in recent months. Concomitantly, it reported constriction of the peripheral field without complaint of central visual acuity (VA), and in the right eye (RE) the symptomatology was more exacerbated. Personal pathological history: treatment for hypercholesterolemia and the presence of genu valgum, without other systemic comorbidities or previous ophthalmological disorders. Family pathological history: mother and brother with "whitish" eyes.

At the ophthalmologic exam, VA in the best correction in RE: 20/100 (under refraction: -1,25DE -0,25DC at 180°) and in left eye (LE): 20/20 (under refraction: -1,00DE - 0,50° C to 170°); to biomicroscopy, whitish corneal opacities arranged concentrically sparing central region and limbar, being worse in RE (Figure 1) and funduscopy, poor visualization, requiring ultrasonographic documentation of normal intraocular structures.

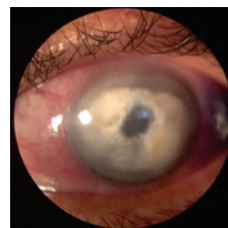
Patient presents an excellent VA in LE and interestingly, the formation of a pinhole (Figure 2) and, therefore, the conduct for this eye, so far, expectant.

Due to the clinical-ophthalmologic findings, the initial diagnosis was lipid degeneration, and as a therapeutic approach to the complaint of the patient in RE, a penetrating transplant was performed, and in the postoperative period (Figure 3), patient, under refraction -0,25DE -3,00DC at 30°, presented VA: 20/40

Due to the diagnostic doubt, we submitted the patient to the in vivo confocal microscopy (IVCM) (Heidelberg Retina Tomograph 3 with Rostock Cornea Module, Heidelberg Engineering GmbH, Heidelberg, Germany), in which we obtained normal images of the transplanted eye (Figure 4) and alterations in LE (Figure 5), such as: reduction of subepithelial nerve plexus density, marked reduction of keratocytes in the stroma and accumulation of needle-shaped material in anterior stroma, signaling a second, more accurate and reliable diagnosis: Schnyder's Corneal Dystrophy, which also fit better into the clinical-epidemiological aspect of this report.

## DISCUSSION

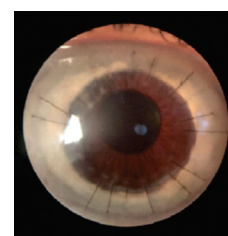
Schnyder's corneal dystrophy (SCCD) is a rare bilateral condition of autosomal dominant inheritance with variable expression. Their characteristics were first described in 1924 by the Germans van Went and Wibaut,<sup>(7)</sup> who took the first step in



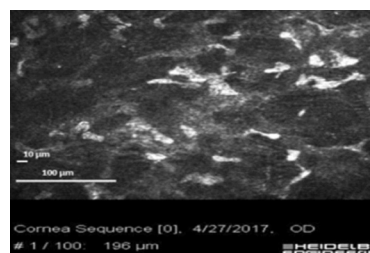
**Figure 1:** Biomicroscopy of the right eye shows whitish corneal opacities arranged concentrically.



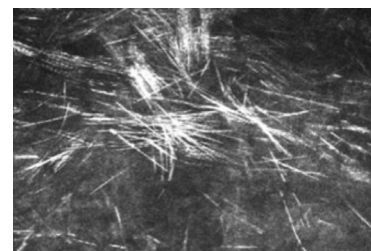
**Figure 2:** Biomicroscopy of the left eye shows a whitish corneal opacity arranged concentrically sparing the central region and the formation of a pinhole.



**Figure 3:** Biomicroscopy of the right eye after corneal penetrating transplantation shows transparent corneal button in 5-year follow-up.



**Figure 4:** Examination of confocal microscopy of the transplanted eye (RE) shows corneal stroma with structure and cellularity within normality.



**Figure 5:** Examination of confocal microscopy of the left eye shows changes such as reduction of subepithelial nerve plexus density, marked reduction of keratocytes in the stroma and accumulation of needle-shaped material in anterior stroma.

describing findings that would later be grouped into a specific corneal dystrophy. This pathology is formed by the appearance of polychromatic thin subepithelial crystals in the central region of the cornea, which can reach the stroma and assume a discoid pattern in most of the affected ones. <sup>(8)</sup> Histologically, there are accumulations of cholesterol and neutral fat in the epithelium, Bowman's layer and anterior corneal stroma. <sup>(9,10)</sup>

The corneal alterations can already be seen in the first decade of life, with slow progression until the 20 and 30 years of age, and an intensified increase of the opacities after the fourth decade <sup>(1)</sup> manifestation analogous to that of our patient, as he resorted to ophthalmologic care when it was already in late adulthood.

The main systemic finding is hypercholesterolemia, however, it has already been reported in the literature that there is no correlation between blood cholesterol levels and the severity of the disease <sup>(11)</sup> and that its systemic reduction does not prevent the progression of the disease. <sup>(12)</sup> In addition, we have a description of genu valgum as another possible component of the clinical picture of SCCD, <sup>(5)</sup> both of which are present in our report.

Often, the SCCD hypothesis requires complementary tests to be validated, due to the countless possibilities of differential diagnoses, including Bietti's crystalline dystrophy, Tangier's disease, cystinosis, type 2 tyrosinemia, infective keratopatiacristalinea, gout, multiple myeloma, as well as, after using certain substances used for treatment under the most diverse conditions, being exemplified by chloroquine, clofazimine, chlorpromazine and gold. <sup>(13)</sup>

An important weapon for distinguishing such pathologies is genetic analysis and biomolecular profile. In this context, the description of the mutation in the UBIAD1 gene is responsible for the development of Schnyder's Dystrophy <sup>(14)</sup> making the diagnosis more accurate. However, genetic mapping often remains within an ideal world, forcing us to look for other diagnostic tools. Invented in 1955, confocal microscopy in vivo, a method that allows the diagnosis of numerous corneal disorders, <sup>(15,16)</sup> including the diagnosis of Schnyder's Dystrophy.

The IVCM allows non-invasive corneal optic section and other structures in real time and at the cellular level. Images are obtained from different depths and allow an 800-fold increase of the corneal structures. <sup>(1)</sup>

The trajectory for the creation of this equipment was not banal. The contact with the microscope universe was first made in the mid-1950s, when pioneers Marvin and Minsky <sup>(17)</sup> developed the first confocal microscope in order to study neural networks in vivo. In 1986, LempEt al. <sup>(18)</sup> inaugurated in vitro cornea research, and his study contributed to the development of tandem scanning confocal microscope (TSCM) with the objective lens horizontally, which made it suitable for ophthalmologic use. Already in the early 90s, Cavanagh <sup>(13)</sup> was the pioneer of corneal studies in vivo with confocal microscopy. To finish the script, Masters and Thaeer, in 1994 made a new variation of the IVCM, generating SSMC (scanning-slit confocal microscope), base system used in the current models. <sup>(19,20)</sup>

This device was shown to be an advance on specular microscopy because it is effective in evaluating all layers of the cornea, including partially opaque corneal conditions, due to edema or scarring, <sup>(5)</sup> which makes it very useful in SCCD, even for this report, in view of the high degree of opacity present, which would preclude an accurate evaluation of all corneal lamellae.

In our case, left-sided IVCM findings, such as: decreased subepithelial nerve plexus density associated with marked reduction of stroma keratocytes and accumulation of needle-shaped material in anterior stroma are corresponding characteristics evidenced in scientific publications correlated with the diagnosis of Schnyder's dystrophy. <sup>(5,15,16)</sup>

## CONCLUSION

Finally, we did not present histopathological and genetic evidence due to sufficient clinical-epidemiological data and typical findings of the SCCD in the confocal microscopy to close the diagnosis, highlighting the magnitude of this equipment in the arsenal of complementary examinations of Ophthalmology.

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### Corresponding author:

Paula Katagui  
Rua Caraíbas, 666 - apto.101 - São Paulo - SP - Brazil  
ZIP Code 05020-000  
Phone/Fax: (11) 98135-9627  
E-mail: paula.katagui@gmail.com