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Nodulo-ulcerative squamous cell carcinoma of the conjunctiva mimicking necrotizing sclerokeratitis in a young patient

Otávio de Azevedo Magalhães [a,*], Maria Paula Sandri Facchin [a], Karoliny Krause Monico [a], Valentina Oliveira Provenzi [b], Marcelo Blochtein Golbert [a]

[a] Cornea and External Disease Division, Porto Alegre Eye's Bank Hospital, Brazil
[b] Department of Pathology, Hospital Conceição, Porto Alegre, Brazil

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ABSTRACT

Purpose: A delay in diagnosing and treating ocular surface squamous neoplasia (OSSN) with an atypical manifestation can lead to a progression to more advanced stages, resulting in a decrease in cure rates and treatment effectiveness.

Observations: This case report describes a 21-year-old white male who presented to our Cornea Division with peripheral nasal corneal and scleral thinning with prolapse of uveal tissue in the right eye for over four months and who had received a sclerocorneal patch graft. The patient underwent systemic immunosuppressive therapy for presumed Mooren's ulcer after laboratory evaluation eliminated a collagen vascular disorder. Approximately three months after the procedure the patient returned with an inferior and superior sclerocorneal perforation. Six months after the first visit to our department, he returned to our ophthalmological emergency department with self-evisceration of the intraocular contents. He underwent an emergency evisceration procedure, and histopathological analysis of the intraocular contents revealed a poorly differentiated nodulo-ulcerative squamous cell carcinoma of the conjunctiva with intraocular invasion. A tomographic evaluation suggested orbital invasion. Subsequently, he underwent exenteration.

Conclusions and Importance: OSSN should be considered in the differential diagnosis of corneal or scleral thinning, perforation, and inflammation of an unknown cause even in young patients, especially after systemic disorders have been excluded.

1. Introduction

Intraocular and orbital invasion of ocular surface squamous neoplasia (OSSN) is rare and has been reported in only 1%–13 % of OSSN cases.[1,2] Such invasion occurs either by direct invasion of the tumor through the sclera or inoculation through a previous intraocular surgery incision or along the tract of the anterior ciliary vessels.[3,4] It is reported to mainly affect elderly men who live in areas of increased sun exposure.[5] The lesions typically present unilaterally as a gelatinous mass in the limbic area and are leukoplakic, opalescent, and/or papillomatous lesions with irregular borders and dilated and tortuous vessels and in the sun-exposed interpalpebral region.[6] However, OSSN of the conjunctiva without a distinct mass can be found and can resemble sclerokeratitis, peripheral ulcerative keratits, or scleromalacia.[7,8] Based on histopathology, intraocular or orbital invasion of OSSN is more commonly observed with aggressive variants, including spindle-cell, mucoepidermoid, and adenoid squamous variants.[9,10]

We describe an unusual presentation of a nodulo-ulcerative squamous cell carcinoma of the conjunctiva (SCCC) presenting as necrotizing sclerokeratitis in a young male.

2. Case report

A 21-year-old white male presented with redness of the right eye (RE) and mild discomfort for over four months. He had a history of receiving a conjunctival flap to treat scleral thinning two months earlier in his city of origin. The first examination at our Cornea Division revealed nasal peripheral corneal and scleral thinning with prolapse of uveal tissue in the RE from the 3 to 5 o'clock positions with engorged vessels and adjacent chemosis (Fig. 1). The best corrected visual acuity was 20/200 in this eye. The left eye was normal. A systemic evaluation was initiated and was negative for collagen and infectious diseases. A

* Corresponding author. 333 Mostardeiro st, office 503, Porto Alegre, RS, 90430-001, Brazil.
E-mail address: otaviomaga@yahoo.com.br (O.A. Magalhães).

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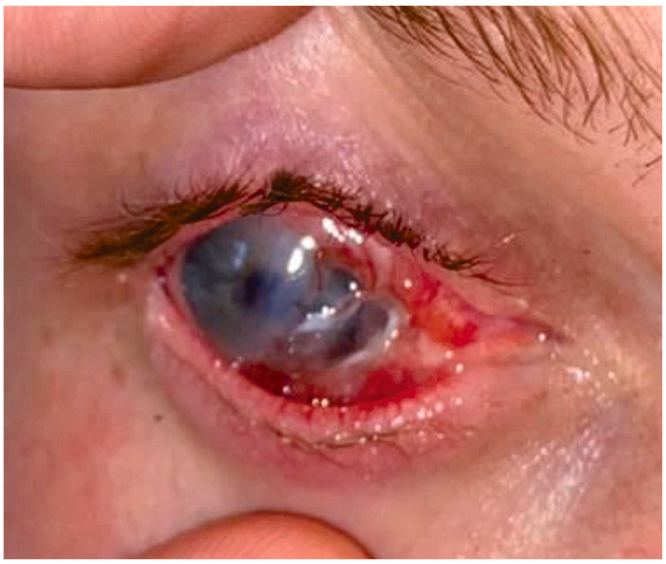

Fig. 1. Right eye image showing nasal peripheral corneal and scleral thinning with prolapse of uveal tissue in the right eye from the 3 to 5 o'clock positions with engorged vessels and adjacent chemosis.

diagnosis of Mooren's Ulcer was the first clinical hypothesis, and immunosuppressive therapy was initiated. The patient received a sclerocorneal patch. Three months later, however, he developed inferior and superior necrotizing sclerokeratitis with perforation and iris entrapment in the RE, and another corneal patch was provided (Fig. 2). Approximately six months after the first visit to our department, he returned to our ophthalmology emergency department with fixed esotropia and a new perforation with self-evisceration of the intraocular contents. A linear ultrasound did not show expansive intraocular lesions, and surgical completion of evisceration was performed. A post-operative orbital computed tomography (CT) scan showed a hyperdense oval lesion that measured 1.6 cm at the largest diameter in the right orbit without extraocular muscles and optic nerve compromise (Fig. 3A–C). Subsequently, orbital exenteration was performed in the RE and revealed poorly differentiated SCCC extending up to the conjunctival fornix. The patient was followed up for 24 months and had no recurrence.

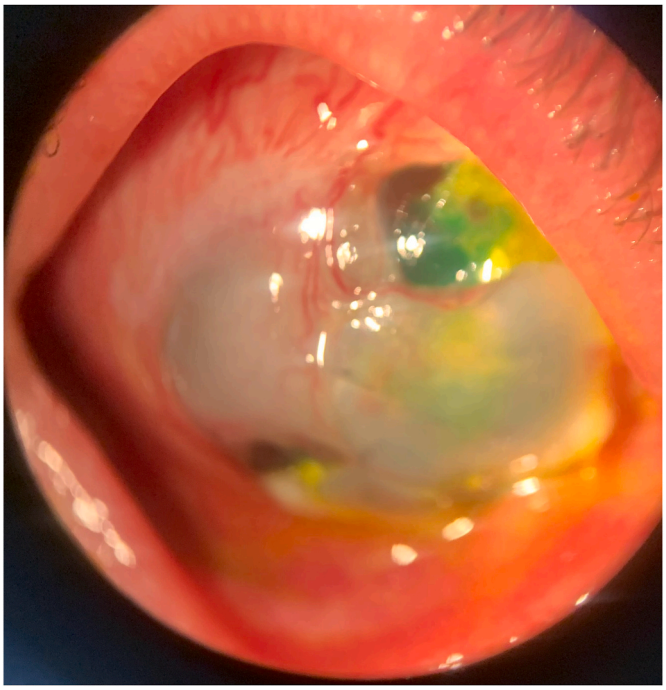

Fig. 2. Right eye image showing Inferior and superior necrotizing sclerokeratitis with perforation and iris entrapment.

3. Histopathology

The tumors from the initial biopsy and definitive exenteration were assessed. The biopsy from the corneoscleral tissue showed a moderately differentiated SCCC on a bed of capillary proliferation and a dense lymphoplasmacytic infiltrate (Fig. 4A). In some areas the tumor appeared differentiated and had thin strands of infiltrative tumor demonstrating loss of cohesiveness and individual cell keratinization. The conjunctival biopsy showed a localized area of superficially invasive SCCC associated with an area of dense chronic inflammation (Fig. 4B). The exenteration specimen showed invasive, moderately differentiated SCCC limited to the anterior orbital tissues. Inferiorly, the conjunctival tumor extended along the surface of the globe to the area of the inferior fornix. A zone of inflammatory cells and desmoplastic stroma surrounded the invading tumor strands. Intraocularly, the tumor filled the anterior chamber angle and spread extensively onto the retinal tissues (Fig. 4C). The p63 and p40 immunohistochemical markers confirmed the SCCC diagnosis (Fig. 4D).

4. Discussion

Our literature review using the terms *nodulo-ulcerative SCCC* and *necrotizing sclerokeratitis SCCC* could find a total of 13 cases on PubMed and Google Scholar in December 2023.[7,8,11–13] All patients described in these cases were males ranging from 31 to 78 years old. Although human immunodeficiency virus (HIV)-positive patients are reported to have more aggressive and atypical presentations, only two patients described in these cases who had nodulo-ulcerative SCCC were positive for HIV.[12] Most of these patients, including our case, were immunocompetent and had no significant comorbidities.

All subjects with nodulo-ulcerative SCCC presented unusual features of tissue inflammation and thinning of the cornea or sclera without any mass formation. Therefore, a delay in the diagnosis in almost all the cases in the literature was reported, as occurred with our case due to the unusual clinical appearance.[8,12,13] Necrosis leading to inflammation may be the result of a very rapidly growing tumor with an intraepithelial lateral growth pattern and vascular invasion. None of the described cases had metastatic disease despite uveal involvement.[7,12]

In most case reports, the patients underwent screening for infectious and rheumatic diseases, and no pathologies were identified.[12] Additionally, topical and systemic corticosteroids were used, which delayed the diagnosis and specific treatment for OSSN.[14] In our case, initially, immunosuppressive therapy was initiated due to the suspicion of Mooren's ulcer.

The treatment of nodulo-ulcerative SCCC depends on tumor extension. Once intraocular extension is diagnosed, enucleation is indicated. If an associated orbital or muscle involvement is present, an exenteration is required. Diffuse growth with inflammation and vascular invasion appears to contribute to thinning, necrosis, and perforation of the surrounding ocular tissues, resulting in intraocular spread even without the presence of a tumor mass. The delay in diagnosis confirmation explains the fact that the disease is usually diagnosed at advanced stages; hence, the majority of patients have undergone exenteration.[7,8,12,13] Although limited in various institutions, it is important to highlight that adjuvant ocular surface radiotherapy can be performed using brachytherapy, proton or electron beam radiation therapy for invasive carcinomas.[15] Radiation therapy could salvage the eye from exenteration even if the eye becomes phthisical as would be expected.

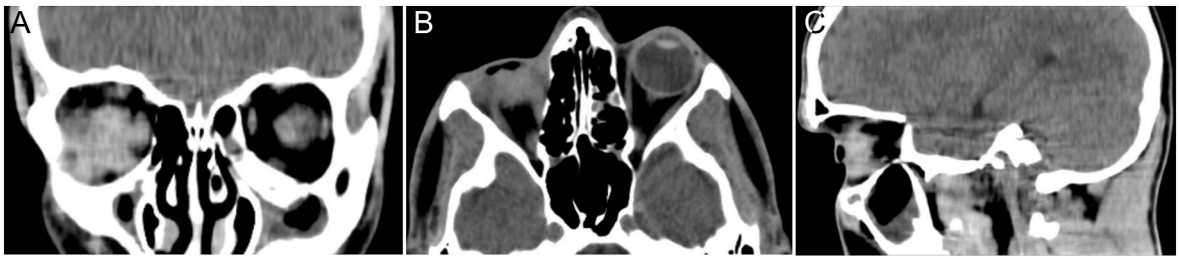

Fig. 3. Post-evisceration orbital CT scan showing a hyperdense oval lesion, measuring 1.6 cm in the largest diameter in the right orbit without extraocular muscles and optic nerve compromise. A-C.

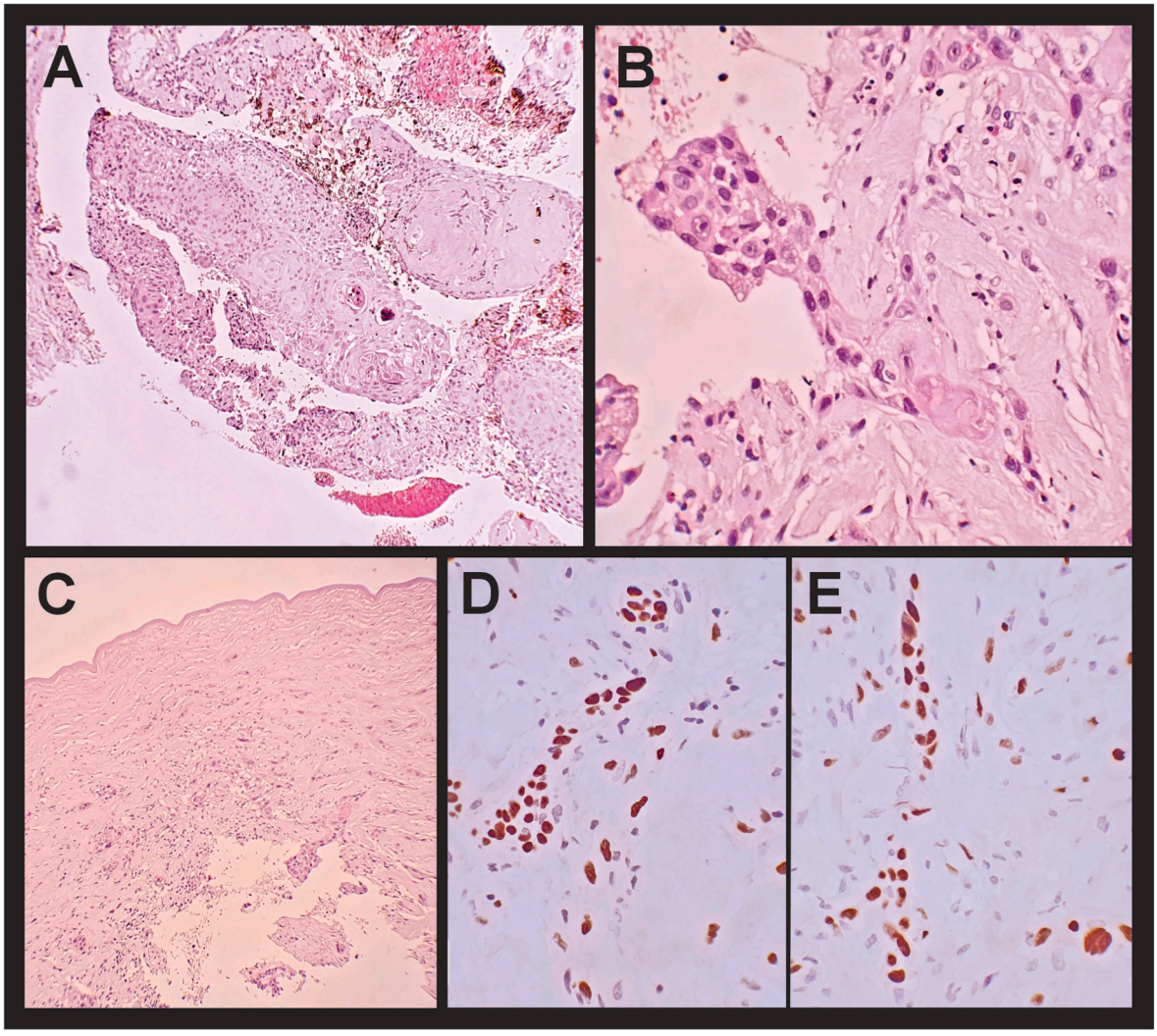

Fig. 4. Biopsy from the corneoscleral tissue showing a moderately differentiated squamous cell carcinoma on a bed of capillary proliferation and a dense lymphoplasmacytic infiltrate (Fig. 4A). Conjunctival biopsy showing a localized area of superficially invasive squamous cell carcinoma associated with an area of dense chronic inflammation (Fig. 4B). Exenteration specimen showing invasive, moderately differentiated squamous cell carcinoma limited to the anterior orbital tissues (Fig. 4C). Immunohistochemical markers p63 and p40 confirming the diagnosis of squamous cell carcinoma (Fig. 4D).

5. Conclusion

Though rare, it is important for all ophthalmologists to be aware of nodulo-ulcerative SCCC presenting as necrotizing sclerokeratitis. Such a diagnosis should be considered in the differential diagnosis of corneal or scleral thinning, perforation, and inflammation of unknown causes in males at any age, especially when systemic diseases have been excluded.

Patient consent

The patient has consented to the submission of the case report for submission to the journal.

CRediT authorship contribution statement

Otávio de Azevedo Magalhães: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project

administration, Methodology, Investigation, Formal analysis, Conceptualization. **Maria Paula Sandri Facchin:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Karoliny Krause Monico:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Formal analysis, Data curation, Conceptualization. **Valentina Oliveira Provenzi:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Formal analysis, Conceptualization. **Marcelo Blochtein Golbert:** Writing – review & editing, Writing – original draft, Validation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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None.

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