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Early Diagnosis of Invasive Conjunctival Squamous Cell Carcinoma in a Young, Immunocompetent, Melanoderma Patient at the Ziguinchor Peace Hospital

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Abstract

Squamous cell carcinoma of the conjunctiva (SCC) is a malignant tumor arising from the conjunctival epithelium, relatively rare in our setting. We report a case of SCC with an atypical epidemiological and clinical presentation, discovered incidentally at an early stage, in an immunocompetent patient of dark skin treated at the Ziguinchor Peace Hospital. Observation: This is a 42-year-old patient, admitted to the ophthalmology department for an inflammatory conjunctival lesion in the right eye, resistant to topical corticosteroid therapy and evolving for more than a month. The ophthalmological examination revealed a rounded, nasal, paralimbic, inflamed conjunctival swelling with overlying vascular dilation. It presented a smooth, regular surface. A marginal, juxtalar corneal ulcer was noted. The remainder of the examination was normal. Excision and biopsy were performed with intraoperative application of an antimitotic agent. Histopathological examination of the specimen led to the diagnosis of a well-differentiated, mature, and infiltrating squamous cell carcinoma. Complete surgical excision (biopsy and excision) with clear 2 mm margins was performed, combined with intraoperative topical application of 5-Fluorouracil (5-FU). Conclusion: Squamous cell carcinoma of the conjunctiva in our setting is a rare condition that can affect young, immunocompetent males. This lesion can mimic a benign lesion, leading to diagnostic uncer-

tainty. Histopathological examination after surgical excision is of paramount importance for management.

Keywords

Conjunctiva, Squamous Cell Carcinoma, Ophthalmology, Histology, Ziguinchor

1. Introduction

Squamous cell carcinoma of the conjunctiva (SCC) is a primary malignant tumor arising from the conjunctival epithelium, which can affect not only ocular function but also the patient's life [1] [2]. Although relatively rare worldwide, it is the most common malignant tumor of the conjunctiva [2] [3].

The epidemiology of this cancer varies considerably depending on the region of the world and age. Certain environmental and individual factors have been implicated in the occurrence of the initial lesion, with chronic sun exposure being the main one [2] [3].

In sub-Saharan African countries, SCC is particularly aggressive and occurs preferentially in young individuals, often female, in close association with human immunodeficiency virus (HIV) infection [3] [4]. In contrast, in Caucasian populations of temperate countries, it mainly affects men over 60 years of age [2] [3].

In this context, we report an exceptional and highly instructive case of invasive conjunctival squamous cell carcinoma diagnosed at an early stage in a young, dark-skinned, immunocompetent patient. Through this case, we discuss the epidemiological and clinical characteristics, the biomicroscopic diagnostic criteria for early detection, and the modalities of adjuvant surgical management with a local antimitotic agent (5-Fluorouracil) in a semi-rural setting in Senegal.

2. Observation

The patient was a 42-year-old teacher residing in the Ziguinchor region (southern Senegal) who was admitted to the Ophthalmology Department of the Peace Hospital for a swollen, inflammatory conjunctival lesion in his right eye. This lesion, which had been present for over a month, had proven completely refractory to first-line topical corticosteroid therapy prescribed at a local health facility (See **Figure 1**). A thorough medical history revealed no significant past medical conditions, including any suspicious dermatological lesions suggestive of xeroderma pigmentosum. It should be noted that the patient did not routinely wear UV-protective eyewear.

The ophthalmological examination revealed bilateral visual acuity of 10/10 and normal intraocular pressure of 10 mmHg in both eyes. A detailed examination of the ocular structures is recorded comparatively in **Table 1**.

Table 1. Elements of the detailed clinical examination, including biomicroscopy.

CLINICAL PARAMETER	RIGHT EYE	LEFT EYE
Distance Visual Acuity	10/10[e]	10/10[e]
Near Visual Acuity	Parinaud 2	Parinaud 2
OCULAR ADNEXA	- rounded, nasal, paralimbic, inflammatory conjunctival swelling with a smooth and regular surface - gelatinous content - *perilesional vascular dilation* (sentinel vessels)	Healthy
ANTERIOR SEGMENT	- marginal, juxtalar corneal ulcer	Normal
INTRAOCULAR PRESSURE	10 mm Hg	10 mm Hg
FUNDUS	Normal appearance	Normal appearance

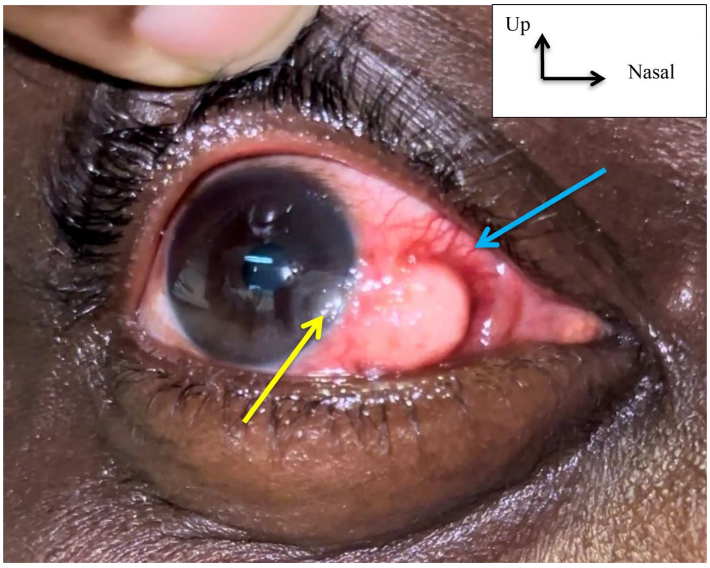


Figure 1. Preoperative appearance of the lesion. 1) Blue arrow: perilesional vascular dilation; 2) Yellow arrow: marginal, juxtalimbic corneal ulcer.

The clinical examination was unremarkable. The regional lymph node areas were clear. The orbital and cerebral CT scan was normal. The retroviral serology was negative.

Given this conjunctival lesion which, despite a smooth surface of benign appearance, presented highly suspicious warning signs of malignancy (perilesional vascular dilation, juxtalesional corneal ulcer and resistance to topical corticosteroid therapy) A wide excision-biopsy was decided from the outset. This choice was reinforced by the impossibility of considering adjuvant external beam radiotherapy in the Ziguinchor region, due to the unavailability of this therapeutic modality throughout southern Senegal and the patient's significant professional and socio-economic constraints precluding transfer to a center in Dakar.

The surgical procedure consisted of complete macroscopic excision of the lesion, respecting a 2 mm safety margin in healthy conjunctival tissue, according

to oncological guidelines. To compensate for the absence of adjuvant radiotherapy, we performed a local intraoperative application of an antimitotic agent, 5-Fluorouracil (5-FU). A sterile surgical sponge (cotton swab) was soaked in a pure 50 mg/mL 5-FU solution (without prior dilution) and applied directly to the exposed sclera for a strict duration of 5 minutes, taking meticulous care to avoid any direct contact with the corneal epithelium. Immediately after the application time, the surgical site was thoroughly and copiously rinsed with 50 mL of isotonic saline to remove any remaining product and stop the cytotoxic effect (see Figure 2).

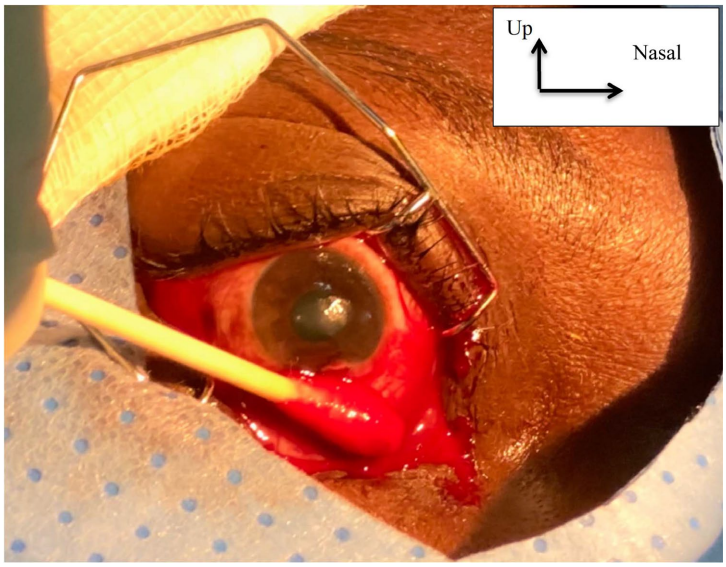


Figure 2. Application of the cotton swab soaked in antimitotic to the excision area, intraoperatively.

The excised specimen was sent to the Anatomy and Cytology-Pathologies laboratory, preserved in 10% buffered neutral formalin.

Histopathological examination led to the diagnosis of a well-differentiated, mature squamous cell carcinoma of the conjunctiva arising from the conjunctival epithelium and infiltrating the conjunctival stroma. This proliferation consisted of well-differentiated carcinomatous cells, dyskeratotic in places, generally arranged in clusters and trabeculae centered on keratinized globules. These cells exhibited moderate to severe cytological atypia, including anisocytosis, anisokaryosis, nuclear hyperchromatism, and a high nucleocytoplasmic ratio, with some mitotic figures. The stroma was polymorphic fibro -inflammatory and necrotic in places. This neoplasm was at least 0.5 mm from the excision margins (see Figure 3).

Close monitoring was instituted post-operatively. Clinical progress was meticulously documented during scheduled visits.

On postoperative day 1 (D1): biomicroscopic examination showed a clean excision bed, undergoing normal healing. Diffuse conjunctival hyperemia was noted, perfectly consistent with the expected reactive inflammatory syndrome in

the early postoperative period (Figure 4).

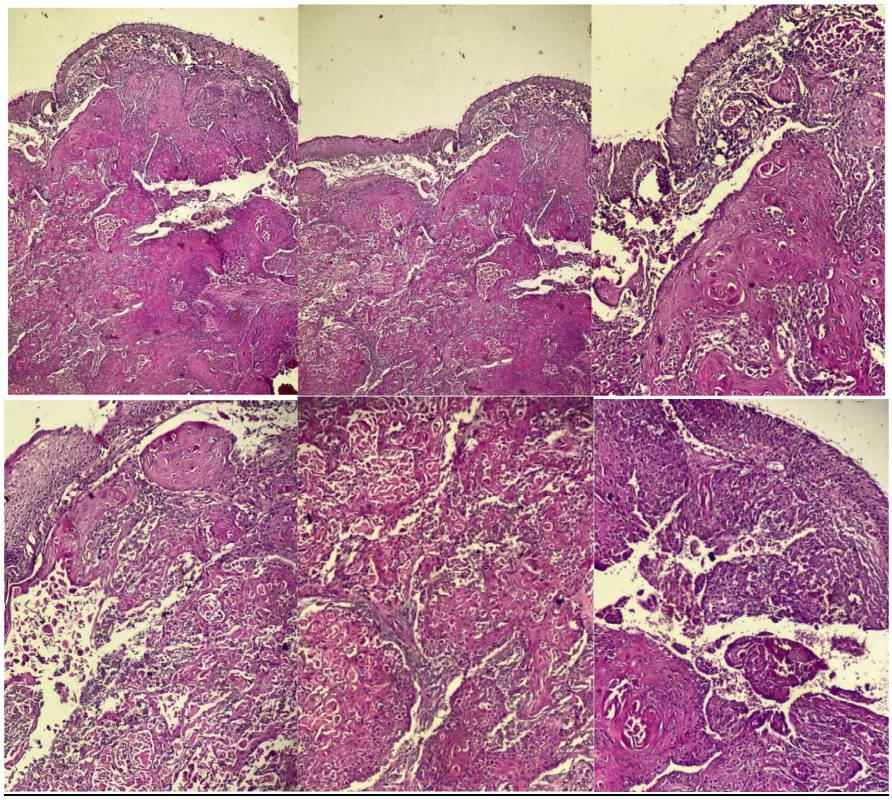


Figure 3. Histological section of the excised specimen.

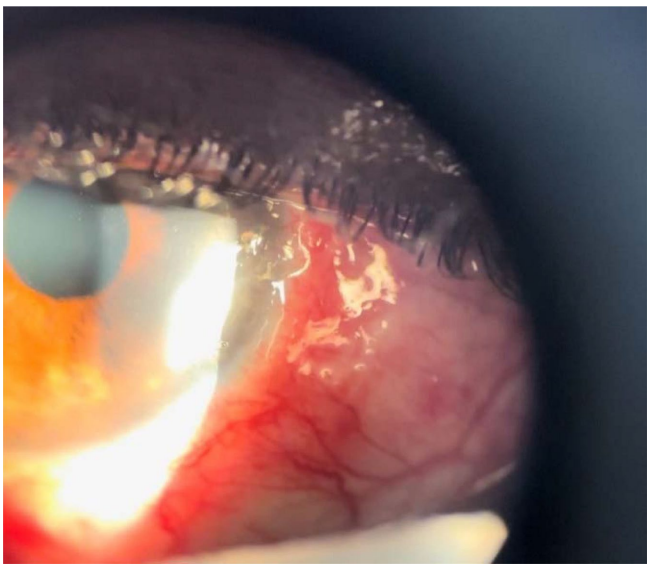


Figure 4. Post-Operative day 1: Inflammation of the ocular surface.

Postoperative Day 10 (D10): Slit-lamp examination revealed complete conjunctival healing. We observed total regression of hyperemia (absence of any inflammation) and a perfectly healthy tumor bed. The marginal corneal ulcer adjacent

to the lesion was completely healed. No granulation tissue or conjunctival elevation suggestive of recurrence was observed (Figure 5).

At 6 months post-operative (M6): The examination of the ocular surface was strictly normal, without any signs of inflammation or tissue growth suspicious of local recurrence.

Long-term monitoring schedule: Given the inherent risk of recurrence of these invasive carcinomas, monitoring remains a critical phase of our management. We asked the patient to consult at the slightest ophthalmological symptom and scheduled a follow-up visit 1 year post-surgery, then implemented systematic annual clinical follow-up within our ophthalmology department.

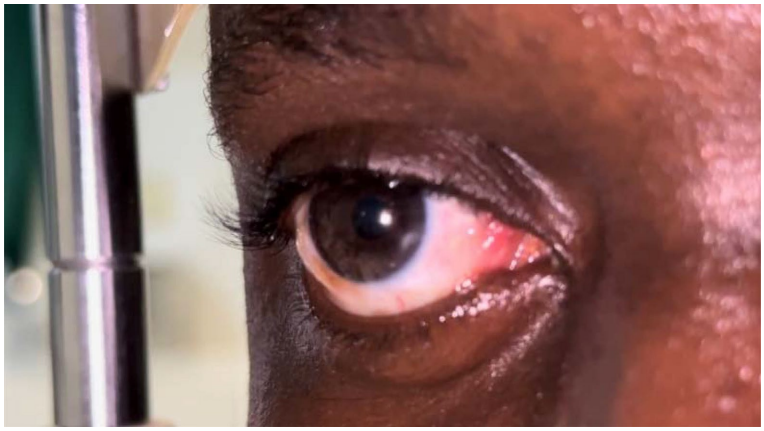


Figure 5. Post-Operative day 10: Complete healing of the conjunctiva; regression of conjunctival hyperemia, healthy tumor bed, healing of the marginal corneal ulcer.

3. Discussion

Squamous cell carcinoma (SCC) is the most common non-pigmented malignant tumor of the ocular surface [2] [3]. Its annual incidence varies considerably worldwide: it is estimated at only 0.03 cases per 100,000 inhabitants in the United States, rises to 0.13 per 100,000 in Uganda, and reaches a peak of 1.9 per 100,000 in Australia [2] [3]. In Senegal, there is no national incidence registry for this cancer. However, hospital prevalence data indicate that it represents a significant proportion of ocular oncology activity. For example, Seck *et al.* (2015) reported that SCC accounted for 15.08% of all primary ocular cancers in adults (in a cohort of 111 cases collected at a national reference center in Dakar) [4].

Race is not a risk factor according to Pisella [5], although two epidemiological profiles are generally described in the literature: on the one hand, young, dark-skinned, female subjects in sub-Saharan Africa, presenting with a state of severe immunosuppression linked to HIV/AIDS; on the other hand Caucasian male subjects, aged over 55 - 60 years, residing in countries near the equator [2] [3].

Our case report is therefore an exception: it concerns a male patient in his forties, with dark skin, and who is immunocompetent. Our patient's immunocom-

petent status was defined based on the following elements:

- a negative HIV serology
- Absence of diabetes: Metabolic assessment revealed a fasting blood glucose level strictly within normal limits, ruling out a state of immunosuppression secondary to uncontrolled diabetes.
- No history of immunosuppressive therapy: The detailed medical history revealed no underlying chronic disease or long-term medication use that could impair immunity (such as long-term systemic corticosteroid therapy or immunosuppressive treatment).

Several epidemiological studies have indeed demonstrated a direct correlation between proximity to the equator, ambient UV radiation intensity, and the incidence of conjunctival sclerosis (SCC) [6] [7]. Other risk factors have been implicated in the development of CSS, including human papillomavirus (HPV) infections (strains 65 and 66), xeroderma pigmentosum, and HIV infection at the AIDS stage [8]. HPV is, moreover, more readily considered a cofactor in conjunctival carcinogenesis rather than a direct initiating factor, as it can be found on the ocular surface of healthy individuals [5] [8].

In our patient, exposure to ultraviolet radiation is strongly suspected as the primary risk factor. Our patient works in southern Senegal (Ziguinchor), a geographical area characterized by constant and extremely intense ultraviolet radiation throughout the day. Furthermore, the patient interview revealed that he never wore UV-protective sunglasses. We also emphasize that in our region, even when people choose to wear sunglasses, their UV protection remains highly questionable, due to the total lack of control over the market for the sale of this equipment.

From a diagnostic standpoint, the originality of this case lies in its extremely early detection. In Africa, squamous cell carcinoma (SCC) is notoriously known for its late diagnosis, occurring at stages of major intraocular or orbital invasion, leading to high rates of enucleation or exenteration and a poor prognosis, as described by Seck in Senegal and Bamanta in Mali [4] [9]. Clinically, distinguishing between certain benign lesions, precancerous lesions, and certain early cancerous lesions of the ocular surface can be difficult, as there is a similarity in the clinical signs observed on biomicroscopic examination [10]. In general, invasive squamous cell carcinoma presents clinically as a raised, multilobulated lesion. Occasionally, it can exhibit atypical features such as the "masquerade syndrome" [11]. It is often located on the exposed area (palpebral cleft area), near the limbus and extends onto the cornea. The satellite vessels are dilated. Intraocular and orbital invasion is possible, especially in advanced forms [1] [5]. In our case, the early diagnosis is explained by two key elements: firstly, rigorous clinical suspicion based on specific biomicroscopic warning signs (absence of the classic triangular shape, intense satellite vascular dilation, marginal corneal ulcer and resistance to topical steroidal anti-inflammatory treatments) which made it possible to quickly rule out the reassuring but erroneous hypothesis of an inflammatory pterygium or pinguecula [10] [11]. On the other hand, the immediate proximity and responsiveness of the

Anatomical Pathology service operating within the Peace Hospital of Ziguinchor made it possible to obtain a definitive histological diagnosis in less than 10 days, thus avoiding the diagnostic uncertainty that is common in these semi-rural contexts.

Regarding therapeutic management, the international oncological standard for invasive conjunctival squamous cell carcinoma recommends complete surgical excision with clear margins (R0) ideally complemented by systematic adjuvant external beam radiotherapy or brachytherapy to prevent frequent local recurrences [1] [6] [12].

Given the unavailability of radiotherapy in the Ziguinchor region and the patient's limited resources, which precluded a prolonged medical evacuation to Dakar, we opted for a high-performing alternative approach: the intraoperative topical application of 5-Fluorouracil (5-FU) at 50 mg/mL for 5 minutes. This rigorous protocol, initially validated by Smith *et al.* (1992) for filtering surgery and the ocular surface, has proven extremely effective [13]-[15]. It inhibits the proliferation of potential residual microscopic tumor cells on the scleral bed without inducing major intraocular or systemic corneal toxicity, provided that copious rinsing with 50 mL of saline is performed as a precaution.

A CT scan performed did not reveal any regional lymph node involvement. A CT scan is necessary for TNM classification [12].

Anatomopathological analysis was crucial in confirming the diagnosis and guiding our treatment. Histopathological examination of the excision biopsy (preserved in formalin) revealed a carcinomatous proliferation arising from the conjunctival epithelium, actively infiltrating the conjunctival stroma. Anatomopathological analysis confirmed the completeness of the excision with clear margins. Clinically, the lesion was paralimbic with a marginal corneal ulcer adjacent to the lesion. The superficial corneal involvement (marginal reactive ulcer) was not of a direct infiltrating tumor nature, which was confirmed by its complete and rapid healing after simple excision of the primary conjunctival lesion.

The absence of tumor recurrence after 6 months of clinical follow-up and the perfect conjunctival healing achieved in our patient validate our combined therapeutic approach. Nevertheless, given the high long-term recurrence rate associated with invasive squamous cell carcinomas (SCCs), rigorous clinical monitoring must be continued annually, which is an essential step in our patient's follow-up. This will allow us to detect any potential recurrence very early and to initiate appropriate and effective management.

4. Conclusion

Conjunctival squamous cell carcinoma (CSC) is the most common non-pigmented tumor of the ocular surface. It can affect young, dark-skinned, and immunocompetent individuals, independent of any association with HIV. In our region, it is still rare or possibly underdiagnosed. This lesion can mimic a benign lesion. The presentation of clinical cases therefore serves to draw the attention of

the ophthalmological community to the potential for underdiagnosis at an early stage of this pathology, due to a presentation that can lead to diagnostic uncertainty. Furthermore, it aims to highlight for the authorities the importance of having a functioning histopathology department, as histopathological examination is crucial for establishing the diagnosis and guiding definitive management.

Informed Consent

We formally confirm that the patient's oral informed consent was duly obtained for the taking of the images and the publication of this clinical case report, as well as for the use of all of its associated clinical photographs.

Ethical Approval

In accordance with local regulations in force at the Ziguinchor Peace Hospital, the publication of a single and anonymized clinical case does not require formal approval from an institutional ethics committee, subject to strict respect for the confidentiality and anonymity of patient data, which has been rigorously guaranteed.

Author Contributions

The specific roles and contributions of all co-authors are defined as follows:

- Dr. Irma Eneida Almeida dos Santos: Principal clinical examiner, performed the surgical excision-biopsy and intraoperative topical 5-Fluorouracil application, coordinated patient follow-up, and authored the initial manuscript draft.
- Dr. Fabrice Senghor & Dr. Ibou Thiam: Performed the histopathological examination of the excised tissue specimen, conducted cytological and architectural analysis confirming invasive conjunctival squamous cell carcinoma, and prepared histological figures.
- Dr. Joseph Matar Mass Ndiaye & Pr. Paule Aida Ndoye: Provided senior clinical supervision, participated in overall diagnostic strategy and patient management protocol design, critically revised the manuscript for intellectual content, and granted final approval.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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