Conjunctival Candidiasis Mimicking Ocular Surface Squamous Neoplasia

Zhiyu Peng
Fudan University Eye Ear Nose and Throat Hospital
https://orcid.org/0000-0001-8318-8878

Jiang Qian
Fudan University Eye Ear Nose and Throat Hospital

Yinan Han (yinanhan2021@126.com)
Fudan Eye & ENT Hospital, Shanghai

Brief report

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Abstract

Purpose

To report a case of conjunctival candidiasis mimicking ocular surface squamous neoplasia.

Case presentation

A 71-year-old man presented with a history of persistent redness, swelling and watering in the left eye accompanying an enlarging mass in the conjunctiva. He underwent excisional biopsy which showed granulomatous inflammation accompanied by irregular and atypical squamous epithelium hyperplasia. Periodic acid-Schiff stain and methenamine silver stain revealed a fungi infection. Further secretion smear was performed to clarify the pathogen as *Candida albicans* and a chronic fungal maxillary sinusitis was found through imaging test. Thus a diagnosis of conjunctival candidiasis was made.

Conclusions

Conjunctivitis caused by fungi is rare and a trigger such as agriculture trauma, immunocompromise state, contact history to fungal environment or contaminated water or infection of adjacent organs occurs in most cases. We report the case not only to share diagnostic and treatment experience, but also describe the unique histopathological manifestation leading to a speculation that chronic fungal or candida albicans infection might induce squamous metaplasia.

Introduction

Ocular fungal infection is a sight-threatening disease with multiple incentives typically involving the cornea and internal structures of the eye. Fungal conjunctivitis, especially conjunctival lesion alone, is so rare that often reported as case reports. The diagnosis mainly relies on medical history, biopsy and specific staining and requires the exclusion of other diseases. In our study, we report a case of conjunctival candidiasis with pathological presentation similar to ocular surface squamous neoplasia.

Case Presentation

A 71-year-old male was referred to our clinic with complaints of persistent redness, swelling and watering in the left eye for the past 10 months, accompanying a progressively enlarging greyish mass in the conjunctiva for 7 months. He was treated elsewhere with topical antibiotics, corticosteroid, interferon α2b, artificial tear and subconjunctiva injection of Triamcinolone Acetonide twice for a diagnosis of undefined conjunctivitis, conjunctiva scar and dry eye. He underwent a ‘pterygium’ surgery in the same eye 6 years before without pathological examination and was diagnosed with diabetes for 4 years. He was a dealer of plastic and frequently in touch with sand, soil and glass fibre and had a history of exposure to aspergillus associated with winemaking from the 1970s to the 1990s.
Ophthalmic examination revealed a tough and immobile grayish broad basal mass, whose surface was unsmooth with telangiectasia, at the 7-2 o'clock position on the limbus and 4-6 o'clock position near the conjunctiva in the left eye (Fig. 1). The upper palpebral conjunctiva showed a local bulge of 3×2mm on the lateral and proximal edge. The cornea and intraocular part of left eye and the right eye were normal. No palpable cervical lymph nodes were found. Ultrasound biomicroscopy (UBM) revealed a conjunctival mass of low to moderate echo at the limbus except the lower part and subtemporal part in the left eye. The mass, of which the maximum thickness was 2.04mm, had heterogeneous echoes and clear boundary.

The patient received conjunctival mass excisional biopsy and the histopathologic examination revealed granulomatous inflammation accompanied by irregular and atypical squamous epithelium hyperplasia (Fig. 2). Fungi were detected by periodic acid-Schiff (PAS) stain and methenamine silver stain (Fig. 3). Topical voriconazole therapy was given soon after pathological diagnosis and further examination was done. Computed tomography and magnetic resonance imaging suggested a fungal infection on the right maxillary sinus. Serum 1,3-β-glucan was detected elevated to 139.8pg/ml. The secretion smear indicated Candida albicans infection. The patient was diagnosed with an ocular fungal infection and chronic maxillary sinusitis. Voriconazole 200mg for injection was given intravenously every 12 hours for over 20 days, and doubled on the first day.

The mass on left conjunctiva and bulbar conjunctiva completely subsided after excision and continuous anti-fungal treatment. Partial pannus with neovascularization was seen in the upper cornea and no conjunctival congestion was observed.

Discussion

Isolation of fungi from the conjunctival sac occurs in normal eyes. Sisinthy Shivaji et al have tested the healthy human ocular surface fungal microbiome by using next-generation sequencing (NGS). Candida Albicans was present in 17 out of 25 samples.\(^1\) But conjunctivitis caused by fungus was rare and were reported as sporadic cases,\(^2\)\(^-\)\(^4\) probably due to the vascular network and lymphoid structures of the conjunctiva which provide abundant cellular defense.\(^5\) The primary cause of the infection might be related to contaminated water, agriculture trauma, immunocompromise state, long-term exposure to fungal environment\(^1\) or fungal infection elsewhere. Mucopurulent discharge and granulomatous inflammation such as grayish deposit often occur especially in the case of Candida infection\(^6\).

Our case of Candida albicans conjunctivitis was not preceded by obvious trauma, but patient had diabetes and a fungal infection on the right maxillary sinus, his occupation also revealed a long-term exposure to fungal environment. Frequent use of topical antibiotics and corticosteroid were likely to result in and prolonged fungal infection. All might have led to inoculation.

Epithelial hyperplasia is a confirmed classic pathologic feature in oral candidiasis. A study conducted by P. S. S. Pina et al. analyzed 36 cases of chronic hyperplastic candidiasis (CHC) and a dysplastic
epithelium were present in nearly half of the cases. Moreover, Pabuççuoğlu, U. et al have reported histopathology of hyperplastic lesion mimicking squamous cell carcinoma in five cases of laryngeal candidiasis. Our case displayed a similar manifestation, indicated that the chronic fungal or *candida albicans* infection might induce squamous metaplasia. This histopathologic manifestation make it more difficult to distinguish between chronic candidiasis and carcinoma.

In summary, diagnosis and treatment of fungal conjunctivitis usually need excisional biopsy, as well as sufficient general and topical anti-fungal drugs. Discovery of yeast, pseudohyphae and true hyphae in sections is the key to diagnose candidiasis.

**Abbreviations**

UBM: Ultrasound biomicroscopy; PAS: periodic acid-Schiff; NGS: next-generation sequencing; CHC: chronic hyperplastic candidiasis

**Declarations**

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None.

**Authors’ contributions**

All the authors contributed significantly to this report, and all the authors agree to be accountable for all aspects of the work. All authors read and approved the final manuscript.

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**Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Ethics approval and consent to participate**

The study was approved by the ethics committee of Fudan Eye and ENT Hospital.

**Consent for publication**

Written consent for images and data publication and identifying clinical details was obtained from the patient.
**Competing interests**

The authors declare that there is no conflict of interests.

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**Figures**
Figure 1

A, B and C, preoperative photograph of left eye, showing grayish broad basal masses at the 7-2 o’clock position on the limbus and 4-6 o’clock position near the conjunctiva.
Figure 2

Histopathology slide showing irregular and atypical squamous epithelium hyperplasia and granulomatous inflammation (Hematoxylin-Eosin staining stain, original magnification ×10).
Figure 3

Fungal spores (black arrow in A and white arrow in B) and hypha (black arrow in C) can be seen in multinucleated giant cells (A, periodic acid-Schiff stain, original magnification $\times 40$. B and C, methenamine silver stain, original magnification $\times 40$).