

Access this article online

Quick Response Code:



Website:

www.e-tjo.org

DOI:

10.4103/tjo.tjo_46_20

A case of fungal conjunctivitis with giant papillae treated surgically

Asami Shimokawa, Ayaka Kobayashi, Yusuke Saeki, Eiichi Uchio*

Abstract:

Fungal conjunctivitis is a rare disorder, with low incidence and difficulty in diagnosis due to a lack of specific clinical findings. We report a case of fungal conjunctivitis which exhibited a specific clinical feature of giant papilla formation, and its diagnosis was a complex process. A 19-year-old woman with a history of atopic dermatitis and hard contact lens use was referred to us with a 3-month history of giant papillary conjunctivitis of the right eye in spite of treatment with antiallergic and corticosteroid eye drops, complicated by intraocular pressure elevation. The left eye showed no symptom of ocular surface disorder throughout the clinical course. The right eye did not respond to oral corticosteroid. Polymerase chain reaction of conjunctival scrapings against *Chlamydia trachomatis* was negative, and she was treated surgically by total papilla resection. Conjunctival giant papilla recurrence was not observed after surgery. Although the primary histopathological diagnosis was chronic inflammation due to atopic keratoconjunctivitis, repeated histopathological survey of excised conjunctival tissue including immunohistochemical staining revealed histiocytes, yeast type spores and hyphae, and phagocytosed spores and hyphae in macrophages. The causative organism was identified morphologically as a *Candida* species. Later, histopathological examination of a cervical swab revealed the presence of *Candida* sp. This rare case indicates that a fungal organism may underlie refractory conjunctivitis with specific giant papillary hypertrophy mimicking vernal keratoconjunctivitis.

Keywords:

Candida, contact lens, fungal conjunctivitis, giant papilla, surgical treatment

Introduction

Fungal conjunctivitis is a rare disorder in ophthalmic practice because of its low incidence and difficulty in diagnosis due to a lack of specific clinical findings. *Candida* species including *Candida albicans* are known to be the major pathogens of infectious keratitis,^[1] whereas *Candida* spp. are not recognized as frequent pathogenic organisms inducing chronic conjunctivitis. We report a case of fungal conjunctivitis which exhibited a specific clinical feature of giant papilla formation and was treated surgically. The diagnosis was a complex process.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

Case Report

A 19-year-old woman presented with a 3-month history of severe conjunctival giant papillae in her right eye before attending our hospital. She had used hard contact lens in both eyes for several years. She was treated with 0.2% olopatadine hydrochloride, 0.1% betamethasone phosphate, and 0.1% tacrolimus eye drops by a local practitioner, but the conjunctival lesion did not respond to these local treatments, and intraocular pressure (IOP) elevation was observed and contact lens use was suspended. She had suffered from atopic dermatitis (AD) since childhood. Corrected visual acuity was 18/20 in the right eye and 30/20 in the left eye. IOP was 25 mmHg in the right eye and 14 mmHg in the left eye. Densely bristled tall papillae without mucous

How to cite this article: Shimokawa A, Kobayashi A, Saeki Y, Uchio E. A case of fungal conjunctivitis with giant papillae treated surgically. Taiwan J Ophthalmol 2021;11:417-20.

Department of
Ophthalmology, Fukuoka
University School of
Medicine, Fukuoka, Japan

*Address for correspondence:

Dr. Eiichi Uchio,
Department of
Ophthalmology, Fukuoka
University School
of Medicine, 7-45-1
Nanakuma, Jonan-ku,
814-0180 Fukuoka, Japan.
E-mail: euchio@
fukuoka-u.ac.jp

Submission: 25-05-2020

Accepted: 11-07-2020

Published: 21-09-2020

discharge were observed in the upper palpebral and bulbar conjunctiva of the right eye [Figure 1a and b]. The left eye showed no symptom of ocular surface disorder throughout the clinical course [Figure 1c]. Considering the refractoriness to anti-inflammatory and antiallergic local treatment, chlamydia conjunctivitis was suspected, and erythromycin eye ointment was started, whereas combined olopatadine, betamethasone, and tacrolimus eye drops treatment was discontinued, and prednisolone 30 mg/day was given orally to avoid IOP elevation. Three days after her first attendance, conjunctival giant papillae showed no resolution, and both ocular pain and eye discharge showed deterioration with increased abundant mucous discharge. Polymerase chain reaction (PCR) for *Chlamydia trachomatis* DNA in conjunctival scrapings was negative. Considering that the clinical course was poorly responsive to medical treatment including systemic corticosteroid therapy, surgical treatment of total papilla resection was carried out under general anesthesia 9 days after her first attendance. She was treated with local 0.1% dexamethasone and levofloxacin eye drops, which were gradually tapered, while conjunctival giant papilla recurrence was not observed, and no objective symptoms were observed after surgery. The ocular surface status has remained stable for 16 months after surgery [Figure 1d]. Histopathological examination of the excised conjunctival tissue revealed conjunctival inflammation composed of abundant eosinophil infiltration with a low proportion of mast cells [Figure 2a]. Based on the histological findings and clinical signs, atopic keratoconjunctivitis (AKC) with giant papillary proliferation was diagnosed, whereas immunohistological staining or specific staining for fungus was not carried out. However, suspicion remained regarding the diagnosis because the absence

of corneal involvement in this patient throughout the clinical course and unresponsiveness to both systemic and local corticosteroid treatment did not match the clinical characteristics of AKC. Asymmetry of the clinical findings in the cornea and conjunctiva between the eyes also made the diagnosis doubtful. Therefore, further histopathological evaluation was carried out including immunohistochemical staining, 1 year after the previous surgery. Immunohistochemical staining for CD68 showed numerous positive cells, indicating the presence of histiocytes [Figure 2b]. Yeast type spores and hyphae were observed in the conjunctival stroma by periodic acid–Schiff (PAS) [Figure 2c] and Grocott [Figure 2d] staining. These bodies were morphologically considered to be *Candida* species (sp.). Phagocytosed spores and hyphae were also found in polynuclear giant cells by PAS staining, suggesting features of granulomatous inflammation [Figure 2e]. From these histopathological findings, fungal conjunctivitis was diagnosed. She reported atypical genital bleeding and white vaginal discharge, and a cervical swab was examined histopathologically. This revealed low-grade squamous intraepithelial lesion with *Candida* sp. infection 2 years after the surgical treatment.

Discussion

Fungal conjunctivitis is a rare disorder and its clinical features have been reported in a few studies.^[2-4] In unbiased metagenomic RNA deep sequencing to identify pathogens causing conjunctivitis, 2 of 14 patients were positive for *Vittiforma corneae* (a parasitic fungal species of the microsporidia group).^[3] By conventional bacterial and fungal culture in clinically diagnosed cases of acute conjunctivitis, 14 out of 102 samples showed evidence of fungal infection.^[4] A case of fungal conjunctivitis presenting as a salmon-pink tumor in the bulbar conjunctiva^[5] and a case of punctate epithelial keratoconjunctivitis^[6] were diagnosed by a microbiological study of conjunctival scrapings as sporotrichosis and microsporidial infection, respectively, whereas cases of fungal conjunctivitis were confirmed by histopathological examination of excised tissue as sporotrichosis^[7] and scedosporium^[8] infection, respectively, indicating the difficulty of diagnosis of fungal conjunctivitis. From the standpoint of fungal conjunctivitis due to *Candida* sp., the infection route in our case was unclear. It is reported that *Aspergillus fumigatus* was detected in a retained soft contact lens covered by a granuloma-like lesion in the bulbar conjunctiva in a case with prominent mucoid discharge and marked papillary conjunctival reaction and severe superficial punctate keratitis.^[9] Cases of fungal penetration through a contact lens with corneal ulcers induced by the same fungus and fungal growth on and in the soft contact lens matrix associated with

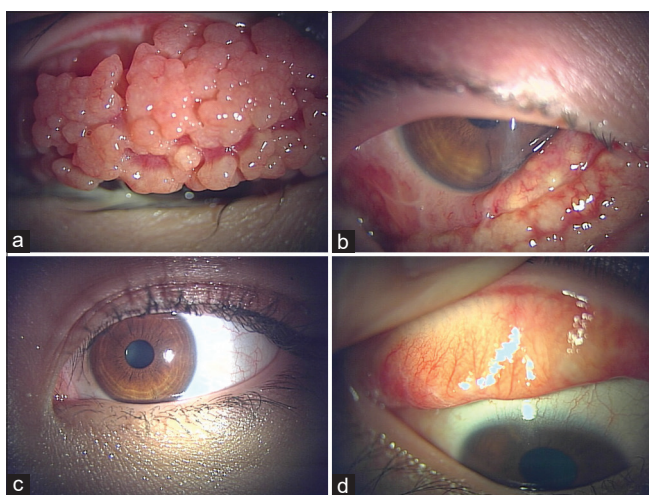


Figure 1: Slit-lamp examination findings and external ocular photographs. Palpebral (a) and bulbar (b) conjunctival findings of the right eye showed dense giant papillary hypertrophy without mucous discharge at the first visit. External ocular finding of the left eye at the first visit (c) showed normal findings. No recurrence was observed in the affected eye 16 months after surgery (d)

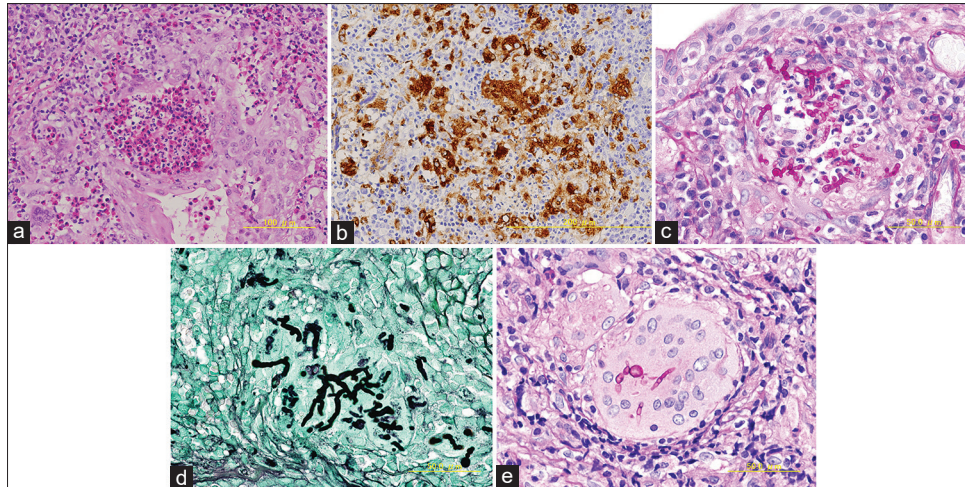


Figure 2: Histopathological and immunohistological findings of the resected lesion. (a) The lesion is composed of abundant eosinophils (H and E, $\times 200$). (b) There are numerous CD68-positive cells, indicating the presence of histiocytes ($\times 200$). (c and d) A positive-stained yeast type fungal spore and hyphae are observed in conjunctival tissue ($\times 400$) with periodic acid-Schiff (c) and Grocott (d) staining (e) A phagocytosed fungal spore and hyphae are observed inside a multinuclear giant cell (periodic acid-Schiff staining, $\times 200$)

conjunctivitis and punctate fluorescein staining of the corneal epithelium were reported in extended-wear soft contact lens users.^[10] These reports suggest an association between fungal conjunctivitis and contact lens wear, although our patient had used hard contact lens for a long time. There was a discrepancy in the clinical appearance between giant papillary hypertrophy in our case and papillary conjunctivitis in these reports,^[9,10] and the exact pathogenesis cannot be explained by contact lens factors. Regarding the past history of AD, indicating an allergic tendency in this case, an interesting study was reported on the correlation between allergic conjunctivitis and latent fungal infection.^[11] Conjunctival scrapings were evaluated cytologically in patients with allergic conjunctivitis without evidence of infection, and latent infection due to *C. albicans* was found in 55.2% of cases.^[11] The incidence of concurrent infection strongly correlated with the percentage of eosinophils.^[11] These findings suggest that chronic allergic disorders might be associated with latent fungal infection. Although corneal infection with *C. albicans* was not confirmed, its possible pathological route to the conjunctiva in atopic keratitis might also be considered.^[12] Collecting these points regarding the etiology and risk factors of this case, contact lens use, an atopic background related to latent fungal infection, and prolonged instillation of corticosteroid^[13] eye drops in this case might be possible risks for fungal conjunctivitis. It was reported that in patients attending gynecological and obstetric outpatient clinics, 50% of vaginal swabs were positive for *C. albicans* by PCR and 30% of conjunctival swabs were PCR positive, indicating that ocular *C. albicans* is frequently associated with genital *C. albicans* in women.^[14] As shown by the later gynecological examination in our case, her ocular involvement could have been associated with the vaginal flora rather than a contact lens-related route as mentioned above.^[14]

Regarding the specific clinical appearance in this case presenting with giant papillary hypertrophy, several factors can be considered. It could be considered that the clinical picture of giant papillae was a consequence of allergic inflammation, since this case had a history of AD. However, the poor responsiveness to systemic corticosteroid treatment does not support this hypothesis, and fungal invasion should be considered an infectious disease. Long-term use of corticosteroid might induce conjunctival proliferative change caused by an increase in *Candida*, as observed in oral candidiasis patients using inhaled steroid.^[15] Thus, the granulomatous inflammation observed in our case might have been part of the pathological findings in the chronic phase of fungal infection. The complete clinical resolution without additional antifungal treatment after surgical resection raises the suspicion that the histologically proven *C. albicans* in the surgical specimen might not have been the causative organism in this case. However, there are several case reports of refractory fungal keratitis that was successfully treated by deep anterior lamellar keratoplasty, which enabled complete removal of fungus from the corneal tissue.^[16] This might support the possibility of the total disappearance of fungal lesions in our case by surgical treatment.

In conclusion, this rare case indicates that a fungal organism may underlie refractory conjunctivitis with specific giant papillary hypertrophy mimicking vernal keratoconjunctivitis. Detailed histopathological evaluation, especially PAS or Grocott staining which is essential for the diagnosis of fungal infection and is more sensitive than hematoxylin and eosin staining,^[17] should be carried out in cases in which the diagnostic dilemma of an infectious or allergic mechanism cannot be resolved.

Acknowledgments

We thank Dr. Yoshihiro Hamada for his contribution to the histopathological evaluation of this case.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent. The patient has given consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, although anonymity cannot be guaranteed.

Financial support and sponsorship

This work was supported by a Grant-in-Aid for Encouragement of Scientists (18K09466) from the Ministry of Education, Science, Sports and Culture of Japan.

Conflicts of interest

The authors declare that there are no conflicts of interest of this paper.

References

1. Mahmoudi S, Masoomi A, Ahmadikia K, Tabatabaei SA, Soleimani M, Rezaie S, *et al.* Fungal keratitis: An overview of clinical and laboratory aspects. *Mycoses* 2018;61:916-30.
2. Thalasselis A, Taie GF, Cabanne GR, Tiano R. Mycotic conjunctivitis: An overview. *J Am Optom Assoc* 1985;56:498-500.
3. Lalitha P, Seitzman GD, Kotecha R, Hinterwirth A, Chen C, Zhong L, *et al.* Unbiased pathogen detection and host gene profiling for conjunctivitis. *Ophthalmology* 2019;126:1090-4.
4. Boralkar AN, Dindore PR, Fule RP, Bangde BN, Albel MV, Saoji AM. Microbiological studies in conjunctivitis. *Indian J Ophthalmol* 1989;37:94-5.
5. Kashima T, Honma R, Kishi S, Hirato J. Bulbar conjunctival sporotrichosis presenting as a salmon-pink tumor. *Cornea* 2010;29:573-6.
6. Dhakal R, Ramappa M, Sharma S. Punctate epithelial keratoconjunctivitis: A microsporidial infestation. *Indian J Ophthalmol* 2018;66:1327-8.
7. Hampton DE, Adesina A, Chodosh J. Conjunctival sporotrichosis in the absence of antecedent trauma. *Cornea* 2002;21:831-3.
8. Fernandez-Flores A, Lopez-Medrano R, Fuster-Foz C. Histopathological clues in the diagnosis of fungal infection by *Scedosporium* in a case of endophthalmitis starting as conjunctivitis. *J Cutan Pathol* 2016;43:461-7.
9. Perry HD, Donnenfeld ED, Grossman GA. Retained *Aspergillus*-contaminated contact lens inducing conjunctival mass and keratoconjunctivitis in an immunocompetent patient. *CLAO J* 1998;24:57-8.
10. Wilson LA, Ahearn DG. Association of fungi with extended-wear soft contact lenses. *Am J Ophthalmol* 1986;101:434-6.
11. Forte R, Cennamo G, Del Prete S, Farese E, Del Prete A. Allergic conjunctivitis and latent infections. *Cornea* 2009;28:839-42.
12. Nivenius E, Montan P. *Candida albicans* should be considered when managing keratitis in atopic keratoconjunctivitis. *Acta Ophthalmol* 2015;93:579-80.
13. Wilson FM 2nd. Adverse external ocular effects of topical ophthalmic medications. *Surv Ophthalmol* 1979;24:57-88.
14. Khattab RA, Abdelfattah MM. Study of the prevalence and association of ocular chlamydial conjunctivitis in women with genital infection by *Chlamydia trachomatis*, *Mycoplasma genitalium* and *Candida albicans* attending outpatient clinic. *Int J Ophthalmol* 2016;9:1176-86.
15. Fukushima C, Matsuse H, Tomari S, Obase Y, Miyazaki Y, Shimoda T, *et al.* Oral candidiasis associated with inhaled corticosteroid use: Comparison of fluticasone and beclomethasone. *Ann Allergy Asthma Immunol* 2003;90:646-51.
16. Xie L, Shi W, Liu Z, Li S. Lamellar keratoplasty for the treatment of fungal keratitis. *Cornea* 2002;21:33-7.
17. Erami M, Afzali H, Heravi MM, Rezaei-Matehkolaei A, Najafzadeh MJ, Moazeni M, *et al.* Recurrent arthritis by *Candida glabrata*, a diagnostic and therapeutic challenge. *Mycopathologia* 2014;177:291-8.