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Case report

Adult inclusion conjunctivitis diagnosed by polymerase chain reaction and Giemsa stain

Wan-Ju Annabelle Lee[a,b,c], Chien-Chin Chen[d,e,*]

[a] Department of Ophthalmology, Chi Mei Medical Center, Tainan, Taiwan
[b] School of pharmacy & Institute of Clinical Pharmacy and Pharmaceutical Sciences, College of Medicine, National Cheng Kung University, Tainan, Taiwan
[c] Department of optometry, Chung Hwa University of Medical Technology, Tainan, Taiwan
[d] Department of Pathology, Ditmanson Medical Foundation Chia-Yi Christian Hospital, Chiayi, Taiwan
[e] Department of Cosmetic Science, Chia Nan University of Pharmacy and Science, Tainan, Taiwan

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ABSTRACT

Adult inclusion conjunctivitis, caused by *Chlamydia trachomatis*, is easily underdiagnosed with nonspecific ocular manifestation. Combined scrape cytology and molecular testing may be a useful strategy for its early diagnosis. A 24-year-old healthy male complained of blurred vision, foreign body sensation, and watery discharge in his right eye for four weeks. His visual acuity was 20/20 bilaterally at his first visit. Allergic conjunctivitis was the first impression, and topical treatment with corticosteroid and anti-histamine was prescribed. However, he returned five days later without symptom improvement, and his right eye vision declined to 20/40. Subepithelial corneal infiltration of his right eye was observed. According to his personal history, his girlfriend was diagnosed with sexually transmitted chlamydial infection and genital gonorrhea. Under the suspicion of sexually transmitted adult inclusion conjunctivitis, we collected his conjunctival lavage to both real-time polymerase chain reaction, which proved chlamydial infection, and Giemsa stain, which demonstrated typical basophilic intracytoplasmic inclusions. To diagnose adult inclusion conjunctivitis, we can use real-time polymerase chain reaction or Giemsa stain to help us obtain a quick and correct diagnosis.

1. Introduction

Adult inclusion conjunctivitis is known as chlamydial conjunctivitis. It is a sexually transmitted disease that occurs most commonly in sexually active young adults. The disease is usually transmitted through the hand-to-eye spread of infected genital secretions [1]. Patients with chlamydial infections of the eyes complain about irritation, discharge, red-eye, and sometimes vision decline. It occurs at any age but is most commonly observed in young adults [2]. Chlamydial conjunctivitis is often unilateral disease but may involve both eyes. It is known as inclusion conjunctivitis because its pathogen, *Chlamydia trachomatis*, demonstrates basophilic intracytoplasmic inclusions under Giemsa stain.

2. Case presentation

A 24-year-old college student had bilateral red eyes, watery discharge, irritation, and intermittent blurred vision for four weeks. He denied contact lens use, recent injury, previous ophthalmic surgery, or other ocular diseases. He did not have recent travel, contact with chemicals, or contact with plants and animals within six months, either. On examination, his best visual acuity was 20/20 bilaterally with normal intraocular pressure. He went to other clinics, and topical antibiotics were given for his discomfort based on recurrent conjunctivitis. Therefore, acute on chronic allergic conjunctivitis was first diagnosed, so topical corticosteroid and anti-histamine eye solutions were prescribed. However, he returned to the clinic earlier than the appointment time because his irritation from the eye aggravated, and he had blurred vision in his right eye this time. His vision of the right eye declined to 20/40. Under the slit-lamp, we observed subepithelial corneal infiltrates in his right eye, accompanied by severe congestion and follicular reaction involving the bulbar conjunctiva and semilunar folds (Fig. 1A and B).

We rechecked the patient's past histories, including medication use, tobacco exposure, and sexual exposure, when he returned to our department this time. Though the patient denied having multiple sexual partners, he mentioned that his girlfriend was recently diagnosed with sexually transmitted chlamydial infection and genital gonorrhea and was treated at the obstetrics and gynecology

* Correspondence to: No. 539, Zhongxiao Rd., East Dist., Chiayi City, Taiwan.
E-mail address: hlmarkc@gmail.com (C.-C. Chen).

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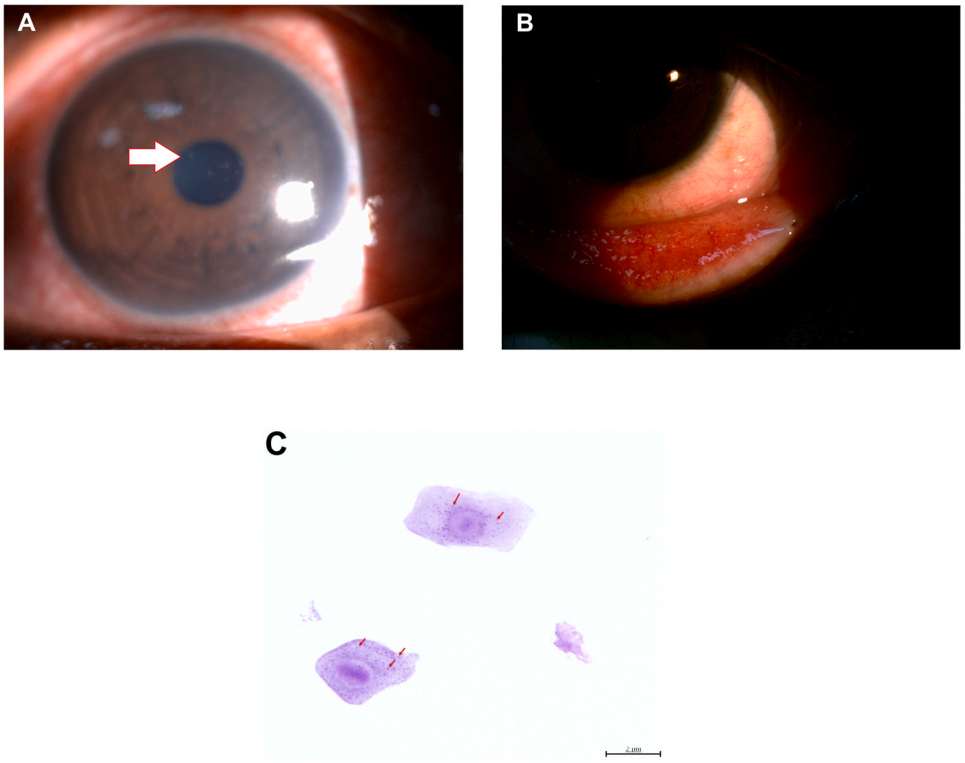

Fig. 1. (A) External photography of the right eye. Corneal subepithelial infiltration was observed in the central part of the cornea (*white arrow*). (B) Follicular conjunctivitis with congestion of bulbar conjunctiva was seen in the lower tarsus. (C) Epithelial cells of the conjunctiva reveal basophilic cytoplasmic inclusions (*red arrows*) around the nucleus (Giemsa staining, 800 × magnification).

department then. Therefore, we performed conjunctival lavage with sterile normal saline (0.9% NaCl) as the irrigation solution under the suspicion of conjunctival chlamydial infection. Then, the lavage samples were collected in sterile containers without preservatives at room temperature and averagely divided (at least 5 mL in each container) for cytology examination and real-time reverse transcription-polymerase chain reaction (RT-PCR). No alcohol or other preservation solution was added, which might contribute to the degradation of DNA and RNA. His void urine was also sent for RT-PCR under the suspicion of genital chlamydial infection. Both conjunctival lavage and urine revealed positive results in RT-PCR tests for chlamydial infection. We used the BD MAX™ system for detecting Chlamydial infection. Besides, we also collected the conjunctival lavage for Giemsa stain to search for the intracytoplasmic inclusions. After proving chlamydial infection in Giemsa stain (Fig. 1 C) and RT-PCR results, we gave the patient doxycycline 100 mg twice daily for ten days and topical fluoroquinolone four times/day, and tetracycline ointment twice daily. The patient's eye symptoms and signs improved gradually. His vision of the right eye regained to 20/20. We referred the patient to the infectious department for further evaluation of sexually transmitted diseases afterward.

3. Discussion

Chlamydia trachomatis, a human pathogen, is an obligate intracellular bacterium responsible for three different conjunctivitis syndromes: trachoma, adult and neonatal inclusion conjunctivitis, and lymphogranuloma venereum [3]. The adult inclusion conjunctivitis is caused by serotypes D-K. In addition, *C. trachomatis* is the most common cause of chronic follicular conjunctivitis and is responsible for 20% of acute conjunctivitis cases [4]. Patients with inclusion conjunctivitis have a wide range of severity of symptoms. Some patients present as acute and mucopurulent conjunctivitis, since most of the time, patients have mild symptoms that last for weeks or months. This disease mimics acute allergic conjunctivitis or another infectious conjunctivitis because the signs and symptoms are insidious, and most patients have similar nonspecific complaints, such as mucous discharge, pink/red eyes, itch, crusting of eyelashes, lids stuck together, swollen lids, photophobia, tearing, foreign body sensation, irritation, and decreased vision [5]. Close questioning about patients' sexual history is vital because adult inclusion conjunctivitis is related to sexually transmitted diseases (STD) [6]. The follicular reaction is a crucial feature of chlamydial conjunctivitis, and severe follicular reaction over the lower palpebral conjunctiva is widespread. Follicles in the bulbar conjunctiva and semilunar fold are frequently present, too. The cornea may exhibit both fine and coarse epithelial and subepithelial infiltrates.

In a non-endemic area like Taiwan, chlamydial conjunctivitis is not a common disease in our daily practice. A diagnosis is based on symptoms, signs, history, and clinical suspicion. About five decades ago, when there were no RT-PCR or enzyme-linked immunosorbent assay (ELISA) techniques, chlamydial infection was merely diagnosed by clinical presentation and Giemsa stain for its intracytoplasmic inclusion. At that time, the inability of viral culture for this pathogen led the investigators to assume that it was a virus. With improved diagnostic technology, physicians currently use PCR or ELISA to help detect the pathogen [7,8]. In our case, we also performed Giemsa statin and obtained the intracytoplasmic inclusion, which made us more confident of our diagnosis.

Diagnostic tests for chlamydial keratoconjunctivitis include conjunctival cytological examination, inoculation of susceptible cell lines followed by observation of cytopathic effect or visualization using various chemical or immunological staining agents, eye tears for various antibodies, and detection of chlamydial antigens in conjunctival and corneal specimens. The traditional cytological investigation with Giemsa stain is insensitive and somehow subjective. Although the specificity could be above 90%, the sensitivity of Giemsa cytology was only 36%. Meanwhile, culture isolation

requires viable organisms necessitating special transport media and prompt transport of specimens between patient and laboratory. It is costly and time-consuming but remains the "gold standard" as isolating an infectious agent is definitive and allows further characterization. Madhavan et al. reported that the McCoy cell culture method's sensitivity for detecting *C. trachomatis* was only 54%, while the specificity was above 90%. In addition, the sensitivity of ELISA for detecting *C. trachomatis* ranged from 40% to 71%, although the specificity reached 97–100% [9]. Moreover, the detection of *C. trachomatis* DNA from ocular swabs using commercial PCR assays was as valid as using urogenital samples and reached 95.71% in sensitivity and 90.00% in specificity[10]. In summary, PCR tests may be a quick and ideal tool for detecting ocular C. trachomatis infection, although it is relatively expensive than Giemsa stain and ELISA.

Chlamydial conjunctivitis can be treated topically with erythromycin, gentamicin, tetracycline, and fluoroquinolones. Owing to the high prevalence of concomitant genital tract infection, systemic antibiotic therapy is strongly recommended when chlamydial conjunctivitis was diagnosed. Though there are some variations in the recommendation for antibiotics, accepted treatment options include doxycycline 100 mg twice daily, azithromycin 1000 mg single dose daily, tetracycline 100 mg 4 times daily for 7–10 days, or erythromycin 500 mg 4 times daily for seven days [11,12]. Due to the poor medical compliance or re-infection and relapse of this disease, weekly oral azithromycin was recommended for 2–4 weeks. If left untreated, adult chlamydial conjunctivitis may resolve spontaneously in 6–18 months, but repeated infections may lead to cicatricial entropion/ectropion or even corneal opacities. In our case, we used topical fluoroquinolone, gentamicin ointment, and oral doxycycline simultaneously. Topical fluoroquinolone was used to to reduce follicular conjunctivitis that persisted for several weeks and prevent further severe keratitis in the ocular surface. Systemic oral doxycycline was aimed to control systemic chlamydial infection [13].

Adult inclusion conjunctivitis can mimic any conjunctivitis or even progress to keratitis. Concomitant infections for genital chlamydial infection or gonorrhea should be considered if chlamydial conjunctivitis is confirmed. RT-PCR and Giemsa stain of conjunctival samples help physicians to have an easy and fast diagnosis of this greater imitator.

Ethical Approval

We have read and complied the policy of the journal on ethical consent, as stated in the Guide to authors.

Informed consent statement

Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patient (s) to publish this paper.

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Author contributions

Both authors had equal efforts for this report: **Wan-Ju Annabelle Lee:** Conceptualization, Investigations, Patient's data collection, Writing – original draft. **Chien-Chin Chen:** Conceptualization, Writing – review and editing, Visualization, Supervision, Submission.

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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