

***Neisseria meningitidis* Keratitis in Adults: A Case Series**

Colin SH Tan,¹MBBS, MMed (Ophth), MRCEd, Prabha U Krishnan,²MD, MRCPATH, DTM&H (Lond), Fong Yee Foo,¹MBBS, James CH Pan,¹MBBS, MMed (Ophth), FRCSEd, Li Wern Voon,¹MBBS, MMed (Ophth), FRCSEd

Abstract

Introduction: The aim of this case series is to describe the clinical course of 2 patients with *Neisseria meningitidis* corneal ulcers. **Clinical Picture:** A 49-year-old man (Patient 1) and a 22-year-old man (Patient 2) both experienced eye pain and were found to have corneal ulcers with surrounding infiltrate and ground-glass appearance. Gram-negative diplococci were seen in the first case. *N. meningitidis* was isolated in culture of corneal scrapings from both patients. **Treatment:** Patient 1 was treated with levofloxacin (0.5%) and cefazolin (50 mg/mL) eye drops hourly and intravenous ceftriaxone and oral rifampicin. Patient 2 was treated with cefazolin (50 mg/mL) and gentamicin (14 mg/mL) eye drops hourly, as well as intravenous ceftriaxone. **Outcome:** The corneal ulcers resolved with anterior stromal scarring and no impairment of vision. **Conclusions:** Corneal ulcers caused by *N. meningitidis* may respond well to treatment without permanent visual sequelae. However, in view of the potential ocular and systemic complications, it is important to investigate and treat patients with *N. meningitidis* infection aggressively.

Ann Acad Med Singapore 2006;35:837-9

Key words: Bacterial, Corneal ulcer, Eye infections

Introduction

Neisseria meningitidis has been reported as a causative organism for conjunctivitis¹ and endogenous endophthalmitis,^{2,3} more commonly in neonates and young children.³⁻⁵ A search of the literature on Medline revealed very few reports on infective keratitis caused by *N. meningitidis*.^{6,7} Thus the characteristic features and natural history of *N. meningitidis* keratitis are not well documented. We describe the clinical course of 2 patients with *N. meningitidis* corneal ulcers and their rapid response to topical and systemic antibiotics.

Case Reports

Patient 1

A 49-year-old man experienced left eye pain after a plastic foreign body injury. At presentation, visual acuity in the left eye was 20/80; there was conjunctival injection, 3+ anterior chamber cells and a 1 x 1.1-mm corneal ulcer with surrounding infiltrate and ground-glass appearance. He refused antibiotic treatment and defaulted follow-up, only

to present again 4 days later, by which time the ulcer had increased to 2 mm in diameter (Fig. 1).

Upon confirmation of *N. meningitidis* from culture of the corneal scrapes, the patient was treated with hourly levofloxacin (0.5%) and cefazolin (50 mg/mL) eye drops, intravenous ceftriaxone and oral rifampicin, and kept isolated for 24 hours. By day 6, the epithelial defect had healed and the ulcer resolved with scarring and 10% corneal thinning (Fig. 2). Household contacts and healthcare professionals who had close contact with the patient were offered chemoprophylaxis.

Patient 2

A 22-year-old soldier experienced sudden pain in his left eye on waking up. Prior to this he did not experience any ocular symptoms and did not have conjunctivitis. There was no history of contact lens use, trauma or foreign body contact, although he had been out on field training the previous week. Visual acuity was 20/25 OS, the conjunctiva was injected and there was a 1.7 x 1.3-mm corneal ulcer

¹ The Eye Institute at Tan Tock Seng Hospital, National Healthcare Group, Singapore

² Department of Pathology and Laboratory Medicine, Tan Tock Seng Hospital, National Healthcare Group, Singapore

Address for Reprints: Dr Colin SH Tan, The Eye Institute, National Healthcare Group, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore 308433. Email: Colintan_eye@yahoo.com.sg

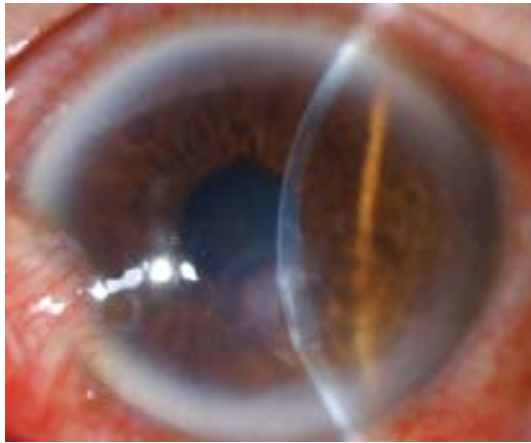


Fig.1. (Patient 1) – Paracentral corneal ulcer with corneal thinning and ground glass appearance.



Fig. 2. (Patient 1) – At 1 week, the epithelial defect has healed and the ulcer has scarred with mild stromal thinning.

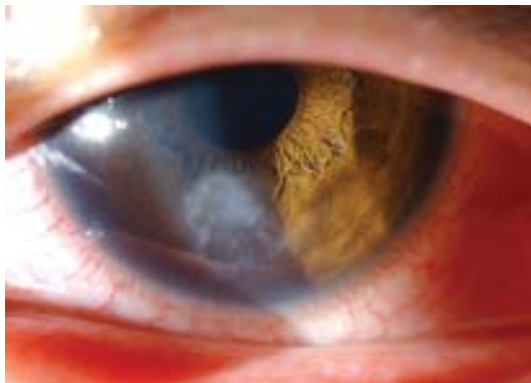


Fig. 3. (Patient 2) – Paracentral corneal ulcer with surrounding ground glass appearance on initial presentation.

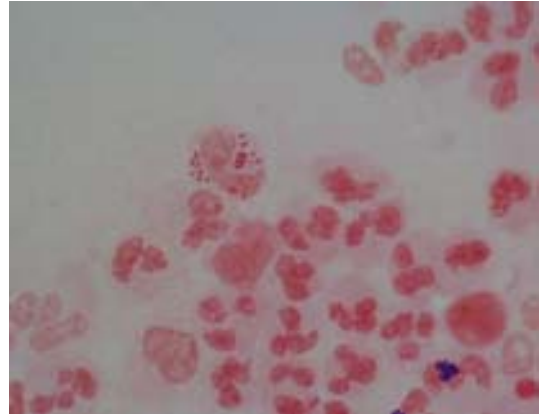


Fig. 4. Gram stain of the corneal scrape demonstrates intracellular gram-negative diplococci, suggestive of *Neisseria* sp.

with surrounding ground glass appearance (Fig. 3). After a corneal scrape was performed, he was started on cefazolin (50 mg/mL) and gentamicin (14 mg/mL) eye drops hourly. The ulcer reduced in size with resolution of the anterior chamber activity and by day 4, there was minimal residual infiltrate and a scar had formed.

Culture of the corneal scraping grew *N. meningitidis*. Although the patient was afebrile and had no clinical signs or symptoms of meningitis, he was admitted in isolation and treated with intravenous ceftriaxone. After 48 hours, blood cultures produced no growth and he was discharged.

Microbiological Methods

Microscopic examination of the corneal scrapes taken from Patient 1 showed intracellular gram-negative diplococci (Fig. 4); scrapes taken from Patient 2 did not show inflammatory cells or microorganisms. The corneal scrapes were inoculated onto a battery of media including a selective agar for *N. gonorrhoeae* and incubated at 35°C in a CO₂ atmosphere. Smooth, round, translucent, oxidase-positive colonies measuring slightly more than 1 mm were

isolated on blood and chocolate plates (but not on nutrient agar) after overnight incubation from both cases. These were identified using the API-NH identification kit (bioMérieux Inc, France), which is a standardised system for the identification of *Neisseria*, *Haemophilus* and *Moraxella* species. A preliminary report of *N. meningitidis* was sent based on these findings.

Additional enzyme substrate tests showed that this isolate acidified glucose and maltose but not lactose, fructose or sucrose. The organisms were identified as *N. meningitidis* and *N. gonorrhoeae* was excluded based upon biochemical and a negative GonoGen II (New Horizons Diagnostics, MD, USA) tests. A β -lactamase detection test using chromogenic cephalosporin, the Cefinase™ disc (BD BBL™) showed that the isolate was not a β -lactamase producer. Minimum inhibitory concentrations (MICs) for penicillin using the E-test (AB Biodisk, Sweden) determined the MICs as 0.064 mg/L (Patient 1) and 0.19 mg/L (Patient 2).

Neither of the isolates were groupable using antisera available locally in the first case or in a referral laboratory in the second case (i.e., antisera to Groups A, B, C, D, X, Y, Z, W135).

Discussion

Ocular infections with *N. meningitidis* conjunctivitis has been recognised for a long time in adults, children and particularly neonates, and may develop as a complication of systemic infection and haematogenous dissemination of the organism.³ It is therefore important to investigate and treat systemically patients with a positive ocular culture of *N. meningitidis*.

In recent years, however, primary meningococcal conjunctivitis has been recognised as a distinct clinical entity.^{4,6} Ocular complications included corneal ulcers, keratitis, subconjunctival haemorrhage and iritis. Some of these patients with *N. meningitidis* ocular infections do not develop neurologic or systemic signs of meningococcal infection.^{2,4,8}

These case reports are unusual in that a corneal ulcer developed in young, healthy adults although the source of the organism is uncertain in both cases. Although Patient 1 had a small foreign body injury, inanimate foreign bodies are not a common source of *Neisseria* species. Patient 2 had no history of ocular trauma and no risk factors that would predispose to corneal ulcers. In both these cases, the source of the organism is uncertain. Neither patient had a history of contact with a person infected with *N. meningitidis* although Patient 2 lived in army barracks and came into close contact with fellow soldiers who could have been harbouring the organism in the nasopharynx.

N. gonorrhoeae is known to penetrate intact corneal epithelium,⁹ thus explaining its virulence and potentially devastating consequences in ocular infections. In a review of 47 patients with ocular infections secondary to *N. gonorrhoeae* seen over a 5½ year period at the Bascom Palmer Eye Institute, 30 patients (63.9%) manifested with conjunctivitis, 16 patients (34%) had corneal involvement and 1 patient (2.1%) with previous enucleation developed orbital cellulites in the socket.¹⁰

In this series, of the 16 patients with corneal involvement, 10 (62.5%) had mild keratitis and no visual consequences. The most frequent corneal manifestation in this group was a limbal anterior stromal infiltrate, with trace punctate epithelial staining, which resolved after several days with faint anterior stromal scarring. The remaining 6 patients (37.5%) with corneal involvement developed severe ulcerative keratitis resulting in permanent visual loss and 5 (31.3%) required surgery to repair a corneal perforation.¹⁰ Patients with isolated conjunctival involvement had a delay in initiating parenteral antibiotic treatment for a mean

of 3.3 days compared to 9 days for all patients with corneal involvement ($P < 0.005$). The 10 patients with mild corneal involvement had symptoms for a mean of 5.1 days compared to 8.7 days for those who suffered permanent visual loss.¹⁰ This highlights the need for prompt and accurate diagnosis, and effective parenteral antibiotics.

In our series, there was a delay of 4 days before starting systemic antibiotics in the first case because of patient non-compliance and 2 days in the second case due to a negative microscopy. However, both patients responded well to therapy and did not develop any significant visual impairment even though the ulcers occurred just off the visual axis. The ulcers healed with mild scarring between days 4 and 6 after initiating treatment with topical and systemic antibiotics. Even in Patient 1, who initially defaulted treatment for 4 days, bacterial keratitis did not result in progressive corneal thinning or perforation, although the ulcer did increase in size from the initial presentation. A larger series would be required to comment on the virulence of meningococci in the pathogenesis of severe eye infections.

Conclusion

Our case series illustrates 2 patients in whom the clinical course of *N. meningitidis* was mild and resolved without any permanent visual sequelae. However, in view of both the potential ocular and systemic sequelae of *N. meningitidis* infection, it is important to investigate and treat these patients promptly and aggressively.

REFERENCES

1. Jackson TL, Eykyn SJ, Graham EM, Stanford MR. Endogenous bacterial endophthalmitis: a 17-year prospective series and review of 267 reported cases. *Surv Ophthalmol* 2003;48:403-23.
2. Brinser JH, Hess JB. Meningococcal endophthalmitis without meningitis. *Can J Ophthalmol* 1981;16:100-1.
3. Gartaganis SP, Eliopoulou MJ, Georgakopoulos CD, Koliopoulos JX, Mela EK. Bilateral panophthalmitis as the initial presentation of meningococcal meningitis in an infant. *J AAPOS* 2001;5:260-1.
4. Anderson J, Lind I. Characterization of *Neisseria meningitidis* isolates and clinical features of meningococcal conjunctivitis in ten patients. *Eur J Clin Microbiol Infect Dis* 1994;13:388-93.
5. Lehman SS. An uncommon cause of ophthalmia neonatorum: *Neisseria meningitidis*. *J AAPOS* 1999; 3:316.
6. Barquet N, Gasser I, Domingo P, Moraga FA, Macaya A, Elcuaz R. Primary meningococcal conjunctivitis: report of 21 patients and review. *Rev Infect Dis* 1990;12:838-47.
7. Andreoli CM, Wiley HE, Durand ML, Watkins LM. Primary meningococcal conjunctivitis in an adult. *Cornea* 2004;23:738-9.
8. Al-Mutlaq F, Byrne-Rhodes KA, Tabbara KF. *Neisseria meningitidis* conjunctivitis in children. *Am J Ophthalmol* 1987;104:280-2.
9. Duke-Elder S, editor. *System of Ophthalmology*. Vol 8. Part 1. Diseases of the outer eye. St Louis: CV Mosby, 1965:167-74.
10. Ullman S, Roussel TJ, Culbertson WW, Forster RK, Alfonso E, Mendelsohn AD, et al. *Neisseria gonorrhoeae* keratoconjunctivitis. *Ophthalmology* 1987;94:525-31.