CASE REPORT

Immune stromal keratitis: a rare ocular presentation of tuberculosis

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SUMMARY

An 11-year-old female patient presented with diminution of vision in both the eyes for the last 4 days. She had redness, watering and photophobia for the past 11 days. Slit lamp examination revealed multiple disc-shaped corneal stromal infiltrates with an overlying epithelial defect and hypopyon in both the eyes. A provisional diagnosis of infective keratitis was made. The patient was started on empirical antimicrobial therapy. However, no improvement was noted over the next 72 hours. Microbiological examination of the corneal scraping from both the eyes was negative. Considering the above, provisional diagnosis was changed to immune stromal keratouveitis and the patient was started on topical steroids. Further evaluation revealed a positive Mantoux test (30×20 mm) and contrast enhanced CT chest showing pulmonary nodules, suggestive of tuberculosis. The patient was subsequently started on antitubercular treatment. The infiltrates along with the ulcer and anterior uveitis responded dramatically to the revised treatment and resolved completely within 7 days of therapy.

BACKGROUND

Tuberculosis (TB), an infection caused by *Mycobacterium tuberculosis*, can involve any organ system, including the eye. It primarily affects the lungs. Ocular TB can involve any part of the eye with or without systemic involvement.¹ The ocular manifestations can be divided as either immune mediated or due to the direct invasion of bacilli.² Immune manifestations include scleritis, episcleritis, interstitial and phlyctenular keratitis, uveitis, Eale's disease and optic neuritis. Lupus of lids, conjunctivitis, epithelial keratitis and miliary retinitis are due to direct invasion of the bacilli. Corneal involvement in ocular TB is rare. The various corneal manifestations reported as of this time includes phlyctenulosis, interstitial keratitis and peripheral ulcerative keratitis.^{2–7}

All these forms of keratitis are often associated with granulomatous uveitis. To the best of our knowledge, immune-mediated stromal keratitis with non-granulomatous uveitis as a manifestation of ocular TB has never been reported in literature. Herein, we report a case of bilateral immune-mediated stromal keratitis with non-granulomatous uveitis due to TB.

CASE PRESENTATION

An 11-year-old girl presented to the cornea clinic with redness, watering, photophobia and foreign body sensation for the past 11 days along with diminution of vision in both eyes for the past 4 days. There were no systemic complaints and family

history was not significant. On ocular examination, best-corrected visual acuity (BCVA) in the right eye was 6/24 and 3/60 in the left eye on Snellen acuity chart. Diffuse as well as circumciliary conjunctival congestion along with upper and lower lid oedema was noted in both eyes.

Slit lamp examination revealed multiple disc-shaped stromal infiltrates with overlying corneal ulcers in both eyes. In the right eye, three such lesions were seen. One was superonasal: 2×4 mm, and the other two were temporal: 0.5×1 mm (figure 1). The left eye also had three such lesions, located superonasally (5×2 mm), superiorly (2×1.5 mm) and superotemporally (3×2 mm) (figure 2). Both eyes had signs of non-granulomatous anterior uveitis with 1.5 mm hypopyon in the left eye. Corneal sensations were normal in both eyes. The intraocular pressure was 12 mm Hg in the right eye and 14 mm Hg in the left eye. Fundus examination was normal within the visible area.

INVESTIGATIONS

Corneal scraping from the lesions of both eyes was performed and the sample was sent for Gram's stain, potassium hydroxide stain, Ziehl-Neelsen (ZN) stain and culture sensitivity. All these microbiological investigations were negative. PCR for herpes simplex virus of the scraping sample was negative. Routine blood investigations, including complete blood count, liver function tests and kidney function tests were within normal range except an elevated erythrocyte sedimentation rate (34 mm/hour). A detailed systemic evaluation was performed to identify the underlying cause, including Mantoux test, chest X-ray, venereal disease research laboratory, rheumatoid arthritis (RA) factor, serum antinuclear antibodies (ANA) and antinuclear cytoplasmic antigen (ANCA). The results of RA factor, ANA and ANCA were negative. The ELISA for toxoplasmosis, cytomegalovirus, rubella and HIV was negative. The Mantoux test showed a 30×20 mm area of induration and chest X-ray posteroanterior view showed 6–8 mm nodular lesion in the right middle zone. Contrast enhanced CT thorax showed signs of active tuberculosis.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of this case included infective keratitis, interstitial keratitis (IK), phlyctenular keratitis and peripheral ulcerative keratitis (PUK). However, the clinical characteristics and negative microbiological results ruled out the above-mentioned differentials.

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Figure 1 Clinical photograph showing multiple stromal infiltrates in right eye.

TREATMENT

On admission, the patient was provisionally diagnosed as bilateral infective keratitis and started on eye drop concentrated cefazolin 5%, one hourly; concentrated tobramycin 1.3%, one hourly and homatropine hydrobromide 2% four times a day. No clinical improvement was seen in the following 48 hours of starting the therapy. Considering the above, provisional diagnosis was changed to immune stromal keratouveitis and the patient was started on topical steroids with eye drop prednisolone acetate 1% (six times daily), moxifloxacin 0.5% four times daily and eye drop homatropine hydrobromide 2% four times following which there was a significant reduction in symptoms as well as visual acuity. Once further systemic investigations confirmed

Figure 2 Clinical photograph showing multiple stromal infiltrates with hypopyon in left eye.

Figure 3 Clinical photograph showing healing of infiltrates with resolution of inflammation at day 5 in right eye.

TB, anti-TB therapy (category 1) was started according to the standard protocol of four drugs (isoniazid, rifampicin, pyrazinamide and ethambutol) for 2 months and two drugs (isoniazid and rifampicin) for 4 months in a dose of isoniazid (5 mg/kg), rifampicin (10 mg/kg), pyrazinamide (25 mg/kg) and ethambutol (15 mg/kg).

OUTCOME AND FOLLOW-UP

After starting steroids, there was significant reduction in ocular discomfort. BCVA in both eyes improved to 6/12. Stromal infiltrates reduced along with the size of the corneal ulcers. Further, on day 5 there was minimal ocular discomfort with a marked reduction in conjunctival congestion. BCVA improved to 6/9 in both eyes with the healing of all the corneal lesions with absent anterior chamber inflammation (figures 3 and 4). On day 7, the BCVA was 6/9 in both eyes with peripheral corneal scarring. In the right eye, one disc-shaped corneal scar was seen in the superonasal (2×4 mm) and two in temporal (0.5×1 mm) quadrant with thinning near the limbus (figure 5). The left eye had similar scars located superonasally (3×2 mm), superiorly (2×1.5 mm) and superotemporally (3×2 mm) (figure 6).

DISCUSSION

The incidence of ocular TB has been reported to be 1.4% of all primary pulmonary TB cases.¹ Corneal involvement in TB is rare. Various corneal manifestations include phlyctenulosis, interstitial keratitis, disciform keratitis and peripheral ulcerative keratitis.^{2–7} Our case initially presented with features suggestive of infective keratitis. Hence, the patient was treated in line of infective aetiology. However, there was no response to the initial therapy. In addition, microbiological tests were negative. A literature review suggested that it could be an immune-mediated pathology. Topical steroids were started judiciously and the dramatic response to steroids confirmed our suspicion. IK is defined as a sterile and non-ulcerative inflammation of the cornea with features of corneal oedema, infiltration and vascularisation of stroma. This is often associated with granulomatous anterior uveitis.^{2,4} Disciform keratitis presents as a focal disc-shaped area

Figure 4 Clinical photograph showing healing of infiltrates with resolution of inflammation and hypopyon at day 5 in left eye.

of stromal oedema with fine endothelium keratic precipitates and no vascularisation. A single case report of bilateral disciform keratitis with spinal TB has been described in the literature so far. Hypersensitivity to tuberculin antigen is the most likely attributable cause.⁵ PUK presents as a crescent-shaped destructive inflammation at the margin of the corneal stroma with an overlying epithelial defect, stromal infiltrate, progressive stromal degradation and thinning.⁶ Phlyctenular keratoconjunctivitis (PKC) in TB presents as unilateral, localised, elevated pinkish-grey nodule most commonly at the limbus with a soft centre and vascularisation.

Therefore, the clinical manifestation of our case was not similar to any previous reports, and considering the dramatic

Figure 5 Clinical photograph showing completely healed stromal infiltrates at day 7 in right eye.

Figure 6 Clinical photograph showing complete healing of infiltrates at day 7 in left eye.

response to steroids, we made the diagnosis of immune-mediated stromal keratitis with non-granulomatous uveitis with TB. We hypothesise that the pathogenesis of this case could be a hypersensitivity reaction to tuberculin protein, which is similar to PKC. In addition, a negative ZN stain prompted us to arrive at such a diagnosis. However, a direct infective process causing the lesion cannot be completely ruled out since paucibacillary form of TB is often missed with routine microbiological tests. Thus to conclude, immune stromal keratitis can be another ocular manifestation of systemic TB. It is difficult to rule out the role of direct bacterial invasion in such cases considering the rarity of presentation and limitations of currently available diagnostic methods for ocular TB.

Learning points

- ▶ Ocular tuberculosis (TB) can present in a varied way.
- ▶ Immune stromal keratitis can be a rare presentation of ocular TB that may appear to be infective at presentation.
- ▶ A detailed systemic evaluation is required in all cases of bilateral keratouveitis.

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