



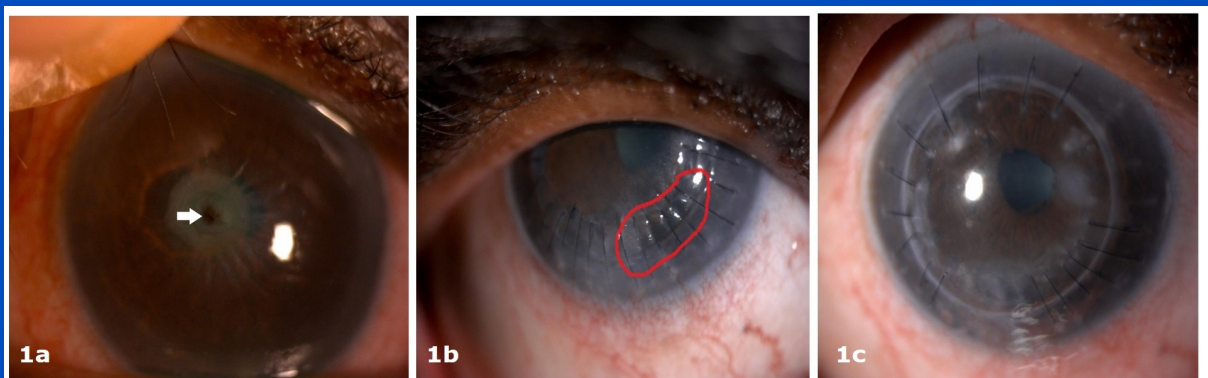
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PERIPHERAL ULCERATIVE KERATITIS: A CASE SERIES OF CORNEAL MELTING.



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ABSTRACT

Corneal melting or keratolysis is an ulcerative inflammation known as peripheral ulcerative keratitis, that results in thinning and ulceration of the cornea in the perilimbal cornea. It is a potentially life and vision threatening condition that usually associated with systemic conditions. We report three cases of corneal melting secondary to multiple aetiologies, which responded poorly to immunosuppressive therapy and required surgical intervention. The rapid course of the disease and unpredicted response to treatment make every case a challenge in its management.

KEYWORDS: Corneal ulcer, Corneal melting, Mooren's ulcer, Penetrating keratoplasty, Peripheral ulcerative keratitis

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Corneal melting or keratolysis is an ulcerative inflammation known as peripheral ulcerative keratitis, that results in thinning and ulceration of the cornea in the perilimbal cornea. It is a potentially life and vision threatening condition that usually associated with systemic conditions. We report three cases of corneal melting secondary to multiple aetiologies, which responded poorly to immunosuppressive therapy and required surgical intervention. The rapid course of the disease and unpredicted response to treatment make every case a challenge in its management.

KEYWORDS: Corneal ulcer, Corneal melting, Mooren's ulcer, Penetrating keratoplasty, Peripheral ulcerative keratitis

INTRODUCTION

Peripheral ulcerative keratitis (PUK) is an inflammatory ulcerative corneal condition that is typically characterized by crescent-shaped stromal thinning with an overlying epithelial defect located at the peripheral cornea, a condition sometimes labelled as corneal melting or corneal keratolysis. The tendency for peripheral location is due to the distinct morphologic and immunologic characteristics of the limbal conjunctiva, which provides access for circulating immune complexes to the peripheral cornea via the capillary network.^{1,2} PUK may be associated with various ocular and systemic infectious and non-infectious diseases.¹ Approximately 50% of non-infectious PUK cases are associated with systemic immune-mediated diseases. The most

common systemic association is rheumatoid arthritis (RA) accounting for 34% of cases.^{3,4}

In contrast, Mooren's ulcer (MU) is a form of PUK that develops in the absence of any systemic disease. The main difference from PUK associated with systemic diseases, is the severity of pain, which is more severe in MU. The central border of the ulcer in MU exhibits an overhanging edge and the sclera is rarely involved.⁵

A thorough systemic evaluation and aggressive management is mandatory in PUK due to the high potential for ocular complications and high mortality rate in the presence of associated systemic diseases. Here, we report three cases of corneal melting or keratolysis of different aetiologies and discussed the challenges encountered in managing these patients.

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CASE 1:

A 60 years old Indian lady presented with one

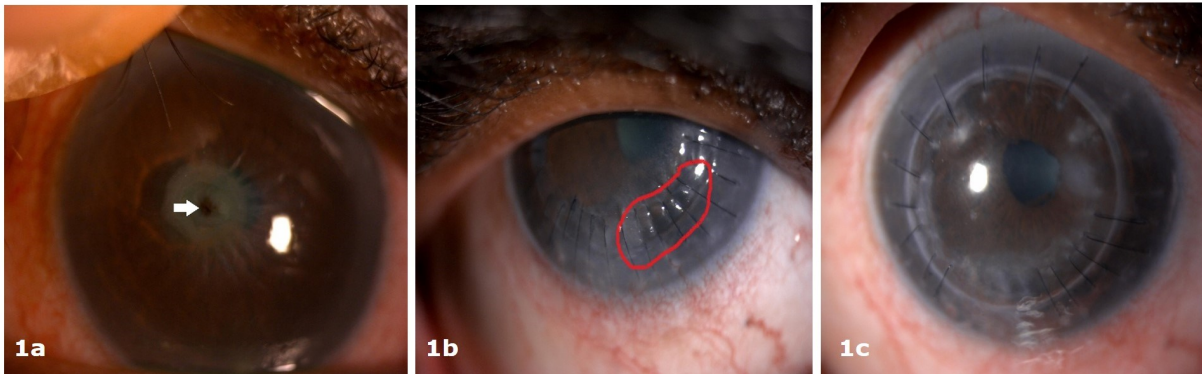


Figure 1: 1a) Right central corneal perforation (white arrow) with shallow anterior chamber, 1b) Persistent right corneal melt at the cornea host junction tissue at 6 weeks post-PK (within red line), and 1c) One year post right penetrating keratoplasty showing no further signs of corneal melt.

week history of ocular pain with progressive deterioration of vision in her right eye. She was diagnosed with sero-positive RA for the past 10 years complicated with pulmonary fibrosis. She was on regular follow up under rheumatology team and was previously on oral sulfasalazine 1g twice daily.

Her visual acuity at presentation was counting finger at 1 metre in the right eye (OD) and 6/12 in the left eye (OS). The slit lamp examination of the right eye revealed central corneal perforation measuring 2.1mm x 2.1mm in dimension with plugged iris and surrounding stromal infiltrates. The anterior chamber was shallow with irido-corneal touched (Figure 1a). The left eye anterior chamber and fundus examination was unremarkable.

She underwent an immediate right cyanoacrylate corneal patch graft upon admission followed by penetrating keratoplasty (PK) performed within two days of admission. She was initiated on oral prednisolone of 1mg/kg/day with weekly tapering dose, oral cyclosporine 50mg twice daily, topical Minims® Dexamethasone 0.1% every four hourly for the right eye and her oral sulfasalazine was continued. Prophylactic antibiotic along with oral doxycycline 100mg twice daily and vitamin C 1g once daily were also started. At 6 weeks post-operatively, she developed per-

sistent corneal melt at the cornea host junction tissue (Figure 1b). Pulsed intravenous (iv) methylprednisolone 500mg twice daily was commenced for 3 consecutive days and was then transitioned back to oral prednisolone of 1mg/kg/day. She responded well with the intensive immunosuppressive therapy with no other episode of cornea melt. However, she developed pneumonia and right fungal keratitis along with raised creatinine level secondary to oral cyclosporine usage. Her creatinine level and infection improved within two weeks of cyclosporine cessation. The oral cyclosporine was replaced with oral azathioprine 50mg twice daily and topical cyclosporine 0.05% four times daily on both eyes. At one year post-PK, her best corrected visual acuity (BCVA) was 6/36 OD with no signs of cornea melt (Figure 1c).

CASE 2:

A 44 years old Malay gentleman with no known medical illness presented with painful progressive visual loss and redness in the left eye over a year duration, which started six months following pterygium excision carried out at another local hospital. He was unable to confirm whether mitomycin C was used during procedure. He denied any history of ocular trauma, symptoms of autoimmune or other associated diseases.

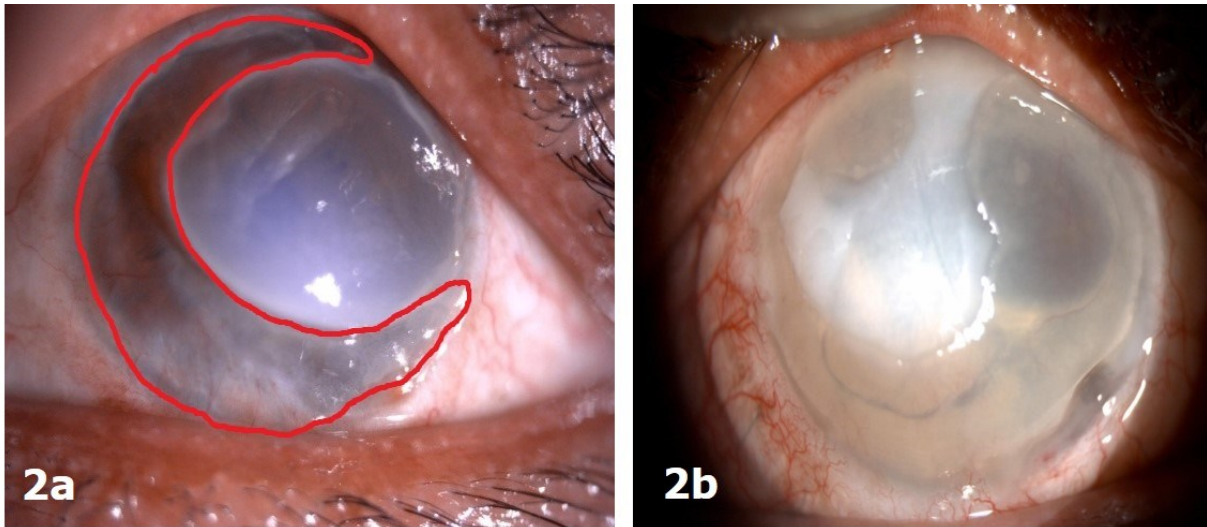


Figure 2: 2a) Left crescent shaped peripheral corneal thinning (within red line) and melting with overhanging edge, 2b) Post four months left lamellar keratoplasty (corneoscleral graft)

His BCVA on presentation was hand motion OD and 6/6 OS. Anterior segment examination of the left eye revealed a crescent shaped 270 degrees peripheral corneal thinning and melting extending from 4 to 1 o'clock (Figure 2a). The overhanging edge and remaining cornea was oedematous. The adjacent conjunctiva was also injected. Examination of the right eye revealed normal ocular findings.

All his relevant investigations were negative including anti cytoplasmic antibody (ANCA), rheumatoid factor (RF), antinuclear antibody (ANA) and hepatitis C screening. Haematological parameters, renal profile and liver function test were normal. Both erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were raised at 22mm/hour and 0.63g/dl respectively. Based on the clinical findings and workups, a diagnosis of MU was made.

Systemic immunosuppressive therapy was initiated with methylprednisolone 500mg iv once daily for three days followed by oral azathioprine 50mg three times daily (tds) and prednisolone of 1mg/kg/day with weekly tapering dose. He was also started on topical prednisolone acetate 1% four times daily,

topical moxifloxacin every 4 hourly, oral doxycycline 100mg twice daily and vitamin C 1g once daily. However at three months after the initial presentation, the cornea melt showed progression to 360 degree peripheral involvement with central island of oedematous cornea. Conjunctival resection was then performed. Despite these efforts, his cornea keratolysis progressively worsen and he underwent tectonic lamellar keratoplasty (LKP) (corneo-scleral graft) under general anaesthesia to prevent further progression. Four month post-operatively, his BVCA ranged from 1/60 to counting fingers and showed stable disease activity (Figure 2b).

CASE 3:

A 40 years old, Malay gentleman with underlying diabetes mellitus, hypertension and history of resolved Steven Johnson Syndrome (SJS) 10 years ago, presented with left eye painless progressive deterioration of vision associated with redness for one year duration. He had bought over-the-counter topical steroid drop regularly to relieve the symptoms without ophthalmologist consultation. He had history of bilateral myopic laser refractive surgery done three years prior to presentation and his vision was initially good post-

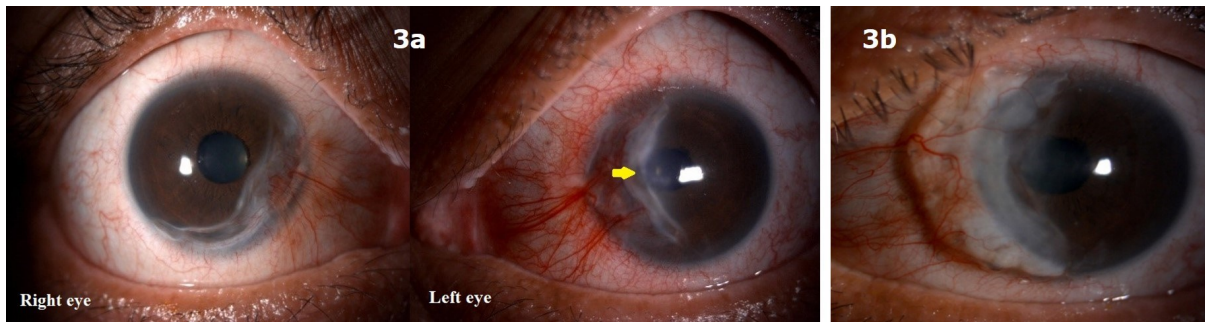


Figure 3: 3a) Bilateral crescent-shaped peripheral cornea thinning nasally with undermined edges with perforation on the left eye (yellow arrow), 3b) Post one year left peripheral corneal banana patch graft.

operatively.

Visual acuity at presentation was 6/24 OD and counting finger OS. Anterior segment examination showed a crescent-shaped peripheral cornea thinning nasally with undermined edges extending from 1 to 8 o'clock in the right eye and 6 to 12 o'clock with limbal involvement in the left eye but no associated scleritis. There was a slow leak over the edge of peripheral cornea thinning on the left eye and the anterior chamber was deep (Figure 3a). There was no sign of secondary infection. Other ocular and systemic examination was unremarkable.

All relevant investigations to rule out causes of PUK were negative except for his inflammatory marker which was moderately elevated with ESR of 46mm/hour and CRP of 1.24mg/dl. Diagnosis of MU was made based on the clinical findings and negative workup for underlying systemic diseases.

He was initiated on systemic immunosuppression of methylprednisolone 500mg iv once daily for three days along with oral cyclosporine 500mg twice daily. The methylprednisolone was transitioned to oral prednisolone of 1mg/kg/day with weekly tapering dose. He was also started with topical prednisolone acetate 1% four times daily and topical moxifloxacin every 4 hourly on both eyes along with oral ciprofloxacin 500mg twice daily (bid) and oral doxycycline 100mg

bid. He underwent left peripheral corneal banana patch graft to seal the linear perforation along the edge of the cornea thinning. Post-operatively, his visual acuity improved to 6/18 OS. However, he developed acute renal impairment and hepatitis secondary to cyclosporine usage, which was then changed to oral mycophenolatemofetil 500mg bid. His renal and liver function improved within one month of cyclosporine cessation. One year post-operatively, his BCVA remains stable with no signs of recurrence (Figure 3b).

DISCUSSION

Corneal melting is a common prelude to the development of corneal perforation. This case series illustrate the different aetiologies of immune-mediated corneal melting and the challenges in its management to halt the disease progression and prevent its recurrence.

Clinical presentation of PUK in RA is variables. Corneal melting in RA occurs late in the disease course with a mean age of onset 19.6 years after diagnosis.⁶ In our first case, the patient presented with PUK after ten years of diagnosis. The serious ocular complications in cases of RA with PUK present challenges to the ophthalmologist at various stages in the management. The primary treatment for acute disease control is systemic corticosteroid and patient with imminent visual loss, pulsed methylprednisolone may be initiated.^{7,8} Corticosteroid alone may not halt the dis-

ease activity and immunomodulatory agent should be started concurrently. Furthermore, these agents have been shown to prolong corneal graft survival rate.^{8,9} Surgical intervention is warranted in cases of corneal perforation to preserve structural integrity of the globe. Nobe *et al.* reported PK in patient with PUK has shown to have high failure rate, most commonly due to graft melt from recurrence of PUK.⁹ Studies have shown that many patients require multiple grafts with 20 to 40% graft survival at six months.^{9,10,11} In relation to our first case, patient underwent PK and showed recurrence of corneal melting post-operatively which responded to the intensive immunosuppression therapy. She was not started on methothrexate, although it is the first line of immunomodulatory agent in RA associated PUK⁴, in view of its side effect causing pulmonary toxicity which may complicate her underlying pulmonary fibrosis.

MU is an idiopathic, progressive and painful ulcerative keratitis that occurs in the absence of any systemic diseases. The exact aetiology of MU is unknown, however, there are evidences suggesting that it is an autoimmune basis.⁵ Zegans *et al.* found that previous history of corneal surgery, trauma or infection was reported in 68% of patient with MU.¹² Both our second and third cases had history of ocular surgery that predisposed them to development of MU. In addition, history of SJS in our third case may result in conjunctival cicatrization which creates a hostile ocular surface environment which may be responsible for triggering the autoimmune mediated keratolysis.

The main approach and goal in the management of MU is to arrest the destructive immune process and promote healing of the corneal surface. Most clinicians advocate on the 'step ladder approach' in the treatment of MU.^{5,12} Initial treatment may include local and pulsed systemic corticosteroid therapy during the acute phase. However, if cortico-

steroid therapy fails to control the disease progression, conjunctival resection should be performed. The use of second line immunosuppressive agents are reserve in cases of bilateral or resistant MU to halt the progressive immune mediated keratolysis.⁵ Both of our patients (case 2 and 3) with MU, however, failed to respond to the aggressive immunosuppressive therapy initiated. The cornea in both cases were progressively melting which warranted surgical intervention. A tectonic LKP (corneo-scleral graft) was performed for the patient in the second case due to presence of extensive peripheral corneal melting with limbal involvement. As for the third case, a peripheral corneal banana patch graft was done to seal the linear perforation along the edge of the cornea thinning. LKP offers several advantages over PK in PUK patients with perforation or impending perforation. The risk of rejection is greatly reduced for lamellar graft.^{5,13} It also permits the preservation of maximum amount of host tissue and adds on to the cornea thickness. This reduce the risk of recurrent perforation if the corneal melting process reactivate.¹³

CONCLUSION

Corneal melting is a vision threatening condition that usually has an underlying systemic aetiology. A systemic workup is crucial in its diagnosis and treatment. The rapid course of the disease and unpredicted response to treatment make every case a challenge in its management. The mainstay of treatment is not only controlling the inflammation of the involved ocular tissues, but may also include controlling the underlying systemic cause. Initiation of appropriate immunosuppressive therapy with corticosteroids and immunomodulatory agent are lifesaving.

Competing interest:

The authors declare that they have no competing interests.

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