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# CORNEAL PERFORATION AS A COMPLICATION OF EPIDERMOLYSIS BULLOSA ACQUISITA

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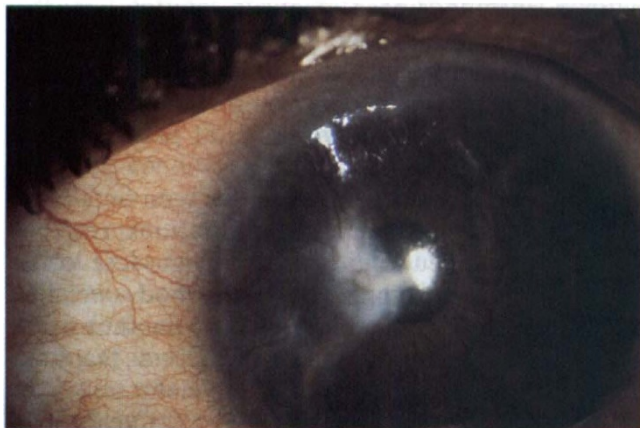
## SUMMARY

Epidermolysis bullosa acquisita (EBA) is now recognised as a histopathologically distinct condition.<sup>1-3</sup> Ocular complications of hereditary epidermolysis bullosa (EB) have been well documented,<sup>4</sup> but little has been reported with respect to the ocular manifestations associated with the acquired form.<sup>5-8</sup>

A patient with EBA and sarcoidosis – an association that does not appear to have been previously reported – developed spontaneous peripheral corneal melting and perforation. The defect healed with the use of a bandage contact lens, antibiotics, mydriatics and pulsed intravenous steroids, and resulted in a satisfactory visual outcome.

## CASE REPORT

A 38-year-old Jamaican woman with sarcoidosis and EBA presented with a short history of intermittent episodes of grittiness and redness of both eyes associated with reduced vision. She was myopic



**Fig. 1.** Healed corneal perforation with pigmentation at site of previous iris 'plugging'.

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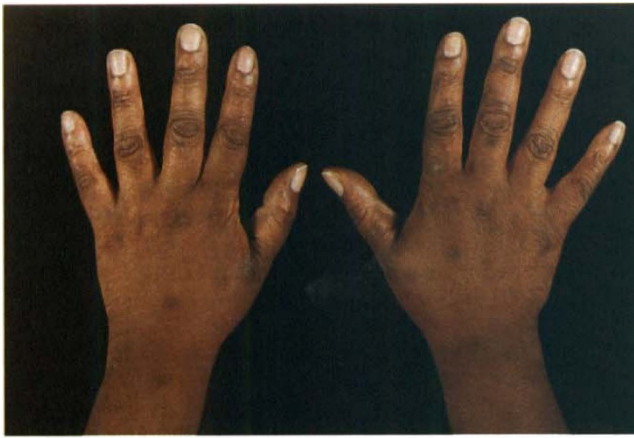
with previously normal corrected visual acuity. She had been treated for one episode of anterior uveitis 8 years earlier.

Sarcoidosis had been confirmed by liver biopsy and raised serum angiotensin converting enzyme (ACE) levels, while the diagnosis of EBA was made on the basis of the clinical presentation and a split skin biopsy. Systemic steroids had previously been used for treatment of her sarcoidosis but had to be stopped because of significant weight gain and depression. A course of dapsone was subsequently tried for her skin condition but proved to be of no benefit. Her condition was well controlled with oral azathioprine 250 mg daily.

On examination there was no sign of blepharitis. The tear film was reduced and there was marked diffuse punctate conjunctival and corneal epithelial erosions but no significant conjunctival scarring. She had 360° of peripheral corneal vascularisation of about 1–2 mm. She also had a mild degree of episcleral injection. These changes were almost symmetrical in both eyes. During the following 5 months the visual acuity fluctuated in both eyes from 6/6 to 6/36 in accordance with the corneal changes and the amount of mucus in her tear film. The



**Fig. 2.** Slit view of healed corneal perforation.



(a)



(b)

**Fig. 3.** Scars on dorsum of hands (a) and feet (b).

blurring of the vision and the irritation responded well initially to topical lubricants.

A corneal infiltrate with only mild stromal thinning and without an overlying confluent epithelial defect developed in the nasal periphery of the left cornea. There was a segmental limbitis and scleritis adjacent to the affected area. The anterior chamber was quiet. In view of the previous problems with systemic steroids, and as she was already on azathioprine 250 mg daily, only topical steroids were added. The infiltrate cleared and the topical steroids were tailed off, but 4 weeks later a corneal perforation occurred at the same site. The cornea was cloudy and the left visual acuity was reduced to counting fingers. The anterior chamber was flat peripherally and very shallow centrally with iris plugging the corneal defect. A bandage contact lens was positioned and topical and systemic antibiotics were commenced. Topical mydriatics were also used initially. Intravenous methylprednisolone (1 g) was administered. Two days later the area of corneal thinning was more limited. The anterior chamber was deeper but the iris was still adherent to the cornea and peripheral anterior synechiae were developing elsewhere. The mydriatics were stopped and pilocarpine 4% drops were started. This succeeded in breaking the anterior synechiae including, surprisingly, that to the site of the corneal perforation. The bandage contact lens was removed. Seidel test was negative and the perforation remained well sealed. The cornea cleared gradually over the following few days and the scar started to become vascularised (Figs. 1, 2). The visual acuity returned to 6/18 unaided, and could be corrected to 6/6. The associated scleritis was also settling. A second bolus dose of 1 g methylprednisolone was administered 5 days after the initial injection. Oral prednisolone 10 mg daily was commenced and appeared to be well tolerated by the patient. The steroids were tailed off

over a few weeks. Within a month only topical lubricants were needed. During the following year the corneal scar became more vascularised and there has been no recurrence of the scleritis or the corneal melting. The corrected visual acuity remains 6/6 in each eye.

## DISCUSSION

EBA is a rare non-inflammatory condition, predominantly adult in onset, thought to affect females and blacks more commonly. There is no family history and the blisters arise classically as a result of trauma on the dorsum of hands, feet, elbows and knees. Linear atrophic scars and milia are common.<sup>9,10</sup> Nail dystrophy and scarring alopecia may be seen.

There is known to be an increased frequency of class II HLA-DR2 haplotype in those patients.<sup>10</sup> The characteristic histopathological and immunological features include linear deposits of IgG at the basement membrane zone (BMZ) and IgG deposits beneath the lamina densa recognised by immunoelectron microscopy; circulating IgG anti-BMZ antibodies are found in two-thirds of patients some time in their disease.<sup>3,10-13</sup>

Mucous membrane involvement is seen in 50% of cases.<sup>5,7,8,14</sup> The systemic manifestations respond poorly to therapeutic measures.<sup>15</sup> High-dose corticosteroids (prednisolone 1-2 mg/kg body weight), cyclophosphamide, azathioprine and methotrexate have all been used without much success. Dapsone has been found to be of little benefit either in conjunction with or without steroids.<sup>16</sup> Cyclosporin A has been more successful in some patients who failed to respond to other lines of treatment.<sup>17,18</sup> Plasmapheresis has been performed in some cases.<sup>19</sup>

The association of EBA and sarcoidosis has not been previously reported but many systemic diseases<sup>20-23</sup> including rheumatoid arthritis, inflammatory bowel disease and thyroiditis have been

associated with EBA, suggesting a possible common autoimmune aetiology.

The ocular manifestations of EBA reported so far<sup>5-7</sup> include conjunctival and corneal scarring, symblepharon and 'blindness'.<sup>5,7</sup> However, the diagnosis of EBA was not confirmed in all cases. Some patients appear to have developed the changes more typical of pemphigoid, with subepithelial scarring and fibrosis leading to symblepharon formation and eventually corneal problems due to exposure.<sup>24</sup> Only one reported patient<sup>5</sup> with a proven diagnosis of EBA has developed corneal perforation, and in common with our patient she did not have significant conjunctival scarring, but her response to treatment was poor and she eventually required a therapeutic keratoplasty.

The patient we report had sarcoidosis and went on to develop blisters which left her with scars on her hands and feet (Fig. 3). Her HLA DR subtype (14 and 15) is consistent with DR2 haplotype. A split skin biopsy was performed. Sections of markedly hyperkeratotic skin showed a subepidermal bullous lesion. Some regenerating epidermal keratinocytes were seen in the base of the bulla. No eosinophils or other inflammatory cells were seen. Immunofluorescent and immunoperoxidase studies were performed, the latter using the pronase technique. Linear deposition of IgG and C3 at the epidermo-dermal junction was demonstrated which supports a diagnosis of EBA. Our patient had dry eyes but did not have the diffuse conjunctival scarring seen in other bullous conditions. She developed a corneal infiltrate without significant melting. She was on systemic azathioprine and the addition of topical steroids appeared to help initially, but she went on to develop a corneal perforation. Topical steroids are sometimes useful in the management of sterile marginal corneal ulcers with an infiltrative component<sup>25</sup> and their use (with caution) for EBA has been advocated,<sup>26</sup> but the risks of perforation are well documented.<sup>27</sup> Marginal corneal ulceration and melting occur in a number of autoimmune and vasculitic conditions, but are not a typical feature of sarcoidosis and are therefore more likely to have been a manifestation of EBA. The exact pathogenesis of these lesions is unclear but may involve local ischaemia or collagenase production. This might be the underlying mechanism in our patient, who had no confluent epithelial defect or signs of infection and only a localised segment of scleritis. A regime of 'pulsed' intravenous steroids as recommended for other types of peripheral corneal melting<sup>28</sup> has resulted in a satisfactory anatomical and visual outcome.

### CONCLUSION

The availability of specific tests and criteria for the

diagnosis of EBA provides an opportunity for more accurate assessment of its ocular manifestations and the recognition of signs specific to this recently better identified entity. It is important to appreciate the potential visual morbidity, even in eyes that do not show the diffuse type of scarring seen in other cicatricial bullous diseases. The use of pulsed steroid treatment may be worth considering.

Key words: Corneal melting, Corneal perforation, Epidermolysis bullosa acquisita, Pulsed steroid, Sarcoidosis.

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