Aggressive mucous membrane pemphigoid: a cross-specialty dilemma

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Introduction

This article presents a case of a 56-year-old man with aggressive mucous membrane pemphigoid and widespread systemic involvement. Although his ocular disease led to his eventual diagnosis, his other manifestations of oral ulcers, severe erosive gingivitis, nasal ulceration and penile ulceration had persisted for almost 3 years. Despite being seen by clinicians from multiple specialties, a variety of incorrect diagnoses had been provided. The patient is currently on intense immunosuppressive treatment.

Case report

A 56-year-old man presented to his optometrist with complaints of discomfort in his left eye, leading to a referral to the oculoplastic clinic for suspected upper lid entropion. The patient's ocular symptoms had lasted for 6 months, but direct questioning revealed a 3-year history of severe gingival disease, oral mucosal ulcers, difficulty swallowing and recurrent nasal ulcers, as well as penile glans ulceration. He had no family history of autoimmune disease and was a non-smoker with a negligible intake of alcohol. His dentist had previously diagnosed his gingivitis, which had eventually led to the loss of multiple teeth. The remaining teeth were exposed to their roots, with the patient wearing cosmetic veneers (Figure 1). His persistent dysphagia was thought to be the result of chronic fungal disease after multiple reviews by the otorhinolaryngologists. Antifungal treatment was initiated with poor results.

Examination revealed extensive loss of his left inferior conjunctival fornix and symblepharon formation, with marked bilateral subtarsal scarring and loss of his plica bilaterally, consistent with cicatrising conjunctivitis (Figure 2). Examination of the mouth revealed ulceration in the buccal mucosa with severe erosive gingivitis. Nasendoscopy revealed widespread ulceration in his nasal mucosa. He also had balanitis which, left untreated, can progress to scarring leading to phimosis and loss of the coronal sulcus (Figure 3). Urgent bilateral superior bulbar conjunctival biopsies were taken in addition to bilateral buccal mucosa biopsies. Histopathological analysis as well as direct immunofluorescence was performed, demonstrating linear binding of IgG, C3 and IgA to the epithelial basement membrane, thereby diagnosing mucous membrane pemphigoid.

Oral mycophenolate mofetil was started at 1 g twice daily in addition to a tapering course of oral prednisolone (initial dose 1 mg/kg). At subsequent review, he reported an increase in discomfort affecting the left eye, soreness in his cheeks, difficulty swallowing and new adhesions between his foreskin and glans penis. This demonstrated a flare in disease activity despite his current immunosuppression, and so his treatment was changed to pulsed oral cyclophosphamide.

How to cite this article:
Abdallah Y, Ogra S, Madge SN. Aggressive mucous membrane pemphigoid: a cross-specialty dilemma. Br J Hosp Med. 2020. https://doi.org/10.12968/hmed.2019.0327

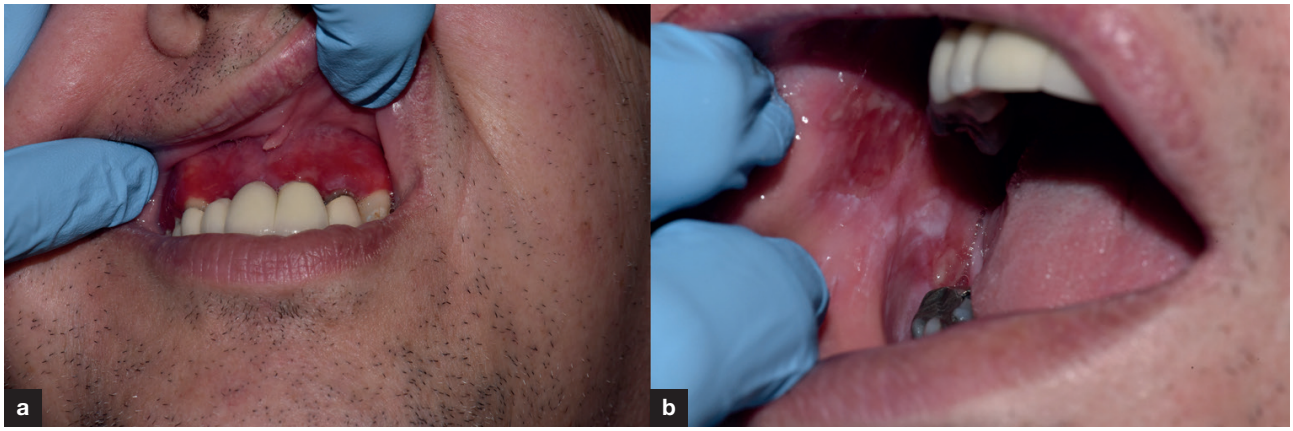

Figure 1. a. Severe gum recession and erosion. b. Ulceration of the buccal mucosa.

Figure 2. Left-sided symblepharon formation inferiorly and loss of the inferior conjunctival fornix.

Figure 3. Inflammation of glans penis (balanitis).

Discussion

Mucous membrane pemphigoid is a group of chronic autoimmune subepithelial blistering diseases with significant morbidity and mortality. It occurs mainly in the older population, aged 50–80 years, with a female:male ratio of 2:1 (Taylor et al, 2015). Affecting only stratified squamous epithelia, the conjunctiva and oral mucosa are the commonest sites for disease occurrence (Hong et al, 2019). The oral lesions often predate other sites and, as noted by Carey and Setterfield (2019), three phenotypes of disease in the mouth exist: pure gingival lesions, extragingival lesions or both. In terms of ocular disease, Saw et al (2008) found that 94% of cases of ocular mucous membrane pemphigoid were bilateral and Georgoudis et al (2019) highlight helpful clinical indicators to narrow down the wide differential diagnosis of ocular mucous membrane pemphigoid. Other sites affected include anogenital skin, the upper aerodigestive tract and head and neck skin, the latest presenting with recurring painful vesicles or bullae with a strong tendency to scar.

Mucous membrane pemphigoid is associated with a significant diagnostic delay of 2.5 years (Radford et al, 2012). It is best diagnosed by direct immunofluorescence, which shows linear binding of IgG and C3 (and possibly IgA) to the basement membrane. Setterfield

Learning points

- Mucous membrane pemphigoid is rare with a significant diagnostic delay and is potentially life- and sight-threatening.
- Biopsy of suspicious lesions for direct immunofluorescence is the gold standard investigation and demonstrates linear binding of IgG and C3 (with or without IgA) to the basement membrane.
- Consider mucous membrane pemphigoid when patients present with mucosal ulceration in multiple sites, especially if the oral cavity or ocular surface is involved.
- Ophthalmologists should consider mucous membrane pemphigoid when investigating cases of chronic conjunctivitis especially with cicatrisation.
- Always remember the importance of a general systems review in any new patient consult.

et al (1998) highlight that mucous membrane pemphigoid associated with both IgG and IgA binding is associated with a more aggressive disease process.

In terms of management, there is a lack of high-quality clinical trials of treatments for mucous membrane pemphigoid, but a systematic review by Taylor et al (2015) includes a summary treatment algorithm. Topical corticosteroid treatments can be useful to limit damage caused by skin lesions.

This case serves as a reminder to ophthalmologists, otorhinolaryngologists, dermatologists, oral medicine clinicians and urologists that serious mucosal disease may present to individual specialties separately over a long period of time. The initial diagnosis must be re-evaluated if there are any atypical features.

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