CASE REPORT

Laryngoceles with airway compromise complicating mucous membrane pemphigoid

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SUMMARY

Mucous membrane pemphigoid (MMP) encompasses a group of autoantibody-mediated, subepithelial blistering diseases, which primarily affect mucosal surfaces including oral, ocular, skin, genital, nasopharyngeal and oesophageal sites. We present a first description of laryngoceles as a manifestation of mucous membrane pemphigoid resulting in dynamic airway closure. Mucosal injury at other sites had previously resulted in pathergy and localised cicatrization. We discuss successful combined medical and transcutaneous surgical intervention designed to avoid tracheostomy and minimise iatrogenic laryngeal cicatrization.

BACKGROUND

Mucous membrane pemphigoid (MMP) can manifest in different ways, including gingivitis, erosions, ulcerations, symblepharon, corneal fibrosis, cutaneous vesicles and bullae, odynophagia, genital apthae and anal fissures.¹ MMP can cause significant morbidity due to the pain, tissue destruction and functional limitations resulting from chronic mucosal scarring, ulceration and inflammation.²

Figure 2 CT scan of the neck in coronal view, prior to surgery, demonstrating the two laryngoceles completely obstructing the airway. The red arrow points to the larger laryngocele and the blue arrow points to the smaller laryngocele.

Figure 1 CT scan of the neck in sagittal view, prior to surgery, demonstrating the laryngoceles completely obstructing the airway. The red arrow indicates their exact location.

MMP is caused by autoantibody-mediated injury directed against epithelial basement membrane zone autoantigens. Antibodies to BP180, BP230, Laminin 332, $\alpha 6 \beta 4$ integrin and type VIII collagen have been reported.³ The larynx is affected in 5%–10% of patients with MMP,⁴ and there have been previous reports of life-threatening laryngeal involvement caused by stenosis.⁵

Figure 3 CT scan of the neck in axial view, prior to surgery, demonstrating two cystic structures representing laryngoceles, with the larger cyst measuring 3.5 cm in diameter. The red arrow points to the larger laryngocele and the blue arrow points to the smaller laryngocele.

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Figure 4 Image from the laryngoscopy, confirming airway compromise related to the supraglottic cysts. The red arrow points to the larger laryngocele and the blue arrow points to the smaller laryngocele.

Figure 5 Image from the laryngoscopy demonstrating mucosal erythema and inflammation (red arrow) in the subglottic airway, below the level of the laryngoceles.

Figure 6 Image from the tracheoscopy demonstrating severe mucosal ulceration, erythema and inflammation (red arrows) extending as far as the carina.

This case presents a first description of laryngoceles as a manifestation of mucous membrane pemphigoid and its challenging treatment options due to previous iatrogenic scarring reactions.

CASE PRESENTATION

A 50-year-old man had a background of mucous membrane pemphigoid which had resulted in conjunctival symblepharon, oral lesions, right anterior nasal airway closure secondary to scar tissue, nasal septal ulceration, anal fissure and balanitis. Initial testing revealed negative serum skin autoantibody studies using indirect immunofluorescence. Unfortunately, ELISA for specific autoantibodies are not yet commercially available. A buccal mucosal biopsy demonstrated linear basement membrane staining for immunoglobulin G and complement C3. Further, a crusting pruritic lesion on his scalp was biopsied demonstrating focal clefts at the dermoepidermal junction and fine granular/linear staining along the dermoepidermal junction for complement C3, which established the diagnosis of MMP. There was no evidence of malignancy. Mucosal biopsies were associated with pathergy and localised cicatrising exacerbations of disease.

Initial control of his disease was achieved with a regimen of corticosteroids, azathioprine and infliximab. However, he soon experienced a severe exacerbation, resulting in a change to mycophenolate and rituximab. Clinical control of active inflammation was achieved with combined mycophenolate mofetil, intravenous immunoglobulin, rituximab and prednisone for a period of 4 years following which treatment was weaned. He then relapsed with worsening of his symptoms, including dyspnoea on minimal exertion, stridor, dysphonia, haemoptysis, severe pain with defecation and genital ulcers.

INVESTIGATIONS

CT of the neck showed two cystic structures in the supraglottic larynx causing marked narrowing of the laryngeal inlet (figures 1 and 2). The larger lesion measured 3.5 cm in maximal diameter (figure 3). Dynamic scanning of the larynx performed via CT bronchoscopy showed complete occlusion of the supraglottic larynx during late inspiration and end expiration due to the laryngoceles. Office-based laryngoscopy and tracheoscopy confirmed airway compromise related to supraglottic cysts (figure 4) and demonstrated mucosal ulceration of the trachea extending as far as the carina (figures 5 and 6).

TREATMENT

Impending critical airway compromise due to the laryngoceles needed to be managed in this case with the knowledge that surgical and airway interventions may themselves precipitate further rounds of pathergy and cicatrization by way of mucosal instrumentation.⁶ Prior to the surgery, his immunosuppressant regimen was intensified with pulsed methylprednisolone followed by a weaning plan of high-dose oral corticosteroids, rituximab-mediated B cell depletion, mycophenolate mofetil 1g twice daily and intravenous immunoglobulin to optimise his healing and decrease any scarring reactions. In order to minimise the risk of mucosal trauma he proceeded to external transcutaneous drainage of the supraglottal cysts under local anaesthetic. Guided by flexible transnasal laryngoscopy, a large bore cannula was introduced via the thyrohyoid membrane draining thick, proteinaceous material. Voice and airway improved immediately and no postoperative complications were demonstrated.

OUTCOME AND FOLLOW-UP

Eighteen months postoperatively the patient's voice and breathing have improved with no recurrence of the laryngoceles. Disease activity has stabilised on immune therapies which include B cell depletion, and a medium-to-long term maintenance strategy consisting of mycophenolate mofetil 500 mg twice daily and rituximab every 6 months, with short-term corticosteroids for exacerbations has been devised to prevent future relapses.

DISCUSSION

Laryngoceles as a manifestation of mucous membrane pemphigoid have not been described in the literature to date.

This patient had multiple contributing factors placing him at risk of laryngocele formation. Chronic cough is a recognised risk factor for laryngocele development.⁷ Furthermore, laryngeal inflammation and scarring are likely to have induced obstruction of the laryngeal sacculae causing expansion secondary to build-up of its glandular secretions. This phenomenon has been described in other settings, with reports of laryngeal infection, inflammation and tumours causing outlet obstruction leading to development of laryngomucocele.⁸

The increased risk of scarring in patients with MMP may be explained by the site of antibody binding. In MMP, antibody binding occurs primarily in the lower lamina lucida and lamina densa of the basement membrane zone.⁹ This deeper location of antibody binding may account for the increased risk of scarring, making it difficult to safely perform sterile procedures involving the mucous membranes. Pathergy has previously been demonstrated in a patient with anti-p200 pemphigoid (anti-laminin- γ 1 pemphigoid), a relatively rare bullous disease.¹⁰ Pathergy occurs due to a hypersensitivity reaction, with development of an erythematous papule or pustule at a site of trauma within 48 hours, and has historically been associated with Behcet's disease.¹¹

In patients with severe MMP, aggressive immunosuppressive regimens may lead to improvement. B cell depletion using rituximab has been shown to be efficacious and ideally would be used early¹²; however, being off-label and unfunded, a more conventional 'step-up' approach to immunosuppression, guarding against excessive corticosteroid exposure is favoured. Immunosuppressants such as azathioprine, mycophenolate mofetil or cyclophosphamide are combined with systemic corticosteroids until disease is controlled, then with a slow corticosteroid taper over 4–6 months.¹³ Our patient received an aggressive treatment regime with pulsed methylprednisolone, mycophenolate mofetil and intravenous immunoglobulin prior to surgery to reduce the risk of long term postoperative scarring. This regime has had a positive outcome by prevention of further scarring and remission of his MMP.

Learning points

- Laryngoceles are a potential life-threatening manifestation of mucous membrane pemphigoid.
- Surgical management of laryngoceles can pose a challenge due to pathergy and cicatricial wound healing.
- The risk of scarring can be reduced through optimisation of medical management and use of minimally invasive procedures.

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REFERENCES

- 1 Fleming TE, Korman NJ. Cicatricial pemphigoid. *J Am Acad Dermatol* 2000;43:571–94. quiz 91–4.
- 2 Chan LS, Ahmed AR, Anhalt GJ, et al. The first international consensus on mucous membrane pemphigoid. *Arch Dermatol* 2002;138.
- 3 Rashid KA, Gürcan HM, Ahmed AR. Antigen specificity in subsets of mucous membrane pemphigoid. *J Invest Dermatol* 2006;126:2631–6.
- 4 Schmidt E, Zillikens D. Pemphigoid diseases. *The Lancet* 2013;381:320–32.
- 5 Schempf U, Plentz R, Stueker D, et al. Scarring mucous membrane pemphigoid presenting as double stenosis of the larynx and esophagus: precautions during therapy can avoid complications. *Endoscopy* 2014;46:E617–8.
- 6 Salihoglu Z, Dikmen Y, Demirel S, et al. Oral aphthous ulcers after difficult intubation in a patient with Behcet's disease. *Anaesthesia* 2002;57:606–25.
- 7 Amin M, Maran AG. The aetiology of laryngocele. *Clin Otolaryngol Allied Sci* 1988;13:267–72.
- 8 Fraser L, Pittore B, Frampton S, et al. Laryngeal debridement: an alternative treatment for a laryngopyocele presenting with severe airway obstruction. *Acta Otorhinolaryngol Ital* 2011;31:113–7.
- 9 Bédane C, McMillan JR, Balding SD, et al. Bullous pemphigoid and cicatricial pemphigoid autoantibodies react with ultrastructurally separable epitopes on the BP180 ectodomain: evidence that BP180 spans the lamina lucida. *J Invest Dermatol* 1997;108:901–7.
- 10 McCarty M, Zillikens D, Fiverson D. Anti-p200 pemphigoid (anti-laminin- γ 1 pemphigoid) demonstrating pathergy. *Int J Womens Dermatol* 2015;1:173–4.
- 11 Davatchi F, Chams-Davatchi C, Ghodsi Z, et al. Diagnostic value of pathergy test in Behcet's disease according to the change of incidence over the time. *Clin Rheumatol* 2011;30:1151–5.
- 12 Le Roux-Villet C, Prost-Squarcioni C, Alexandre M, et al. Rituximab for patients with refractory mucous membrane pemphigoid. *Arch Dermatol* 2011;147:843–9.
- 13 Kourosh AS, Yancey KB. Therapeutic approaches to patients with mucous membrane pemphigoid. *Dermatol Clin* 2011;29:637–41.

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