Laryngeal involvement in a patient with bullous pemphigoid

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Bullous pemphigoid (BP) is a subepidermal blistering disease predominantly seen in older individuals.¹ Lesions usually consist of 1- to 3-cm blisters situated on either normal appearing or inflamed skin.² Oral mucosa can be involved in one-third of patients. The diagnosis is made on the basis of clinical presentation, histology, and immunopathological studies. In about 50 percent of patients with oral pemphigoid, the disease can progress to extraoral sites, such as the eye, larynx, pharynx, or esophagus.² We report a unique case of bullous pemphigoid that presented with laryngeal edema and critical airway narrowing manifesting as stridor.

Case

An 81-year-old male was seen in the otolaryngology clinic for oral ulceration noticed for the past 3 months. There was no history of skin rash, drug intake, fever, diarrhea or dysuria. On oral examination the patient was found to have ulcers involving the oral mucosa and tonsils with an inflamed base. On routine indirect laryngoscopic examination, a similar ulceration was noticed in the larynx. As the location of ulcers was peculiar, with laryngeal involvement, a biopsy of the oral, tonsillar and laryngeal ulcers was performed under general anesthesia. The pathology was inconclusive. Three months after biopsy the patient presented in our emergency room with complaints of gradually worsening shortness of breath and hoarseness of voice. He was admitted to the intensive care unit with a diagnosis of upper airway obstruction and stridor. On physical examination there were multiple scattered tense bullae measuring 1 to 3 cm seen predominantly on the extremities, axilla, and upper trunk (anteriorly and posteriorly). The skin surrounding the blisters was inflamed in some areas and normal looking in others. The ruptured blisters revealed an inflamed base. A loud inspiratory stridor was audible. Oral examination revealed two ulcers on the buccal mucosa. His arterial blood gases revealed acute respiratory acidosis. He was given a 70:30 helium-oxygen mixture, less dense than air or oxygen alone, to decrease the work of breathing and dyspnea. Simultaneously, he was started on intravenous dexamethasone. The patient responded well and his respiratory acidosis disappeared in the next 12 hours. As the patient refused bronchoscopic inspection, computed tomography (CT) of the neck was done, which revealed supraglottic edema. The narrowest airway diameter was around 5.5 mm. Skin biopsy was performed for histopathology and immunofluorescence, which found cell-poor subepidermal bullae with scant perivascular inflammation. Immunofluorescence revealed linear deposition of fibrinogen and C3 at the dermoepidermal junction while IgG, IgM, IgA and C1q were negative (Figure 1). The findings were consistent with bullous pemphigoid complicated by laryngeal involvement. He was started on high-dose methylprednisolone (1 mg/kg) every six hours. The patient

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Figure 1. Top: Cell-poor subepidermal bulla in the upper dermis with sparse perivascular lymphocytic infiltrate (H&E). Bottom: Complement deposition at dermo-epidermal junction.

responded and resting stridor disappeared by day 3. He was switched to oral prednisone (1 mg/kg). A subsequent CT of the neck on day 10 revealed improvement in airway diameter (Figure 2). Pulmonary function tests (PFT) revealed a forced expiratory volume in the first second (FEV1) of 77% of predicted and a forced vital capacity (FVC) of 51% of predicted. Airflows were decreased in both inspiration and expiration for most of the FVC with a more marked decrease in inspiration. Maximal flow during inspiration was 0.7 L/sec and expiration was 1.7 L/sec. Two weeks after discharge the patient continued to improve on steroids. Repeated PFTs revealed a FEV1 of 102% of predicted and an FVC of 88% of predicted. Maximal inspiratory and expiratory flows were 1.2 L/sec and 2.3 L/sec, respectively.

Subsequently, the patient was referred to the dermatology clinic in Riyadh where he was put on azathioprine as attempts to withdraw steroids resulted in a recurrence of the skin lesions. Until the last contact with the patient (six months from the admission

in our ICU), he was on azathioprine and skin lesions were decreased markedly with no oral ulceration.

Discussion

This case report of upper airway involvement in bullous pemphigoid (BP) is the first from this part of the world. We found not only a rare association of laryngeal involvement in BP but also demonstrated the timely use of helium-oxygen mixture along with steroids, which prevented surgical intervention for critical airway narrowing. Use of helium and oxygen is well documented in large airway obstructions. Helium is less dense than oxygen and air and thus decreases turbulence due to airway narrowing, which in turn decreases the work of breathing. This therapy is generally used as a bridging therapy in the management of large airway obstructions until definitive therapy is available. This approach can sometimes prevent invasive airway management, as happened in our case.

BP is typically a chronic disease characterized by periods of exacerbation and partial remission. Lesions tend to predominate on the lower trunk, axilla, groin, or flexor surfaces of the extremities.² The differential diagnosis of BP is diverse and includes autoimmune diseases like pemphigoid gestationis, IgA dermatosis, epidermolysis bullosa acquisita, dermatitis herpetiformis, bullous lesions in systemic lupus erythematosus, and other rare disorders. Non-immunological diseases mimicking BP may include bullous erythema multiforme, drug reactions, and porphyrias. Most of these diagnoses can be differentiated by detailed history, careful physical examination and appropriate investigations. Differentiating BP from mucous membrane pemphigoid (MMP) at times can be difficult especially with the first episode of the either disease. Another difficult disease to differentiate is epidermolysis bullosa acquisita (EBA), which may require specialized studies (specific antigen detection). Bullous pemphigoid antigen 1 (BPAG1 or BP230) and BPAG2 (BP180) act as auto-antigens in this immune-mediated disorder.^{2,3} Autoantibodies bind to these antigens thus fixing complement and triggering tissue injury as manifested by clinical symptoms and signs. In MMP, autoantibodies are predominantly directed towards BPAG2 and laminin 5 (epidermal antigens), while in EBA IgG antibodies are formed against basement membrane auto-antigen collagen VII.² Immunopathology is the mainstay in differentiating these disorders. Despite exhaustive testing, a clear distinction cannot be made in a significant number of patients.²

Figure 2. Left: CT scan showing narrowed airway diameter due to airway edema. Right: CT scan on day 10 showing improved airway diameter.

Immunosuppressive agents are the mainstay of treatment for this disease. Systemic glucocorticoids are the most commonly employed medications. Topical steroids can be used in milder forms of BP. Involvement of ocular, laryngeal, esophageal, and/or genital mucosae require more aggressive therapy.^{2,4} Steroids are generally used in the doses ranging from 0.75 to 1 mg/kg per day. Patients with extensive or recurrent disease may require steroid-sparing immunosuppressives (e.g., azathioprine, cyclophosphamide, mycophenolate mofetil). Involvement of the supraglottic area with BP causing airway compromise has only been reported

once before.⁵ The patient showed marked improvement after the use of a helium-oxygen mixture.⁵ Our case further emphasizes the role of helium-oxygen in upper airway obstruction due to BP as a possible intervention that may prevent aggressive airway management (emergent tracheotomy) when combined with steroids.

In conclusion, blistering skin diseases should be considered in older patients presenting with upper airways obstruction. A helium-oxygen mixture can be a life-saving bridging modality and should be routinely used in such patients along with immunosuppressive therapy.

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