

Obstructive respiratory failure in cicatricial pemphigoid

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ABSTRACT A 20 year old woman died of respiratory failure due to cicatricial pemphigoid of the trachea and bronchi. This is the first case with the lower airways affected to be reported.

Cicatricial pemphigoid, or benign mucus membrane pemphigoid,^{1,2} is a chronic bullous disease primarily affecting mucus membranes and less frequently the skin. It occurs from the second to the eighth decade of life, but is more common in the elderly. Its course is usually benign, though conjunctival scarring may cause visual impairment. The respiratory tract is rarely affected, and in previously reported cases disease has been limited to the larynx.^{1,2} We present a patient who died of respiratory failure caused by lesions in the trachea and bronchi.

Case report

A 20 year old Bolivian woman was admitted to our hospital from another centre with mucosal ulceration and respiratory dysfunction. She had been healthy until September 1986, when a painful blistering eruption had developed in the mouth and vulva, which partially resolved with prednisolone. One month later typhoid fever was diagnosed, and she was treated with chloramphenicol, sulphamethoxazole, and trimethoprim. A few days later there was an abrupt onset of a generalised cutaneous bullous rash, thought to be erythema multiforme, so antibiotics were discontinued. The rash resolved but the mucosal lesions persisted. A lip biopsy specimen taken at the time was reported as showing the histological changes of pemphigus vulgaris, though no immunofluorescence studies were carried out. Prednisolone (70 mg/day) was reintroduced, again with partial improvement, but it was withdrawn after three weeks, after the onset of depressive psychosis. At this time the patient also began to complain of dyspnoea, cough, and wheeze. The respiratory symptoms progressively worsened; bron-

chodilators and steroids afforded some relief but again steroids had to be discontinued, and she was transferred to our care.

On admission she was afebrile but distressed, dyspnoeic, and cachectic, with painful ulceration and scarring of the vulva and mouth and blistering of the face and trunk. The conjunctivae were ulcerated and scarred, and early synechiae were present. There was prolonged expiration and wheeze, and chest radiography and computed tomography showed hyperinflated lungs and distended bronchi (fig 1). Arterial oxygen tension was 7.3 kPa and arterial carbon dioxide tension 8 kPa; FVC was 1.08 (pred 3.64) l, FEV₁ 0.53 l (pred 2.99 l), PEF 108 l/min (pred 379 l/min), and FEF 25-75% 0.23 (pred 3.68) l/s. The airways obstruction was unaffected by inhaled salbutamol. Oesophageal and tracheal ulcers surrounded by cicatricial areas were seen at endoscopy.

Laboratory investigations showed mild anaemia, a total white cell count of $4.8 \times 10^9/l$, and reactive bone marrow. Antinuclear factor, lupus erythematosus cells, rheumatoid factor, circulating immune complexes and anti-basement membrane antibody were absent; serum complement and immunoglobulin concentrations were within normal limits.

Biopsy material from the vulva, lip, mouth, and trachea

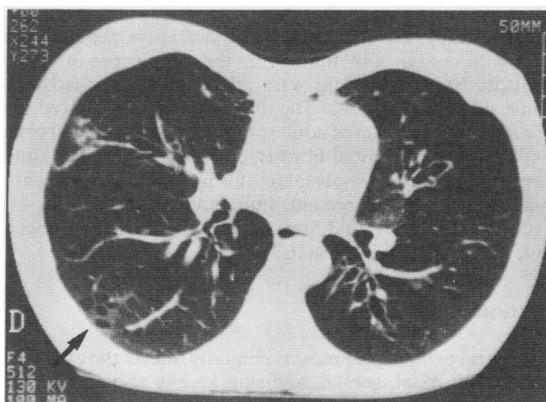


Fig 1 High resolution computed tomogram of the thorax showing cystic subpleural air spaces (arrow), central and peripheral bronchiectasis, and some areas of alveolar consolidation.

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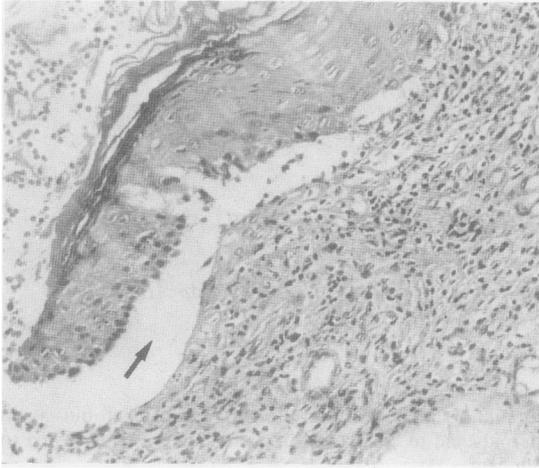


Fig 2 Tracheal biopsy showing squamous metaplasia with a subepidermal bulla (arrow) and underlying chronic inflammation. (Haematoxylin and eosin.)

showed subepithelial bullae with underlying fibrosis, proliferation of blood vessels, and a heavy plasma cell infiltrate (fig 2); there was no acantholysis. The basement membrane was either on the floor of the bullae or attached to the desquamated epithelium. Direct immunofluorescence tests for IgG, IgM, IgA, C3, and fibrinogen gave negative results.

The clinical and pathological features were considered to be consistent with cicatricial pemphigoid. Despite treatment with triamcinolone, dapsone, cyclophosphamide, and later azathioprine, the bronchial obstruction and mucosal ulceration progressed and new bullous lesions appeared. After three weeks on ventilatory support the patient died of respiratory failure and secondary infection.

At necropsy lesions were seen to affect the cornea, conjunctivae, mouth, oesophagus, skin, vulva, and respiratory tract (from the larynx to the small bronchi). Histologically, there was superficial ulceration, proliferation of small vessels, and fibrosis in the submucosa of large bronchi. Smaller bronchi were dilated and ulcerated with some subepithelial clefts. The lung parenchyma showed the characteristic changes of adult respiratory distress syndrome, with areas of interstitial fibrosis, epithelial hyperplasia, and deposition of intra-alveolar fibrin. Severe bronchopneumonia was also present. Immunofluorescence tests for IgG, IgA, IgM, C3, and fibrinogen in the trachea, bronchi, and skin gave negative results.

Discussion

Cicatricial pemphigoid most commonly affects the eyes and mouth, but nasal, genital, and skin lesions also occur, and oesophageal and laryngeal lesions have been reported.¹² It is thought to be an autoimmune disorder, and immunoglobulin

and complement have been found in the basement membrane of the mucosa, skin, and conjunctiva of 50-97% of patients.² Circulating anti-basement membrane antibodies may be present,^{2,3,6} but their absence does not exclude the diagnosis.

This case was unusual in that the respiratory tract was affected, culminating in respiratory failure. Although mechanical ventilation may have contributed to the ulceration of the bronchial mucosa the preceding bronchoscopy and biopsy had shown bullous and erosive lesions. The diagnosis of cicatricial pemphigoid was based on the clinical appearance of the mucosal lesions and the presence of subepithelial bullae with underlying chronic inflammation in the biopsy material.

We are not aware of any previous reports of this complication in cicatricial pemphigoid. Disease affecting the airways has been described in Behçet's disease and erythema multiforme.^{7,8} In our patient, however, the histological appearance did not fit Behçet's disease; and the absence of extensive cutaneous lesions, the prolonged and progressive course, and the onset of mucosal lesions before sulphonamides were given make erythema multiforme unlikely. Negative results in immunofluorescence studies excluded pemphigus vulgaris, and lupus erythematosus is also ruled out as no specific clinical or serological abnormalities were present.

The course of cicatricial pemphigoid is usually benign, though oesophageal and laryngeal lesions may be fatal.^{2,9} Whether the disease in our patient was an aggressive variant of cicatricial pemphigoid or a separate, hitherto undescribed entity is uncertain.

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