

CASE REPORT

Multiple mucosal involvement in cicatricial pemphigoid

Un caso di pemfigoide mucosinechiante con coinvolgimento nasale e laringeo

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SUMMARY

Mucous membrane pemphigoid includes chronic autoimmune sub-epithelial blistering diseases that predominantly affect mucous membranes, with varying combinations of oral, ocular, cutaneous, genital, nasopharyngeal, oesophageal and laryngeal lesions. The case is reported of a man with multiple manifestations of mucous membrane pemphigoid. A 53-year-old male presented at our Department with a 4-year clinical history of diagnosed cicatricial pemphigoid. The patient was affected by ocular and urinary symptoms and presented with nasal obstruction and dysphonia. Nasal endoscopy revealed crusting and synechiae with pale and atrophic mucosa. Computed tomography examination showed hypodense-hyperdense material occupying all paranasal sinuses and nasal fossae. Laryngoscopy showed anterior para-commissural and inter-arytenoidal synechiae. The patient underwent functional endoscopic sinus surgery for incision of synechiae and removal of scars and inflammatory material from all sinuses. Nasal splints were then inserted. A wait-and-see policy was adopted for the laryngeal lesion. One year later, the splints were removed; the upper airways were still free and there were no signs of nasal obstruction. An endoscopic approach appears to be efficacious in the surgical treatment of nasal cicatricial pemphigoid, and long-term stenting may be necessary to avoid recurrence. Although surgery has not a curative role in long-term therapeutic strategies, it may, nonetheless, improve the quality of life and ensure good nasal respiration.

KEY WORDS: Nose • Larynx • Cicatricial pemphigoid • Synechia

RIASSUNTO

Il pemfigoide mucosinechiante è un disordine autoimmune cronico caratterizzato da manifestazioni mucose spesso multiple. Questa rara condizione colpisce prevalentemente alcuni organi, quali, ad esempio, il cavo orale, gli occhi, la cute, i genitali, la mucosa nasale, faringea, esofagea e laringea. Presentiamo il caso di un paziente con coinvolgimento multiorgano. Un uomo di 53 anni è giunto alla nostra attenzione, presso il Dipartimento di Otorinolaringoiatria dell'Ospedale San Raffaele di Milano, con diagnosi antecedente di pemfigoide mucosinechiante e una storia clinica di circa 4 anni, caratterizzata da un intervento di odontocheratoprosi all'occhio destro. Il paziente presentava sintomi oculari e urinari associati a ostruzione respiratoria nasale e disфонia. All'indagine endoscopica nasale era evidente un quadro di rinite crostosa e sinechie diffuse su una mucosa nasale pallida e atrofica. L'imaging radiologico confermava la presenza di materiale infiammatorio occupante i seni paranasali e le fosse nasali. In fibrolaringoscopia erano presenti una sinechia laringea localizzata in sede paracommissurale e una in sede interaritenoidica. Il paziente è stato sottoposto a chirurgia endoscopica naso-sinusale allo scopo di rimuovere il materiale cicatriziale e infiammatorio dai seni paranasali e lisare le sinechie con posizionamento di splints parasettali. Per quanto riguarda il coinvolgimento laringeo si è deciso di effettuare un follow-up stretto sulla lesione senza intervenire chirurgicamente. Gli splints parasettali sono stati lasciati in sede per circa un anno. Al controllo le vie aeree risultavano pervie, senza segni di ostruzione nasale. L'approccio endoscopico nel trattamento chirurgico delle forme di pemfigoide mucosinechiante con coinvolgimento nasale sembra essere efficace soprattutto se associato all'utilizzo di splints nasali a lunga permanenza.

PAROLE CHIAVE: Naso • Laringe • Pemfigoide mucosinechiante • Sinechia

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Introduction

Mucous Membrane Pemphigoid (MMP) includes chronic, autoimmune, inflammatory sub-epithelial blistering diseases that predominantly affect the mucous membranes, with or without skin involvement as defined by the first international consensus conference¹. Any mucosa might

be affected, with varying combinations of oral, ocular, cutaneous, genital, naso-pharyngeal, oesophageal and laryngeal lesions. MMP is typically a disease of the elderly. It occurs most frequently in the sixth and seventh decades of life, although it has been reported to range between the third and ninth decades^{2,3}. Females are affected twice as often as males, and there is no geographic or racial pre-

dominance⁴. MMP is not a common disease. The annual incidence is reported to be 1.16 and 0.87 per million, in France and Germany, respectively^{5,6}.

Although the exact patho-physiological mechanisms have not yet been fully elucidated, experimental data suggest that humoral and cellular immune mechanisms may play a role in the pathogenesis of the disorder⁷⁻⁹. Direct immunofluorescence investigations show continuous linear deposits of IgG and C3, in addition to IgA, in the epithelial basement membrane zone in all MMP patients^{1,10}. Clinical onset varies as it may appear as vesicolo-bullous lesions, with progressive erosion and healing with scars or as erythema, oedema or crusty ulcers that occasionally evolve into scarring and adhesions¹¹. The heterogeneous clinical picture can make diagnosis of MMP difficult. Diagnosis of the condition requires a combination of clinical and immuno-pathological findings together with histological evidence¹¹. Medical therapy is the treatment of choice. Both local and systemic measures may be used to achieve symptomatic control and delay disease progression, but since the aetiology is unknown, treatment is neither specific nor curative. According to the data in the literature, surgery plays a marginal role being used mainly in the presence of complications. Herewith, the case is presented of a multiple mucous involvement, focusing on ENT lesions.

Case report

A 53-year-old male presented at the Department of Otorhinolaryngology at the Vita-Salute University of Mi-

lan, in 2002, with a 4-year clinical history and diagnosis of Cicatricial Pemphigoid (CP). He was affected by scarring of the tarsal conjunctiva with symblepharon and ankyloblepharon formation (Fig. 1A). This condition had progressed until total blindness. He also reported urinary disorders, correlated with the presence of urethral synechiae requiring endoscopic surgery followed by placement of a foley for 50 days in order to ensure diuresis. He came to our attention complaining of nasal obstruction, hyposmia and headache. He also reported having dysphonia since 2001.

Nasal examination using a 30° rigid endoscope revealed crusting and synechiae between the nasal septum and inferior turbinates, which also led to choanal stenosis. Evidence of a pale nasal mucosa confirmed atrophic rhinitis (Fig. 2B). Laryngeal involvement was evaluated with a 70° endoscope showing anterior para-commessural and inter-arytenoidal synechiae (Fig. 2A). Computerized tomography (CT) examination (in 2002) was performed on axial and coronal views, 3 mm thickness (Fig. 3A-D). CT

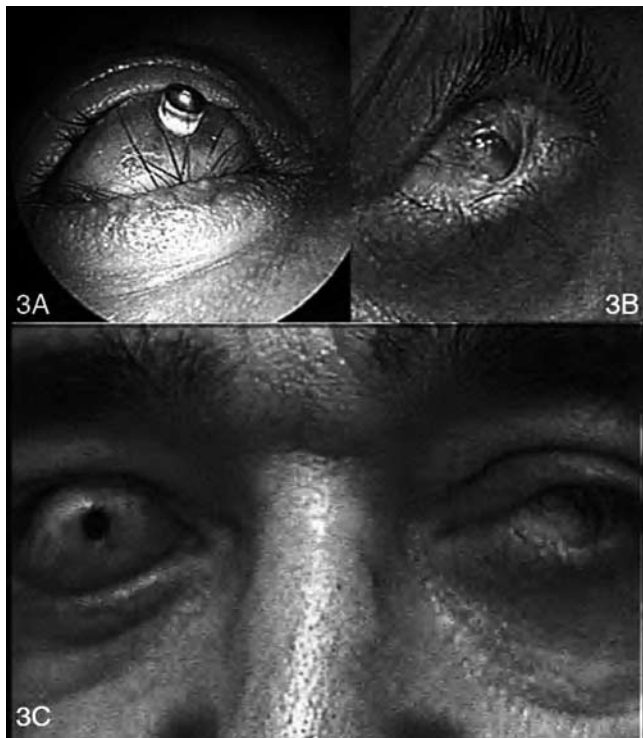


Fig. 1. A: Left eye with conjunctival synechiae. B: Right eye treated by osteo-odonto-keratoprosthesis. C: General view of eyes.

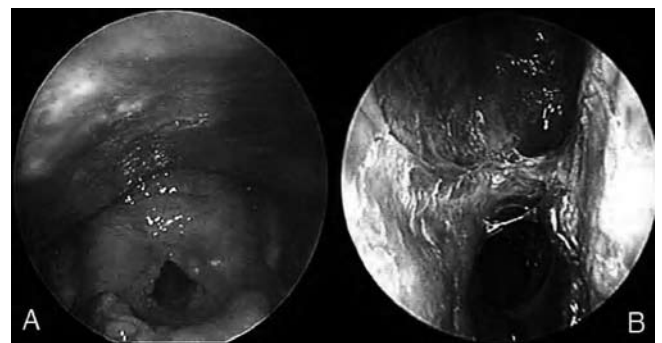


Fig. 2. A: Laryngeal involvement was evaluated with a 70° endoscope showing anterior para-commessural and inter-arytenoidal synechiae. B: Nasal endoscopy shows pale nasal mucosa with atrophic rhinitis, synechiae and crusting.

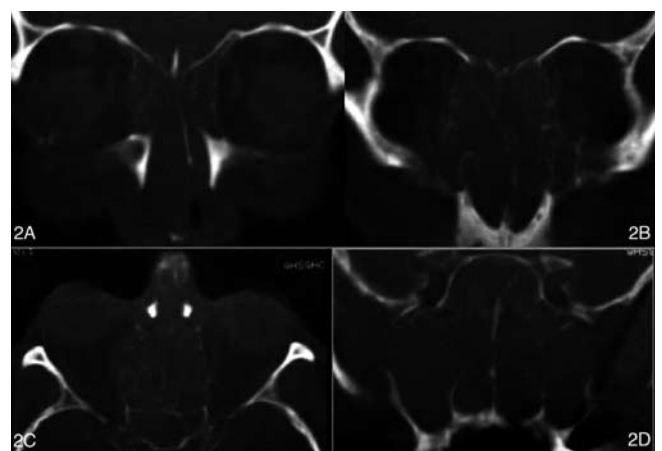


Fig. 3. A-B-D: CT scan (coronal views) shows inflammatory material occupying ethmoid, maxillary, sphenoid sinuses and nasal fossae. C: Axial view of CT examination shows pathological tissue that extends to obliterate the paranasal sinuses.

showed hypodense-hyperdense material occupying the left maxillary sinus, ethmoidal cavities, sphenoidal and left frontal sinus. Material was also present in the right maxillary sinus. Nasal fossae, especially the left, were totally filled. Bone structures were hyperdense, on CT scans, for lateral walls and thin for medial walls that were not easily detected at nasal fossae level, similar to findings observed in chronic inflammatory reactions. Pathological tissue extended anteriorly to the nasal fossae and posteriorly to the choana, particularly on the right side.

Due to the patient's clinical and radiological picture, functional endoscopic sinus surgery (FESS) with diode laser was performed, in order to incise synechiae, remove scars and inflammatory material from all sinuses. Nasal splints were then inserted. One year later, the splints were removed; the upper airways were still free and there were mild signs of nasal obstruction. A wait-and-see policy was adopted for laryngeal lesions. Between 2003 and 2004, the patient underwent ocular surgery, and his right eye was treated using an osteo-odonto-keratoprosthesis (Fig. 1B).

Discussion

Cicatricial pemphigoid is a chronic, progressive, sub-epithelial blistering disease that may affect several mucous sites. According to the literature, this condition involves, in decreasing frequency, the oral cavity (90%), eye (65%), nose, nasopharynx, anogenitals, skin (20-30%), larynx (8-9%) and oesophagus¹². In a recent prospective study, Alexandre et al. investigated the nose and throat manifestations of MMP and reported several symptoms, such as epistaxis (26%), pharyngalgia (24%), dysphagia (40%), dysphonia (18%), dyspnoea (13%), nasal obstruction (37%) and nasal crusting (82%)¹³. Our patient showed nasal obstruction and crusting in addition to dysphonia.

Very limited data concerning ENT involvement by blistering are available, and the frequency of such lesions and correlated symptoms is not well known¹³. Indeed, it should not be forgotten that agreement between symptoms and lesions was only partial. Some symptomatic patients have no lesions at physical examination. At the same time, it cannot be excluded that asymptomatic patients might have lesions. In the literature, clinical lesions have been reported in 25% of cases involving the nose and in 5% and 17% involving the pharynx and larynx, respectively¹³.

Atrophic rhinitis is the most frequent nasal lesion (58%)¹³. In our patient, this condition was associated with crusting and synechiae, which have been reported to represent 26% and 11%, respectively, of nasal lesions¹³. These nasal manifestations lead to choanal or nasal valve stenosis, symptoms which give rise to great discomfort

Postbullous erosions of the pharynx and larynx, associated with erythema and/or oedema, have been reported to occur in 13% and 42% of previously reported cases, respectively¹³. The most frequent laryngeal lesion is erosion

of the epiglottal laryngeal surface (34% of the cases)¹³. These lesions are also seen on arytenoids, interarytenoids and aryepiglottic folds. Synechiae may be observed joining the epiglottis, aryepiglottic folds, arytenoids and false vocal cords resulting in severe obstruction of the laryngeal inlet. Laryngeal involvement is particularly dangerous since it exposes the patient to the permanent risk of acute dyspnoea and death. Our patient presented dysphonia related to two synechiae in the paracommissural and interarytenoidal space.

Severe laryngeal involvement, severe ocular lesions or more than 3 affected sites, other than nose and throat mucous membranes, can be potentially life-threatening¹³. In patients with nasal disease, regular irrigation with isotonic sodium chloride solution and an intra-nasal lubricant are important¹⁴. Atrophic rhinitis requires specific treatment based on local corticosteroid instillations. Vasoconstrictors are contraindicated due to the increased risk of mucous atrophy¹³.

Use of nasal surgery is highly controversial. In the literature, surgical procedures have been considered both unnecessary and detrimental on account of the high risk of relapse¹³. Surgical approaches require repeated divisions and insertion of nasal splints¹¹. Our patient underwent functional endoscopic sinus surgery to improve nasal obstruction removing synechiae, scarring and inflammatory material in addition to splint insertion. The splints were removed one year later and the upper airway was still free. Although surgery does not play a curative and long-term therapeutic role, in this case it improved the patient's quality of life and ensured good nasal respiration.

Laryngeal synechiae and stenosis can result from the typical evolution of the pathological condition or as a consequence of routine intubation. This latter event explains why surgery, to repair the upper aerodigestive tract, should be delayed until MMP is stabilized; anaesthesiologists should be forewarned regarding the fragility of the upper aerodigestive tract to guarantee scrupulous care when intubation is necessary.

The discovery of laryngeal involvement orientates the clinician towards an aggressive systemic therapeutic approach, combining immunosuppressive drugs and inhaled corticosteroids¹³. All previous reports focusing on the surgical treatment of laryngeal stenosis stress the reluctance of surgeons to excise the scarred tissue on account of the recurrent nature of MMP¹⁵. Tracheostomy may, however, be a life-saving procedure in order to stabilize the airway whilst the appropriate therapy is undertaken. Excision of scarring is not recommended in the acute period. Once the disease is stabilized, the laryngeal airway can be restored with a carbon dioxide laser¹¹. This surgical procedure can be repeated during management of the disease and also associated with adjuvant use of mitomycin-C, which appears to reduce the severity of stenosis and prolong the symptom-free interval¹⁶⁻¹⁸. On the basis of the above considerations, it was decided not to treat this patient with

conventional surgical techniques since he presented only dysphonia and not dyspnoea.

In conclusion, an endoscopic approach appears to be effi-

cient in the surgical treatment of nasal cicatricial pemphigoid and long-term stenting is required to avoid acute relapse.

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