Unusual external auditory canal relapse in pemphigus vulgaris

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INTRODUCTION

Pemphigus vulgaris (PV) is an autoimmune mucocutaneous blistering disease characterized by autoantibodies against desmogleins (DSGs), resulting clinically in the formation of blisters.[1] Histopathologic analysis shows suprabasal acantholysis with loss of adhesion between adjacent keratinocytes with a tombstone appearance. Bullous lesions can involve different sites on both skin and mucosa such as oropharyngeal, laryngeal, nasal, conjunctival, genital, anal, and esophageal mucosa. The frequency of ear, nose, and throat (ENT) involvement in PV is clearly highlighted in previous studies, but ear involvement has been only occasionally reported, characterized by pain and ear canal obstruction as reported first symptoms.[2]

We present an unusual case of a patient with mucocutaneous PV who, after a period of clinical and immunologic remission, presented with a relapse manifested only by auricular symptoms and signs that preceded the appearance of oral blisters.

Abbreviations used:

DSG:	desmogleins
ELISA:	enzyme-linked immunosorbent assay
ENT:	ear, nose, and throat
PV:	pemphigus vulgaris

CASE DESCRIPTION

In January 2014, a 47-year-old man was referred to the Oral Medicine Unit, Department of Neuroscience, Reproductive and Odontostomatological Sciences, Federico II University of Naples with blisters and erosions involving the skin of the face, neck, and chest and the oral and nasal mucosa with bilateral conjunctivitis. The patient complained of throat and nasal symptoms such as pain, stinging, nasal obstruction, and crusting. His general medical and dermatologic histories were negative. The patient underwent full ENT evaluation including otomicroscopy and endoscopic examination that confirmed oral and nasal mucosa involvement.

He also underwent laboratory tests, including enzyme-linked immunosorbent assay (ELISA) test to detect antibodies anti- DSG1 and anti-DSG3, instrumental examinations, and incisional oral and skin biopsies with direct immunofluorescence. He underwent examination with routine hematologic and infectious test and tumor markers. No alterations to these laboratory tests were detected. The initial anti-DSG3 antibody titers were greater than 100 RU/mL and anti-DSG1 antibodies were negative as detected by ELISA test. Histopathology found suprabasal acantholysis and intercellular deposits of IgG, confirming the suspected diagnosis of PV. In absence of comorbidities, the patient started conventional systemic therapy with corticosteroids deflazacort (120 mg/d) and azathioprine (100 mg/d) for 60 days without obtaining either clinical or immunologic remission. High-dose intravenous immunoglobulin (2 g/kg/cycle) was started and resulted in a clinical and immunologic remission. The remission lasted 2 years, until right ear canal obstruction and pain appeared without hearing loss. Direct examination of the auricle and auditory canal

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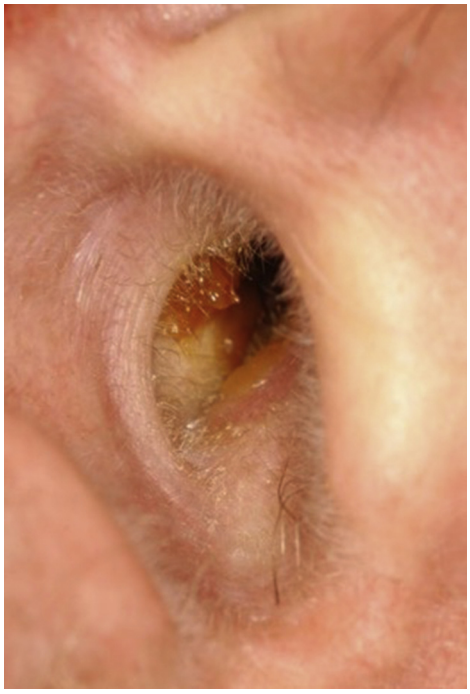

Fig 1. Erosions in right auditory canal.

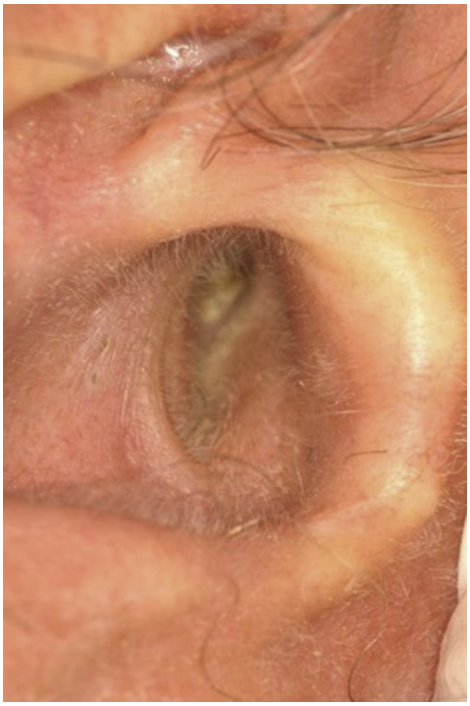

Fig 2. Complete resolution of auricular lesions after complete remission.

showed erosions in the auditory canal and serous otorrhea (Fig 1). Otoendoscopy with rigid 0° endoscope (Storz, diameter 2.7 mm, length 10 cm) confirmed the presence of ear involvement, that lasted 3 weeks, after which the disease spread to involve the face, neck, chest, and conjunctival and oral mucosa. Anti-DSG 3 antibodies titer were 35 RU/mL, and anti-DSG1 antibodies were negative by ELISA test. The mucocutaneous relapse was treated with anti−CD-20 monoclonal antibodies (rituximab) in association with intravenous immunoglobulin in line with the protocol described by Ahmed et al.[3] This treatment resulted in a complete clinical and immunologic remission (Fig 2). The patient is currently in 6-month follow-up remaining in clinical and immunologic remission off therapy.

DISCUSSION

There are few data on ENT bullous manifestations; in fact, at the early stage of illness ENT involvement may not be clearly diagnosed.[4] The frequency of ENT involvement has been described as pharynx (38%-85%), larynx (40%-85%), nasal cavity (11%-76%), and ear (8%-27%).[5] Auricular findings in PV patients with otoendoscopic examination were confirmed and well described in 10.5%,[6] 19%,[7] 26.5%,[2] and 26.8%[8] of patients. The frequency of auricular involvement appears to be greater in the mucocutaneous phenotype than in the mucosal phenotype.[6] The published symptoms associated with ear blistering lesions are earache, blockage of the external auditory canal, and hearing loss, with a frequency rate of 25%,[6] 26.5%,[2] and 26.8%.[8]

Although nasal and pharyngeal lesions are in most cases symptomatic, the ear involvement is often asymptomatic; therefore, in the absence of an otoscopic examination, ear blisters may not be detected, and the diagnosis of auricular PV may be delayed or missed.[6] Few cases of ear blisters have been reported in the literature, but there is no indication of the exact anatomic area affected by bullous lesions; Fawzy et al[2] describes only external lesions; the only patient who described ear blocking on otoscopic examination showed an accumulation of earwax; therefore, the symptom was not related to the main pathology. Fernández et al[9] reported that the pinna (7.5%) and the most external part of the external auditory canal (7.5%) are the most affected sites.

Mahfoudhi and Khamassi[10] described a case of auricular PV with erythematous and crusted lesions of the pretragic region and of the auricle with small lesions of the external auditory canal. Therefore, in the reported cases, the PV-related auricular lesions affected the peri-auricular skin, instead in our case the PV relapse occurred with blistering and erosive

lesions in the innermost part of the external auditory canal. This report is of a rare case of PV in which the onset of the relapse is characterized by a singular bullous lesion of the auricular canal without involvement of other mucosal or cutaneous sites.

The ear, like the oral mucosa, can represent the first manifestation of the disease or relapse; therefore, the ENT specialist must make a careful assessment of the area in question to make an early diagnosis. An endoscopic otorhinolaryngologic examination must be performed at the first manifestation of bullous disease, regardless of the district involved and the phenotype and subsequently in case of relapse of the disease and in the course of follow up.

CONCLUSION

The presence of bullous lesions can involve anatomic areas that are not always examined in routine clinical inspection such as the ENT district and, specifically, the ear. Therefore, the role of the ENT specialist is fundamental in the early diagnosis of PV and in the evaluation of the real disease extension.

Then, for a correct clinical evaluation at the onset and during the course of PV, it is necessary to explore ENT mucosa and skin with endoscopy, not only when the patient reports symptoms but routinely in all PV patients.

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