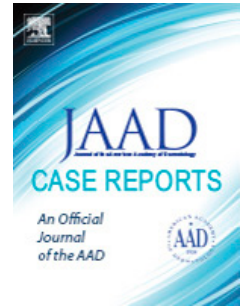


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UNUSUAL EXTERNAL AUDITORY CANAL RELAPSE IN PEMPHIGUS VULGARIS:
A CASE REPORT

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PII: S2352-5126(20)30288-5

DOI: <https://doi.org/10.1016/j.jdc.2020.04.014>

Reference: JDCR 1359

To appear in: *JAAD Case Reports*

Received Date: 5 March 2020

Revised Date: 10 April 2020

Accepted Date: 13 April 2020

Please cite this article as: Coppola N, Cantone E, Valletta A, Mignogna MD, Leuci S, UNUSUAL EXTERNAL AUDITORY CANAL RELAPSE IN PEMPHIGUS VULGARIS: A CASE REPORT, *JAAD Case Reports* (2020), doi: <https://doi.org/10.1016/j.jdc.2020.04.014>.

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1 **Case Report**

2 **UNUSUAL EXTERNAL AUDITORY CANAL RELAPSE IN PEMPHIGUS**
3 **VULGARIS: A CASE REPORT**

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12 **Short running title:** Pemphigus Vulgaris and relapse

13 **Abstract words count:** 140

14 **Manuscript words count:** 1000

15 **Figure count:** 2

16 **References:** 10

17 **Declarations of interest:** The authors have no conflict of interest to declare

18 **Funding Source:** This article has no funding source

19 **Key words:** Pemphigus Vulgaris; autoimmune bullous disease; ear, nose and throat;
20 dermatology; otoscopy.

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27 INTRODUCTION

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

37 We present a peculiar case of a patient suffering from muco-cutaneous PV who, following a
38 period of clinical and immunological remission, presented a relapse manifested only by
39 auricular symptoms and signs that preceded the appearance of oral blisters.

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50 **CASE DESCRIPTION**

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

58 He also underwent laboratory tests, including ELISA test to detect antibodies anti-DSG1 and
59 anti-DSG3, instrumental examinations and incisional oral and skin biopsies with direct
60 immunofluorescence (DIF). He was examined by means of routine hematological and
61 infectious test and tumor markers. No alterations to these laboratory tests were detected. The
62 initial anti-DSG 3 antibodies titer were >100 RU/ml and anti-DSG1 antibodies were negative
63 as detected by ELISA test. Histopathology showed suprabasal acantholysis and intercellular
64 deposits of immunoglobulin G (IgG), confirming the suspected diagnosis of PV. In absence
65 of comorbidities, patient started conventional systemic therapy with corticosteroids
66 (Deflazacort 120 mg/die) and Azathioprine (100mg/die) for 60 days without obtaining both
67 clinical and immunological remission. The second step was the use of high-dose intravenous
68 immunoglobulin (IVIg) (2gr/kg/cycle) with a clinical e immunological remission. The
69 remission lasted 2 years, until right ear canal obstruction and pain appeared without hearing
70 loss. Direct examination of the auricle and auditory canal of the ear showed erosions in
71 auditory canal and serous otorrhea (Fig.1). Otoendoscopy with rigid 0° endoscope (Storz,
72 diameter 2.7 mm, length 10 cm) confirmed the presence of ear involvement, that lasted 3

73 weeks after which the disease widespread involving face, neck, chest, conjunctival and oral
74 mucosa. Anti-DSG 3 antibodies titer were 35 RU/ml and anti-DSG1 antibodies were negative
75 detected by ELISA test. The muco-cutaneous relapse was treated with anti-CD-20
76 monoclonal antibodies (Rituximab) in association with IVIg in line with the protocol
77 described by Ahmed et al [3] with a complete clinical and immunological remission (Fig 2).
78 The patient is currently in six-monthly follow-up remaining in clinical and immunological
79 remission off-therapy.

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96 **DISCUSSION**

97 There are few data on ENT bullous manifestations, in fact at the early stage of illness ENT
98 involvement may not be clearly diagnosed [4]. The frequency of ENT involvement has been
99 described as: pharynx (38-85%), larynx (40-85%), nasal cavity (11-76%), ear (8-27%) [5].
100 Auricular findings in PV patients with otoendoscopic examination were confirmed and well-
101 described in 10.5% [6], 19% [7], 26.5% [2] and 26.8% [8] of patients. The frequency of
102 auricular involvement appears to be greater in the muco-cutaneous phenotype than in the
103 mucosal phenotype [6]. The published symptoms associated with ear blistering lesions are
104 earache, blockage of the external auditory canal and hearing loss, with a frequency rate of
105 25% [6], 26.5% [2] and 26.8% [8].

106 While nasal and pharyngeal lesions are in most cases symptomatic, the ear involvement is
107 often asymptomatic and, therefore, in the absence of an otoscopic examination, ear blisters
108 may not be detected and the diagnosis of auricular PV may be delayed or missed [6]. Few
109 cases of ear blisters have been reported in the literature, but there is no indication of the exact
110 anatomical area affected by bullous lesions; Fawzy [2] describes only external lesions and the
111 only patient who described ear blocking on otoscopic examination showed an accumulation
112 of ear wax, therefore the symptom was not related to the main pathology. Fernández et al.
113 reported that the pinna (7,5%) and the most external part of the external auditory canal
114 (7,5%) are the most affected sites [9].

115 Mahfoudhi et Khamassi described a case of auricular PV with erythematous and crusted
116 lesions of the pretragic region and of the auricle with small lesions of the external auditory
117 canal [10]. Therefore, in the reported cases the auricular lesions PV-related affect the peri-

118 auricular skin, instead in our case the PV relapse occurred with blistering and erosive lesions
119 in the innermost part of the external auditory canal. This case is a rare report of PV patient,
120 where the onset of the relapse is characterized by singular bullous lesion of the auricular
121 canal without involvement of other mucosal and/or cutaneous sites.

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

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141 **CONCLUSION**

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

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

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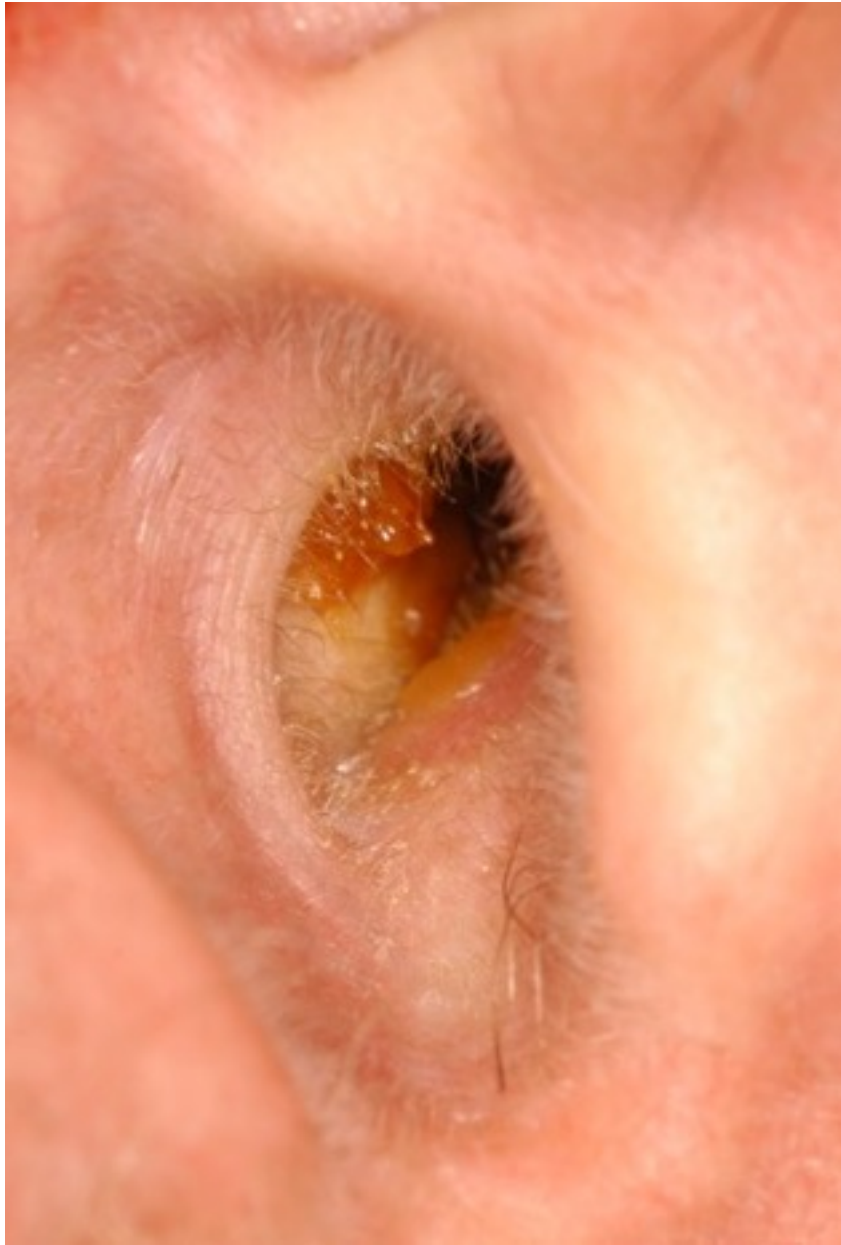
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207 Legend of figures

208 **Fig 1:** Shows erosions in right auditory canal.

209 **Fig 2:** Shows complete resolution of auricular lesions following complete remission.

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