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The role of upper endoscopy in identifying oesophageal involvement in patients with oral pemphigus vulgaris

G. Galloro[a,*], M. Mignogna[b], C. de Werra[a], L. Magno[a], G. Diamantis[a], E. Ruoppo[b], P. Iovino[a]

[a] *Department of General, Geriatric, Oncological Surgery and Advanced Technologies, Special Section of Surgical Digestive Endoscopy, School of Medicine, University 'Federico II' of Naples, Via S. Pansini, 5, 80132 Naples, Italy*
[b] *Department of Oral Medicine, School of Medicine, University 'Federico II' of Naples, Naples, Italy*

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Abstract

Background and aims. The involvement of oesophagus in pemphigus vulgaris is still debated. The aims of this study were to evaluate the prevalence of oesophageal involvement and the gastro-duodenal mucosa appearance before and after high-dose corticosteroid therapy in a group of patients with oral pemphigus vulgaris.

Methods. We prospectively studied 28 consecutive patients with oral pemphigus by oesophageal symptom standardised questionnaire, upper gastro-intestinal endoscopy, exfoliative cytology and histological biopsy. After clinical remission, all patients underwent new endoscopy.

Results. The prevalence of oesophageal symptoms was 57.1%. Endoscopic examination revealed oesophageal involvement with different degrees of severity in 67.8% of patients. After corticosteroid therapy, endoscopy showed normal oesophageal–gastro-duodenal mucosa. No examination-related exacerbations of the oesophageal lesions were seen.

Conclusions. The upper gastro-intestinal endoscopic examination, in oral pemphigus vulgaris patients with oesophageal symptoms, is safe in skilled hands technique and a useful diagnostic tool prior to starting therapy.

Keywords: Dysphagia; Endoscopy; Haematemesis; Oesophagus; Oral pemphigus; Pemphigus vulgaris

1. Introduction

Pemphigus vulgaris (PV) is a rare autoimmune blistering disease involving skin and mucous membranes without sex differences, but with a potentially fatal outcome [1,2]. The skin and the oral mucosa are the most frequently involved sites: oral lesions precede skin lesions in 70% of cases, and when skin is already involved, there is an oral comorbidity in 90% of cases [3]. Nevertheless, any stratified squamous epithelium can be involved.

In PV, acantholysis occurs low in the stratum spinosum with a superbasal cleft [4]. A study reported that, as in the epidermis, the cell adhesion molecule desmoglein 3 (the target antigen of pathogenetic PV antibodies) is strongly expressed in oesophageal epithelia [5,6].

The prevalence of oesophageal involvement is still debated. Some authors suggest that it is rare [7–13]; others reported higher prevalence [3,14]. Because patients with oesophageal involvement may be asymptomatic and endoscopy may not be routinely performed, such involvement may be under-recognised.

The aims of this study were to evaluate in 28 consecutive patients with oral PV:

(1) the prevalence of oesophageal involvement, and
(2) the gastro-duodenal mucosa appearance before and after high-dose corticosteroid therapy.

* Corresponding author. Tel.: +39 081 746 2716; fax: +39 081 746 2815.
E-mail address: galloro.g@tin.it (G. Galloro).

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Table 1
Descriptive statistics of about 28 patients affected with oral PV

Gender	11 M	17 F
Age	49.4 ± 17.1	Range 22–78
	%	No. of patients
Oral involvement	100	28/28
Oral DIF positivity	100	28/28
Oral IIF positivity	92.8	26/28
Negative	7.1	2/28
Weakly positive	0	0
Positive	64.2	18/28
Highly positive	28.5	8/28
Skin involvement	53.5	15/28
Conjunctival involvement	14.2	4/28
Nasal involvement	42.8	12/28
Glans involvement	21.4	6/28
Vulva involvement	35.7	10/28
Oesophageal symptoms	57.1	18/28
Dysphagia	57.1	18/28
Odynophagia	21.4	6/28
Heartburn	0	0
Regurgitation	0	0
Chest pain	0	0
Haematemesis	3.5	1/28
Oesophageal appearance		
Normal	32.1	9/28
Localised erythema	21.4	6/28
Red longitudinal lines	35.7	10/28
Erosions	17.8	5/28
Blisters	28.5	8/28
Ulcers	3.5	1/28

M, male; F, female; DIF, direct immunofluorescence; IIF, indirect immunofluorescence.

2. Population

From November 1991 to December 2002, we prospectively studied 28 consecutive patients, referred from Department of Oral Medicine of Federico II University, with oral PV newly diagnosed on the basis of histology, indirect (IIF) and direct (DIF) immunofluorescence [8]. Details on IIF and DIF technique have been presented in the original article [3]. IIF was scored on the basis of titre (1:20–1:40, weakly positive; 1:80–1:160, positive; 1:160–1:640, highly positive). DIF was positive in all patients. Descriptive statistics of our PV patients is showed in Table 1.

3. Methods

Oesophageal symptoms were scored by a standardised questionnaire, dealing with the presence or absence of dysphagia, odynophagia, heartburn, regurgitation and chest pain. Any other symptom was specified in an open box in the questionnaire [15]. In each patient, we scored the presence of one or more symptoms as cumulative score (0–5).

All patients underwent upper gastro-intestinal endoscopy (UGE) (standard pre-medication by diazepam 10 mg and hyscine bromure 20 mg i.v.) with histological biopsies and cytology. Six histo-biopsy specimens, two from each site (upper, medium and distal oesophagus), were taken by oval, needle biopsy forceps (RL Linx, Boston Scientific Microvasive Miami, FL, USA). When intact blisters were present, we performed biopsies at junction between floor and roof of the blister and adjacent, not blistering mucosa.

All specimens were processed with May Grunwald–Giemsa and haematoxylin–eosin for histopathological examination.

The cytological preparations were obtained either from affected oesophageal mucosa, after rupture of intact blister (smearing the internal roof of the blister), or by mucosal brushing from non-blistering affected areas, immediately smeared on slides, fixed in 95% alcohol. The slides were stained with Papanicolaou technique.

Gastro-duodenal mucosa appearance by UGE was scored as 0, normal; 1, erosions; and 2, peptic ulcers. Biopsy for detection of *Helicobacter pylori* was routinely performed. When the gastro-duodenal mucosa appearance was more than 0, and *H. pylori* was present, we instituted therapy [9], and after a month we re-tested the patient. When the gastro-duodenal mucosa appearance was more than 0 and *H. pylori* was absent, patients were given antisecretory therapy and then a new UGE [16,17].

All patients with a normal gastro-duodenal mucosa appearance (either at first UGE or after any treatment described above) underwent the specific treatment of the PV with the goal of achieving complete control of the signs and symptoms with minimal side effects. The protocol for the initial/induction phase of treatment consisted of systemic deflazacort (120 mg daily in a single morning dose) and topical (oral) corticosteroids. The initial dose of deflazacort was maintained from 2 to 4 weeks, especially in patients with initial severe oral disease [18]. In addition, in the case of PV unresponsive to the conventional high dose of steroids, patients received adjunctive systemic medication, which included azathioprine (50–100 mg daily) or cyclophosphamide (50 mg daily). The end point of the initial high dose treatment was reached when the patient was asymptomatic and clinical signs were under control, as previously described [19]. During steroid therapy, all patients were co-treated with proton pump inhibitors (PPI).

At clinical remission, a new UGE was performed to evaluate the oesophageal and the gastro-duodenal mucosal appearance.

3.1. Statistical analysis

All data are presented as mean ± S.D., unless otherwise indicated. Spearman correlation was used when indicated. Significance was expressed at $p < 0.05$ level. All the data were analysed with SPSS software package for Windows (release 11.5.1; SPSS Inc., Chicago, IL, USA).