Journal of Oral Science, Vol. 48, No. 1, 43-46, 2006

Case report

Characterization of oral pemphigus vulgaris in Thai patients

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(Received 17 August 2005 and accepted 20 January 2006)

Abstract: Pemphigus vulgaris (PV) is a serious mucocutaneous disease that be fatal if left untreated. The oral mucosa is often the first site to be affected by the disease. It is thus important that the dentist is able to recognize oral manifestations of PV and refer appropriately. Although oral PV is a well-characterized condition, the disease characteristics of patients in Thailand have not been previously reported. Here, we describe patient and lesion characteristics of 18 cases of oral PV. For these 18 cases, the mean age was 38 years, and the male:female ratio was 1:2. The most commonly affected sites were the gingiva and buccal mucosa, and the duration of disease was approximately one year. Medications previously used included corticosteroids and interferon, and nine patients reported systemic disease. Histopathologic examination with/without direct immunofluorescence was the method of diagnosis in all cases. (J. Oral Sci. 48, 43-46, 2006)

Keywords: oral mucosa; pemphigus vulgaris; retrospective study; Thai.

Introduction

Pemphigus is one of the classic autoantibody-mediated diseases that can manifest as lesions on the skin and mucous membranes including the oral mucosa. Pemphigus can be classified into 4 types: pemphigus vulgaris (PV), pemphigus vegetans, pemphigus erythematosus, and pemphigus foliaceus (1). In addition, new entities of pemphigus have been described, paraneoplastic pemphigus and IgA-pemphigus (2,3). Only pemphigus vulgaris and the more rare form, pemphigus vegetans, can affect the oral mucosa. Although vulgaris means "common" in Latin, the worldwide incidence of PV has been reported to be 0.1 to 0.5 cases per 100,000 persons per year (4). Importantly, PV, if untreated, is often fatal. Clinically, PV appears to occur in males and females in an equal ratio (1,5) and is mostly frequently reported in patients between the fourth to sixth decades of life, and rarely in juveniles (6). Oral mucosa is often the first affected site, yet the most difficult to treat effectively. The dentist thus plays a critical role in diagnosing and managing oral lesions in patients with PV.

PV is believed to occur idiopathically, as a result of the presence of autoantibodies directed against components of the epithelial desmosomes, desmogleins 3 and 1 (7). As a result, the epithelial cells lose their intercellular adhesion, leading to formation of intraepithelial vesicles or blebs. A recent study demonstrated that PV IgG could activate the intracellular signaling cascades and induced acantholysis *in vivo* (8). Moreover, PV IgG could induce apoptosis of the epithelial cells through the Fas-mediated death signaling pathway (9). These data suggest that apoptosis could be the cause of the acantholytic phenomenon. Although the source of the autoantibodies is unknown, a number of medications, for example penicillamine, captopril, and penicillin, are able to induce pemphigus-like conditions in patients (4,10). Furthermore, a pemphigus-like condition, known as paraneoplastic

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pemphigus, can occur in some patients with underlying malignancies especially lymphoreticular cancers (1,11).

The aim of the present study was to characterize cases of oral PV from the multicentric dental institutes of Thailand in terms of patient demographics, medical history, medication used, systemic disease involvement, and method of PV diagnosis.

Materials and Methods

A retrospective study of 18 patients with oral PV was performed during 1991-2004. The majority of patients were from Chulalongkorn University, Chiang Mai University, Khon Kaen University and Lumphun Provincial Hospital, Thailand. Medical history and demographic data (including age, gender, affected site, duration of the disease, systemic disease involvement, medication used, and method of diagnosis) were collected from each patient, and analyzed using descriptive statistics.

Results

Clinical results are shown in Table 1. The mean age was 37.7 ± 10.6 years, and the male:female ratio was 1:2. The gingiva was the most commonly affected site followed by the buccal mucosa, palatal mucosa, retromolar mucosa, tongue, lips, and floor of the mouth. The duration of disease was approximately one year, and previous medications included corticosteroids (7 cases) and interferon (1 case). Associated systemic diseases were hepatitis B, ovarian cysts and tumors, esophagitis, ovaritis, tubal pregnancy, breast cyst, and lupus erythematosus. For all cases, PV was diagnosed by biopsy and hematoxylin and eosin staining. The clinical features of PV from cases 5 and 17 are shown in Figures 1 and 2, respectively. The histopathologic appearance of the lesion from case 17 is depicted in Figures 3 and 4.

Discussion

In the present study, oral PV most frequently occurred in patients in the fourth decade. These results are consistent with previous reports that the peak incidence of PV occurs between the fourth and sixth decades of life (1). In the present study, females were affected more frequently, with a male-to-female ratio of 1:2. Previously, an equal male to female distribution has been reported (1). Other studies have reported a male-to-female ratio of 3:9 and 1:2 (5,12). The discordance in findings may be due to the different geographic and ethnic natures of patients studied.

The most commonly affected sites in the present study

Table 1 Characteristics of PV cases

Case	Sex	Age	Site								Duration	Medication	Systemic Disease	Methods of Diagnosis	
			G	B	L	Fl	R	P	T	Ex	(months)			Biopsy	DIF-IgG
1	M	43	✓	✓	✓	✓					12	_	_	✓	✓
2	F	27	✓	✓				✓			6	_	_	✓	✓
3	F	37	✓	✓		✓		✓	✓		7	_	Hepatitis B, Ovaritis	✓	✓
4	F	39	✓								2	_	Ovarian tumor (myoma)	✓	✓
5	F	45	✓								2	_	Pharyngitis, Breast cyst	✓	✓
6	F	43	✓	✓			✓			✓	5	_	Esophagitis	✓	
7	M	46	✓					✓			8	Interferon, Lopid	Hepatitis B	✓	✓
8	F	30	✓				✓	✓		✓	12	_	Tubal pregnancy	✓	
9	F	37	✓	✓					✓		98	_	_	✓	
10	F	55	✓	✓	✓		✓		✓		2	Corticosteroid	Ovarian cyst	✓	
11	F	33		✓							_	_	_	✓	
12	F	21	✓	✓							_	Corticosteroid	_	✓	
13	F	54	✓								_	Corticosteroid	_	✓	
14	M	18	✓	✓							_	_	_	✓	
15	M	33	✓	✓	✓	✓	✓				7	Corticosteroid	Esophagitis	✓	
16	F	36	✓						✓	✓	3	Corticosteroid	Lupus erythematosus	✓	✓
17	M	30	✓	✓			✓	✓		✓	2	Corticosteroid	_	✓	
18	M	52	✓					✓			1	Corticosteroid	_	✓	

Sex : M - Male F - Female

Site : G - Gingiva B - Buccal mucosa L - Lips Fl - Floor of mouth R - Retromolar mucosa P - Palatal mucosa T - Tongue Ex - Extraoral

were the gingiva and buccal mucosa. These findings are in line with those of Robison *et al* (5). The majority of the patients in the present study had previously been treated with corticosteroids. One patient, however, had been treated with interferon and this is of special interest here because there are small number of reports in the literature concerning pemphigus induced by interferon given for the treatment for hepatitis C (13,14). In the present case, interferon was used as a treatment for hepatitis B. Collectively, our data support previous reports that the use of interferon may induce development of pemphigus in patients.

Interestingly, we also encountered a case of oral PV with lupus erythematosus (LE). Previous studies have shown that few cases of PV are associated with LE (7,15), raising the question as to whether there is a true association or whether this is a coincidental finding.

In conclusion, PV is a serious disease that can be fatal if untreated. The skin and mucosa are the major organs involved, and the oral mucosa is often affected first. Therefore, dentists can play a significant role in early diagnosis and managing the oral manifestations of PV. Furthermore, the medical history of patients needs to be carefully evaluated, since several medications including interferon and certain systemic diseases can induce or be associated with PV.

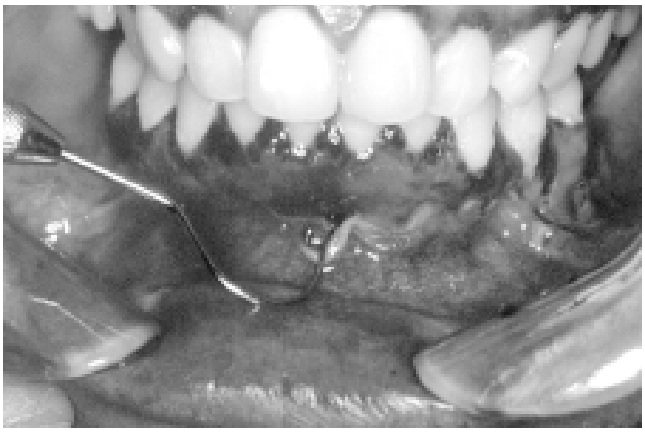

Fig. 1 Clinical presentation of oral PV in case 5, showing generalized desquamative gingiva with ragged shallow erosion.

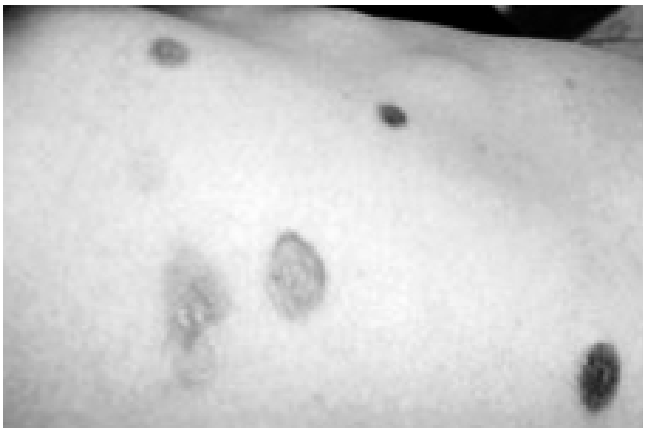

Fig. 2 The skin lesions from case 17 demonstrating multiple flaccid bullae.

Fig. 3 Histopathologic section of case 17 showing a characteristic intraepithelial separation at the suprabasal cell layer (open arrow). (H-E staining, × 100)

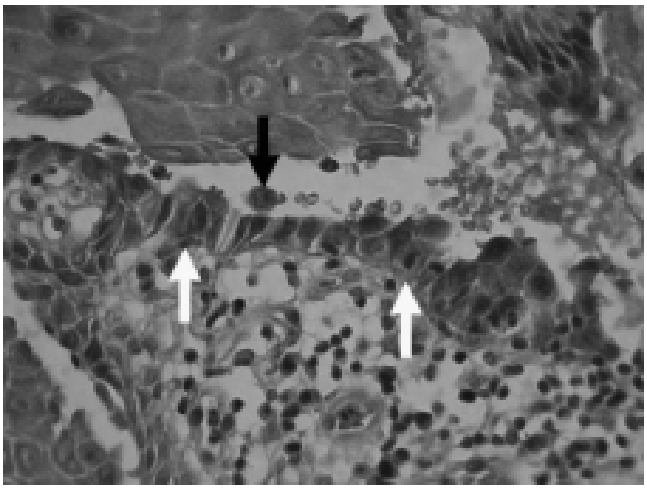

Fig. 4 High power photomicrograph from case 17 revealing the basal cells (open arrows) separating from the whole upper epithelial layer with the appearance of a so-called "row of tombstones." A rounded, acantholytic epithelial cell sitting within the intraepithelial cleft is evident (arrow). (H-E staining, × 400)

Acknowledgments

The authors would like to express their gratitude to the Oral Diseases Group of Thailand (ODGT) and the Research Unit for Oral Diseases, Chulalongkorn University, Thailand for their support.

References

1. Neville BW, Damm DD, Allen CM, Bouquot JE (1995) Oral and Maxillofacial Pathology. WB Saunders, Philadelphia, 559-562
2. Sklavounou A, Laskaris G (1998) Paraneoplastic pemphigus: a review. Oral Oncol 34, 437-440
3. Nishikawa T, Hashimoto T, Shimizu H, Ebihara T, Amagai M (1996) Pemphigus: from immunofluorescence to molecular biology. J Dermatol Sci 12, 1-9
4. Becker BA, Gaspari AA (1993) Pemphigus vulgaris and vegetans. Dermatol Clin 11, 429-452
5. Robinson JC, Lozada-Nur F, Frieden I (1997) Oral pemphigus vulgaris: a review of the literature and a report on the management of 12 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 84, 349-355
6. Rabinowitz LG, Esterly NB (1993) Inflammatory bullous diseases in children. Dermatol Clin 11, 565-581
7. Scully C, Challacombe SJ(2002) Pemphigus vulgaris: update on etiopathogenesis, oral manifestations, and management. Crit Rev Oral Biol Med 13, 397-408
8. Sanchez-Carpintero I, Espana A, Pelacho B, Lopez Moratalla N, Rubenstein DS, Diaz LA, Lopez-Zabalza MJ (2004) *In vivo* blockade of pemphigus vulgaris acantholysis by inhibition of intracellular signal transduction cascades. Br J Dermatol 151, 565-570
9. Wang X, Bregegere F, Frusic-Zlotkin M, Feinmesser M, Michel B, Milner Y (2004) Possible apoptotic mechanism in epidermal cell acantholysis induced by pemphigus vulgaris autoimmunoglobulins. Apoptosis 9, 131-143
10. Mutasim DF, Pelc NJ, Anhalt GJ (1993) Drug-induced pemphigus Dermatol Clin 11, 463-471
11. Mutasim DF, Pelc NJ, Anhalt GJ(1993) Paraneoplastic pemphigus. Dermatol Clin 11, b473-481
12. Lamey PJ, Rees TD, Binnie WH, Wright JM, Rankin KV, Simpson NB (1992) Oral presentation of pemphigus vulgaris and its response to systemic steroid therapy. Oral Surg Oral Med Oral Pathol 74, 54-57
13. Niizeki H, Inamoto N, Nakamura K, Tsuchimoto K, Hashimoto T, Nishikawa T (1994) A case of pemphigus foliaceus after interferon alpha-2a therapy. Dermatology 189 (Suppl 1), 129-130
14. Marinho RT, Johnson NW, Fatela NM, Serejo FS, Gloria H, Raimundo MO, Velosa JF, Ramalho FJ, Moura MC (2001) Oropharyngeal pemphigus in a patient with chronic hepatitis C during interferon alpha-2a therapy. Eur J Gastroenterol Hepatol 13, 869-872
15. Calebotta A, Cirocco A, Giansante E, Reyes O (2004) Systemic lupus erythematosus and pemphigus vulgaris: association or coincidence. Lupus 13, 951-953