

Clinical and Demographic Characteristics of Pemphigus Vulgaris Patients

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ABSTRACT Pemphigus is an autoimmune disease characterized by intraepithelial bullae and erosions in the skin and mucosa. We aimed to evaluate the clinical and demographic characteristics of pemphigus vulgaris (PV) patients who presented to our Department. Patients who presented to our Department between May 2013 and May 2014, were examined dermatologically and diagnosed with PV based on clinical, histological and direct immunofluorescent findings. Name, family name, and gender of the patients, their complaint at presentation, onset time and location of the lesions, the number of lesions, systemic treatments received by patients and patients' medication histories were recorded. Forty-nine PV patients were included in our study. Among these, 22 (44.9%) were female and 27 (55.1%) male. The mean age of the patients was 53.28±14.70 (range 23 to 79) years. The mean duration of the disease was 44.45±45.68 (range 1 to 180) months. The most common complaints at presentation were lesion in the mouth (47/49) and lesion/blister in the skin (39/49). The onset locations of the lesions were the oropharynx (63.3%), the skin and oropharynx combined (16.3%), the skin (18.4%) and the anus (2%). The chronological order for the sites of involvement were as follows: first the oropharynx then the skin (42.9%), first the skin then the oropharynx (18.4%), and the oropharynx and the skin combined (16.3%). Ten patients (20.4%) had mucosal involvement and one (2%) had skin involvement alone, whereas both mucosal and skin involvements were observed in 38 patients (77.6%). Forty-seven patients (95.9%) had not used any medications that could have led to pemphigus. One patient had a history of beta-blocker use and another had a history of ACE inhibitor prior to the emergence of the pemphigus lesions. The clinical and demographic results of the PV patients in our region were consistent with those from other studies.

KEY WORDS: autoimmunity, bullous diseases, pemphigus vulgaris

INTRODUCTION

Pemphigus is an autoimmune disease characterized by intraepithelial bullae and erosions in the skin and mucous membranes (1). The main characteris-

tic of pemphigus is the occurrence of acantholysis, the loss of intercellular connections between the epidermal keratinocytes which caused by autoanti-

bodies in the pemphigus serum (2,3). The IgG type of autoantibodies against desmoglein 1 and/or 3, a cell surface antigen of keratinocytes, are directly detected in immunopathological studies (1-3). According to its clinical and immunopathological characteristics, the pemphigus family can be categorized into four groups: pemphigus vulgaris (PV), pemphigus foliaceus (PF), IgA pemphigus, and paraneoplastic pemphigus (paraneoplastic autoimmune multiorgan syndrome, PAMS) (4). The most common clinical type of the disease is PV, characterized by loose and easily rupturable bullae on normal skin and mucous membranes or on an erythematous base (1). Pemphigus is a widespread disease around the world and is mostly encountered in patients between 40 and 60 years of age (5). It is equally prevalent among females and males. The incidence of the disease is between 0.7 and 5 new cases per million per year (6). The main goal in the treatment of pemphigus is to achieve the remission of the disease in the shortest time and reduce the synthesis of autoantibodies. Early systematic treatment is necessary to control the disease and maintain a long term remission (7,8).

In our study, we aimed to evaluate the clinical and demographic characteristics of the PV patients who presented to our Department.

PATIENTS AND METHODS

Forty-nine patients were enrolled in the study who presented to the Department of Dermatology and/or Bullous Diseases Clinic at the Faculty of Medicine at Karadeniz Technical University between May 2013 and May 2014. They were examined dermatologically and diagnosed with PV based on clinical, histological and direct immunofluorescent findings.

Only the patients whose PV diagnoses were confirmed by histopathologic and immunofluorescent examinations were included in the study. The biopsy material for immunofluorescence was obtained from the perilesional skin. Diagnostic criteria included suprabasal disintegration and inflammatory infiltration in the dermis accompanied by eosinophils in the histopathological examination and intercellular accumulation of IgG in direct immunofluorescence. Name, family name, and gender of the patients, their complaint at presentation, onset time and location of the lesions, the number of lesions, systemic treatments received and patients' medication histories were recorded.

Enzyme-linked immunosorbent assay (ELISA) was used for the detection of anti-Dsg1 and anti-Dsg3 antibodies (Dermatology Mosaic 7 kit, EUROIMMUN, Lübeck, Germany). The ELISA was performed at the time of the inclusion in the study.

Statistical analyses were performed using the SPSS 13.0 software package (IBM, Armonk, NY, USA). Descriptive statistics were summarized as number, percentage, mean and standard deviation.

Results

Of the 49 PV patients included in the study, 22 (44.9%) were female and 27 (55.1%) male. The female:male ratio was 1:1.2. The mean age of the patients was 53.28 ± 14.70 (range 23 to 79) years. The complaints at presentation were lesions in the mouth (47/49), dysphagia/pain (17/49), nosebleed (9/49), hoarseness (12/49), lesion/blister in the skin (39/49) and red eye (7/49) (Table 1).

The mean duration of the disease was 44.45 ± 45.68 (range 1 to 180) months. The onset locations of the lesions were the oropharynx (63.3%), the skin and oropharynx combined (16.3%), the skin (18.4%) and the anus (2%). The chronological order for the sites of involvement were as follows; first the oropharynx then the skin (42.9%), first the skin then the oropharynx (18.4%), and the oropharynx and the skin combined (16.3%), first the oropharynx then other mucous membranes (conjunctiva, anogenital, nasal) (2%), the oropharynx plus other mucous membranes combined (8.2%), still confined to the oropharyngeal region (10.2%) and still confined to the skin (2%) (Table 1).

There were no skin or mucosal lesions at the time of admission in 19 out of 49 patients (38.8%). There were less than 3 lesions in 7 patients (14.3%), 3-5 lesions in 5 patients (10.2%), 6-10 lesions in 6 patients (12.2%) and more than 10 lesions in 13 patients (26.5%)

Ten PV patients (20.4%) had mucosal and one (2%) had skin involvement alone while both mucosal and skin involvements were observed in 38 patients (77.6%). Eleven patients (22.4%) had a consanguineous marriage (mother-father) (Table 1).

The standard initial dose of prednisolone was generally 0.5-1 mg/kg/day in our study. If the disease was not controlled after 15 days of treatment on evaluation, the steroid dose was increased by 25-30%. The assessment of treatment effectiveness was based on the improvement in clinical condition. Epithelialization of more than 80% of existing erosions and ulcers, the cessation of new lesion formation within the last 15 days and the negativity of Nikolsky's sign, if Nikolsky's sign is initially positive, were indications that the disease was under control. Once the disease was under control, steroids were gradually reduced by 25% every two weeks. If the disease could not be controlled, we returned to the initial dose of treatment and added adjuvant immunosuppressive therapy if

Table 1. Clinical and demographic characteristics of PV patients

Age (mean±standard deviation)		53.28 ± 14.70
Gender (n, %)	Female	22 (44.9)
	Male	27 (55.1)
Complaint at presentation (n, %)	Lesion in the mouth	47 (95.9)
	Dysphagia, pain	17 (34.7)
	Nosebleed	9 (18.4)
	Hoarseness	12 (24.5)
	Lesion/blister on the skin	39 (79.6)
	Red eye	7 (14.3)
Onset location (n, %)	Oropharynx	31 (63.3)
	Skin + Oropharynx	8 (16.3)
	Skin	9 (18.4)
	Anal region	1 (2)
Chronological order (n, %)	First the oropharynx then the skin	21 (42.9)
	First the skin then the oropharynx	9 (18.4)
	Oropharynx + skin combined	8 (16.3)
	First the oropharynx then other mucous membranes (conjunctiva, anogenital, nasal)	1 (2)
	Oropharynx + other mucous membranes combined	4 (8.2)
	Still confined to the oropharyngeal region	5 (10.2)
	Still confined to the skin	1 (2)
Clinical type (n, %)	Mucocutaneous	38 (77.6)
	Mucosal	10 (20.4)
	Skin	1 (2)
Duration of the disease (months)		44.45±45.68
Consanguineous marriage (n, %)		11 (22.4)

corticosteroids had been initially given alone. Ten of the patients (20.4%) did not receive any treatment and 39 (79.6%) were under treatment (corticosteroid and/or azathioprine).

Twenty patients (40.8%) in our series were treated with methylprednisolone and azathioprine combined, 16 (32.7%) with methylprednisolone alone and three (6.1%) with mycophenolate mofetil. Ten of the patients (20.4%) did not receive any treatment and 39 (79.6%) were under treatment (corticosteroid and/or azathioprine).

Diagnosis of PV in 47 patients (95.9%) were made by histopathology and this diagnosis was confirmed by direct immunofluorescence in 21 (42.9%) of them.

Dsg1 was investigated in 15 (30.6%) of the 49 patients. The Dsg1 titers varied between <1/10 and >1/1000. The Dsg1 titer was <1/10 in seven patients (46.7%), >1/10 in two patients (13.3%), >1/100 in two patients (13.3%), >1/1000 in one patient (6.7%) and >1/32 in three patients (20%).

Dsg3 was investigated in 20 patients (40.8%). The Dsg3 titers also varied between <1/10 and >1/1000.

The Dsg3 titer was <1/10 in five patients (25%), >1/10 in two patients (10%), >1/100 in three patients (15%), >1/1000 in five patients (25%), >1/32 in two patients (10%) and >1/320 in three patients (15%).

Forty-seven patients (95.9%) did not use any medications that could have led to pemphigus. One patient had a history of beta-blocker use and another had a history of ACE inhibitor prior to the emergence of the pemphigus lesions.

DISCUSSION

Pemphigus is a widespread disease around the world. Although the disease is mostly encountered in patients between 40 and 60 years of age, it may rarely be seen in children and later ages. Studies have shown the mean age for the onset of the disease is 46 in South Africa, 36.7 in Tunisia, 52 in Macedonia and 57 in Finland (5,9-12). In accordance with the literature, the mean age of our patients at the time of diagnosis was 50 and the age of our patients ranged between 23 and 75 years.

Although it is usually acknowledged that the disease is equally prevalent in females and males, some

researchers suggest its prevalence is higher in females while others advocate the opposite (6,13-15). In our study, 44.9% of the participants were female and 55.1% were male, with a female: male ratio of 1:1.2. Despite the slightly higher prevalence in males, this finding is consistent with those from the literature, suggesting an equal prevalence of pemphigus in both sexes.

Whereas pemphigus might involve different mucosal tissue, the most commonly involved one is the oral mucosa (13,16,17). Some studies reported that mucosal involvement in pemphigus was observed in up to 100% of the cases (10,12,15). In our study, 98% of the patients had mucosal involvement. 95.9% of our patients had lesions in the mouth, 34.7% had dysphagia/pain, 18.4% had nosebleed, 24.5% had hoarseness and 14.3% had red eye. In agreement with the literature, the prevalence of mucosal involvement was high and the most common mucosal involvement was the oral mucosa.

In PV, the symptoms on the skin usually appear after the involvement of the oral mucosa (18). The symptoms were observed first in the oral mucosa and then on the skin in 42.9% and first on the skin and then in the oral mucosa in 18.4% of the patients. 16.3% of the patients experienced simultaneous involvement of the skin and oral mucosa. In 2% of the patients, the involvement of the mouth was followed by other mucous membranes (conjunctiva, anogenital, nasal) while oropharyngeal and other mucous had combined involvement in 8.2% of the patients. The involvement was in the oral mucosa alone in 10.2% of the patients and 2% had only dermatological symptoms. These findings were consistent with those of the literature.

Involvement of the mucosa and/or skin is common in PV (10,13,15,17). In our study, 98% of the patients had mucosal involvement and 79.6% had involvement of the skin. These findings support the suggestion of common involvement of the skin and/or mucosa in PV.

In our study, the lesions were located both on the skin and in mucosae in 77.6% of the PV patients. Similar outcomes were exhibited in a Macedonian study (76%), whereas a study from Bulgaria reported lower prevalence (64.8%) and another from our country reported higher prevalence (82.5%) (10,19,20). Our study showed that the lesions were located in mucosae alone in 20.4% of the PV patients. Similar results were obtained again in the Macedonian study (24%); however, the study from Bulgaria reported a lower (10.8%) and the study from Spain reported a higher prevalence (71%) (10,19,21). The study from Bulgar-

ia showed that the lesions were located on the skin alone in 24.3% of the patients whereas localization on the skin was observed in 6.4% and 6.5% of the patients in Iran and Turkey (19,20,22). In our study, 2% of the patients had lesions located on the skin alone and this was a lower rate in comparison to those in the literature. This finding confirms that mucosal involvement is more frequent in PV.

The main histopathological finding in PV is intraepidermal disintegration. Histopathological assessments of the biopsies in PV patients exhibited suprabasal disintegration in 95 to 100% of the patients (23-26). In our study, 95.9% of the patients had suprabasal disintegration and 4.1% had non-specific pathological findings; an outcome consistent with those from the literature.

In our series of 49 patients clinically and histopathologically diagnosed with PV, 15 (30.6%) were examined for anti-Dsg1 antibodies and 20 (40.8%) for anti-Dsg3 antibodies. In the literature, the diagnostic sensitivity for anti-Dsg3 antibodies was reported to vary between 85 and 100% (25-28). In our study, anti-Dsg antibodies were found positive in 75% of the patients. The lower rate in our study, in comparison to that in the literature, was associated with the absence of active lesions in our patients who have been receiving treatment. Positivity rates for anti-Dsg1 antibody values were reported 46% in Europe, 55.6% in Japan, 76.5% in Italy and 77% in Iran (25,27-29). Our rate of 53.3% positivity for anti-Dsg1 antibodies was close to the rate from the Japanese study.

All participants in our study were investigated for consanguineous marriage (mother-father). 22.4% of our PV patients had this type of marriage. In the studies of Tuncbilek, conducted in different cities in Turkey, the rate of consanguineous marriage was between 20 and 25% and in the study of Baki *et al.*, conducted in the city of Trabzon, the rate was 20% (30, 31). We believe the findings of our study represent the nationwide rate of consanguineous marriage.

CONCLUSION

The clinical and demographic data of the PV patients in our region were consistent with other studies.

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