Bullous Pemphigoid in Iranian Patients: A Descriptive Study on 122 Cases

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Abstract- Bullous pemphigoid is an immunobullous disease with high mortality and morbidity. Different aspects and characteristics in the patients vary in different areas in the world. Our objective was to study clinical and demographic characteristics of bullous pemphigoid in Iranian patients. In a retrospective descriptive study, we reviewed 122 patients with bullous pemphigoid within 1987-2007. Demographic characteristics, clinical manifestations, treatment, relapses and outcome were evaluated. The mean age of 122 patients was 65 ± 18.11 years including 35.2% male and 64.8% female. The most common manifestations were cutaneous bullae (97.5%). 27% had oral lesions. 30.3% had eosinophillia. 90 patients (73.8%) received oral prednisolone, 29 patients (23.8%) topical steroid, 2 patients tetracycline and 1 patient dapsone. 89 patients were followed after admission. Out of them 44 patients experienced first relapse and 22 patients second relapse. 41 cases (46%) were completely controlled. 11 cases (12%) were not controlled. Clinical and general characteristics of bullous pemphigoid patients differ in various regions in the world.
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Keywords: Bullous pemphigoid; Iranian; Immunobullous diseases

Introduction

Bullous pemphigoid is an autoimmune, sub epidermal, blistering skin disease characterized by antibodies specific for components of the epidermal basement membrane (1). Bullous diseases are associated with high morbidity and mortality. They are resulted from autoimmune response to one or more components of the basement membrane or desmosomes (2). Previous studies on bullous pemphigoid have reported incidences between 0.2 and 3 per 100000 population in a year; these are higher in older age groups, and some studies report association with sex (3-5). In the United Kingdom, a regional study estimated an incidence of 1.4 per 100000 persons yearly (6). Wide variation in mortality is reported, with one year mortality varying between 6% in the United States and 41% in France (7-8). Studies show that the rate of bullous pemphigoid is increasing (4). Few studies has been carried out about various characteristics such as relapses and response to treatment in Iran (9). In this study, it has been tried to determine general characteristics and co-incidence with other diseases, clinical manifestations and response to treatment in the patients with bullous pemphigoid who referred to Razi Hospital, Tehran, Iran within 1987-2007.

Materials and Methods

This is a descriptive study, which has been designed as a retrospective study. We reviewed the medical files of 122 patients with documented bullous pemphigoid .They had referred to Razi Hospital ,Tehran ,Iran within 1987-2007. All of them had a definite bullous pemphigoid according to pathology and direct immunofluorescence (DIF).

Treatment was mostly including systemic corticosteroids or topical steroids. Systemic corticosteroid was about 1 mg/kg whereas the amounts of topical steroids were depended on severity of disease. Relapses were defined as multiple new lesions appeared after complete control. According to our experts´ opinion in our center, response to treatment was categorized as three parts based on clinical criteria: complete control that was defined as complete healing old lesions and no or a few new lesions. Not control is defined when older lesions has not been repaired while multiple new lesions are appearing continuously. Incomplete control is a condition between complete and not controlled in which older lesions have been repaired incompletely while few new lesions are appearing.

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Demographic data, relapses and treatments were extracted from medical files and recorded in the questionnaires. Then, collected data were analyzed by SPSS software version 13. Since our study is descriptive, we mostly calculated frequencies.

Results

122 patients with documented bullous pemphigoid were enrolled in this study. The mean age at the time of first presentation was 65±18 years (range 12-100). Forty three (35.2%) of them were male and 76 cases (64.8%) were female.

The most common manifestations were cutaneous bullae (97.5%). The other common clinical manifestations were pruritus (80.3%), oral lesions (27%), non-specific rash (19.7%), urticaria (18%), eczema (7.4%), fever (6.6%), malaise (6.6%) and genital lesions (4.1%).

Distal of extremities was the most common site of lesion (77%). The lesions were in 68 cases (55%) in chest, 47 cases (38.5%) in trunk, 31 patients (25.4%) in face, 29 cases (23.8%) in abdomen, 21 cases (17.2%) on scalp, 20 cases (16.4%) on buttock, 10 patients (8.2%) on axillary region. 10 cases (8.2%) had lesions on palm and sole.

Average time since the first presentation until clinical and pathologic diagnosis was 105.7±314.37 days with a median 60 days (range 3-2520 days).

2 patients mentioned a family history of bullous pemphigoid, 2 cases had resent surgery, 2 cases had experienced resent emotional stress, 5 cases stated they have a common cold before presentation and 2 patients had local trauma (burn and vascular fistula).

Coincidence diseases were including: 1 case of cancer, 2 cases of vitiligo, 3 cases of rheumatoid arthritis, 2 cases of ulcerative colitis, one case of multiple sclerosis and 16 cases of diabetes (13.1%).

History of receiving penicillin, antipsychotics and aldosterone antagonist was mentioned in 3 patients.

Elevated erythrocyte sedimentation rate (ESR) (37.3%) was the most common findings in laboratory tests. Eosinophilia (30.3%), leucocytosis (23%), anemia (17.2%) and abnormal liver enzyme level (5.7%) were the other common findings.

Distribution of blood groups in our patients was including 35.2% A, 29.6% B, 26% O and 9.3% AB.

90 patients (73.8%) underwent treatment with oral prednisolone, 29 patients (23.8%) topical steroid, 2 patients tetracycline and one patient received dapsone.

Period time since initiation of treatment until initiation tapering was considered as control period. The mean of control period time was 15.48±13 days (range 3-126).

We followed up 89 patients. Relapse was defined as need for increasing the dose of drugs. 44 patients (69%) had first relapse. The mean of period time between control of disease and first relapse was 177±163.26 days (range 10-630 days). In 2 patients who experienced relapse before one month, treatment interruption by patients and rapid tapering seemed to be the cause of relapse.

Out of 89 followed up patients, 41cases (46%) were completely controlled so that the lesion recovered and drugs tapered. The mean of their oral prednisolone and topical clobetasol was 12.8±10.86 mg/day (range of 1.25-40) and 1.08±0.75 tube/day (range of 0.25-2) respectively.

37 cases (42%) were incompletely controlled so that the lesions were not recovered completely. The mean of their oral prednisolone and topical clobetasol was 19.26±15.09 mg/day (range of 5-60) and 1.59±0.83 tube/day (range of 0.25-3.5) respectively.

Table 1. Comparison of prednisolone and clobetasol amounts and control time in the patients, at the time of diagnosis and in first and second relapses.

	Initiation of treatment	First relapse(out of 89 followed up patients)	Second relapse(out of 89 followed up patients)
Number of cases	122	44(49%)	22(24.7%)
Number of cases treated with oral prednisolone	90(73.8%)	26(59.1%)	15(68.2%)
Number of cases treated with topical clobetasol	29(32.8%)	13(29.5%)	7(31.8%)
Mean of oral prednisolone dose (range)	60.38±21.21 (5-120 mg/day)	32.88±22.5 (10-100mg/day)	27.86±17.24 (8-60 mg/day)
Mean of clobetasol dose(range)	2.3±0.66 (1-3.5 tube/day).	2.23±0.8 (1-3.5 tube/day)	1.4±0.91 (0.25-3 tube/day)
The most common site of lesions	Distal of extremities	Distal of extremities (54.5%)	Distal of extremities (63.6%)
Mean of control Period (range)	15.48 ±13 (3-126 days).	27.6±24.57 (5-136 days)	24.1±10.76 (7-45days)

11 cases (12%) were not controlled so that the new lesions were presented and the dose of drugs was increased. The mean of their oral prednisolone and topical clobetasol was 17.51±8.96 mg/day (range of 7.5-30).

Mean of relapses was 1.02±1.67 times with maximum of 10 relapses. Prednisolone and clobetasole amount, control time in the patients at the time of diagnosis and in first and second relapse have been summarized in table 1.

Discussion

Bullous pemphigoid is an immunobullous disease with high mortality and morbidity. Investigation about clinical manifestations, diagnosis and treatment is useful for understanding about various aspects of this disease. We evaluated 122 patients with bullous pemphigoid in Iran.

The mean age in our patients was 65 ± 18.11 years (range 12-100 years). This mean is similar to Tunisia with mean age of 67.2 years (10), Poland with 67.25 years (11) and Kuwait with 65 years (12). The mean age in our patients is lower than France with mean age of 83 years (13), Germany with mean age of 77.3 and United States with mean age of 77 years (8).

Out of 122 cases, 43 (35.2%) were male and 76 (64.8%) were female. In Tunisia (10) males are more than females, in Kuwait (12) female to male ratio was 5.1 and in the United States (8) males and females are nearly equal.

In majority of investigations cutaneous bullae is the most common sign in the patients with bullous pemphigoid. 119 cases in our study (97.5%) has presented with cutaneous bullae. Oral lesions were seen in 33 patients (27%). Oral lesions were seen in 37% of the patients in Kuwait (12) and 12.8% in Taiwan (14).

Bullous pemphigoid has been reported in association with some diseases such as diabetes, multiple sclerosis, ulcerative colitis and vitiligo (15-16). Association with malignancies has also been reported (17); however we were unable to find any malignancies in our patients.

In our study, eosinophilia was observed in 37 cases (30.3%). Similar findings has been reported in a study in Taiwan (14).

Ninety (73.8%) patients received oral prednisolone and 29(23.8%) patients treated with topical clobetasol. 2 patients received tetracycline and one case received dapsone. Average dose of prednisolone was 60.38 ± 21.2 mg per day (range 5-120) and that of topical clobetasol was 2.36 ± 0.66 tubes per day (range 1-3.5).

In a study in United States 76% of the patients received oral prednisolone with dose of 10-80 mg/day and 5 patients received topical clobetasol (8). Dose of prednisolone in the patients in Kuwait was 20-60 mg/day (12). In recent years, obvious changes have occurred in the treatment of bullous pemphigoid and some introduced topical steroids as first choice of treatment (18).

According to our experts´ opinion in our center response to treatment was categorized as three parts based on clinical criteria: complete control that was defined as complete healing old lesions and no or a few new lesions. Not control is defined when older lesions has not been repaired while multiple new lesions are appearing continuously. Incomplete control is a condition between complete and not controlled in which older lesions have been repaired incompletely while few new lesions are appearing. Forty one (46%) out of 89 followed up patients were controlled completely, 37 cases (42%) controlled incompletely and 11 cases (12%) were not controlled. Complete control in our patients is more than Taiwan (14) and Kuwait (12) which was 30% and 32% respectively.

Clinical and general characteristics of bullous pemphigoid patients differ in various regions in the world. Our study is retrospective and descriptive. Clinical trials or study with a larger sample size is necessary for achieving more findings on various aspects of this disease and introducing more effective treatments with fewer side effects.

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