Bullous Pemphigoid: An Experience in Kuwait

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Abstract:

Bullous pemphigoid (BP) is a rare autoimmune bullous disease (ABD). The data on clinicoepidemiological features of BP is lacking from Arabian Peninsula. This study was aimed to determine the clinicoepidemiological features of BP in Kuwait. A total of 29 cases of Pemphigoid were studied in our ABD clinic. They constituted 22% of the total number of ABD (n =130) seen by us over a span of 12 years. BP was observed to be the second commonest ABD after pemphigus in our ABD clinics. The minimum estimated incidence of pemphigoid in our population was 2.1 cases/million/year. We observed a striking female preponderance (86%).

Ninety-three percent of the patients were Arabs. The mean age at onset of disease was 62.93 and mean duration of disease before coming to us was 3.53 months. Majority (69%) had a moderate severity of the disease. The mucosal involvement was seen in 36%. Systemic steroids were the mainstay of treatment. Adjuvants were added when indicated. The course of the disease and various risk factors were studied for all the patients and the results were compared with those from elsewhere.

Introduction:

Bullous pemphigoid (BP) is a rare autoimmune blistering disease (ABD) characterized clinically by tense blister formation, histologically by subepidermal blister with an inflammatory cell infiltrate in the upper dermis, and immunologically by autoantibodies in patient's circulation that bind to basement membrane zone (BMZ). These autoantibodies show a linear staining at the dermal-epidermal junction (DEJ) and recognize two major hemidesmosomal proteins, the BP 230 (BPAG1) and BP 180 (BPAG2) (BP 180NC 16A)[1]. The clinicoepidemiological features of BP have been described in various surveys from different parts of the world.[2-8] but the data is lacking from our region.

The present study was aimed to determine the incidence and clinicoepidemiological features, and course of BP patients in Kuwait, and to compare the results with those available from elsewhere.

Materials and Methods:

The study was carried out in the National Dermatology Center, Kuwait (ABD). An autoimmune bullous diseases clinic was established in our center in July 1991. All the patients of BP, registered in our ABD clinic between, July 1991 – June 2003 were included in the study.

The diagnosis in all the cases was suspected clinically and confirmed by histopathology showing subepidermal blister with mixed upper dermal infiltrate, and a positive direct/indirect immunofluorescence by linear IgG and/or C_3 in the basement membrane zone (BMZ). The diagnosis was further supported by indirect immunofluorescence performed on saline-split skin, with a positive staining of immunoreactants (IgG/C_3) at the roof of the blister. Doubtful cases, not confirmed by immunofluorescence, were not included in the study. A detailed clinical record including age, sex, nationality, age of onset, site of onset, duration of disease, sites affected, severity of the disease, and associated diseases was maintained for all the patients. Severity of disease was graded as mild if the patient had scattered vesicobullous lesions <20% of skin surface area; moderate when over 20-50%; and severe when over more than 50% skin. The division of severity was arbitrary but more or less constant, since all the patients were followed by same group of investigators. Systemic steroids (Prednisolone 20 – 60 mg daily) were the mainstay of treatment. Adjuvants including tetracyclines, azathioprine, dapsone, IVIG were added for the resistant cases when indicated. A follow-up record was maintained to study the course and outcome of the patients.

Results:

A total of 29 cases of pemphigoid were seen in our ABD clinic during the study period. They were observed to constitute 22% of total number of ABDs (n = 130) registered over a span of 12 years. Pemphigoid was the second commonest ABD in our clinic after pemphigus. The minimum estimated incidence of pemphigoid cases among a referral population of 1.14 millions for our clinic was 2.1 cases per million per year. The 29 cases

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with pemphigoid included 28 patients (96.6%) of bullous pemphigoid (BP) and one (3.5%) cicatricial pemphigoid (CP).

Among 28 patients with BP, there were 26 Arabs (93%) and 2 non-Arabs (7%). The various nationalities among Arabs included Kuwaitis 16 (62%), followed by Bedouns 5(19%), Saudi Arabian 2 (7.6%) and one patient each from Syria, Egypt, and Jordan (3.5%). Two non-Arabs one from India and other one from Bangladesh.

The age of onset ranged from 32 to 99.75 years with a mean of 62.93 ± 20.23 years. The duration of disease before coming to us ranged from 2 days to 12 months with a mean of 3.53 months. There were 4 males (14%) and 24 females (86%) with a male to female ratio of 1:6. The extremities were the commonest site of onset (69%). The oral mucosal involvement was seen in 10 patients (36%). A mild severity of the disease was noticed in one patient (3.5%), moderate in 20 (71.4%); and severe in 7 patients (25%).

Among the associated diseases, 14 patients (50%) were observed to have diabetes mellitus, followed by hypertension in 11 (39%), ischaemic heart disease 8 (29%), cardiovascular accidents 2 (7%), and chronic renal failure, parathyroid adenoma, psychiatric ailments, bronchial asthma, squamous cell carcinoma of vulva, hypothyroidism, epilepsy, old tuberculosis, vitiligo and psoriasis in one patient each (3.5%).

Sixteen patients (57%) received prednisolone alone (20-60mg daily) to control their disease whereas, adjuvants including azathioprine, dapsone, tetracyclines, or IVIG were added in 12 patients (43%). The follow-up period ranged from 2 months to 9 years.

In the present study, till last follow-up, we observed a mortality rate of 39% (11 among 28 patients). Among the 11 patients, 9 died while still on treatment for BP, whereas, 2 were off therapy. The cause of death included septicemia in 5 patients (45%), ischaemic heart disease with congestive heart failure in 3 (27%), extensive disease with disease related complications in 2 (18%) and squamous cell carcinoma of vulva with secondaries in one patient (9%). Among these 11 patients, (36%) died within first six months of diagnosis, and 5 (45%) within 6 months to one year and 2 patients (18%) died between 1-3 years. Hypoalbuminemia and eosinophilia were observed to be the bad prognostic factors ($P = <0.05$).

Discussion:

Bullous pemphigoid was observed to be the second commonest ABD in Kuwait after pemphigus. It was described to be the second commonest ABD from Malaysia[9] and Tunis,[3] whereas, in France,[8] Germany[7] and Singapore[6] BP was observed to be the most prevalent ABD. The minimum estimated incidence of 2.1 cases per million per year was much lower than reported from Europe[7,8] (6.62–7.64 cases/million/year) and Singapore[6] (7.6 cases/million/year). We feel that the lower incidence of BP in our series may be partially related to referral bias, as has been observed, recently.[6] Some of the cases with mild disease responding to topical treatment may not have been referred to us. Most of the cases in the present series were of moderate to severe disease. Whether some of these differences in incidence are related to ethnic or genetic variations, needs to be settled. An interesting observation in the present series was of striking female preponderance. BP was described to be twice more common in females than males in Singapore,[6] and slight female preponderance was described from Europe as well.[7,8] A male predilection was reported from Tunis.[3] In our series it was observed to be six times more prevalent in females than males (M:F = 1:6) and reasons for this striking female dominance needs to be settled.

Contrary to pemphigus, where high doses of systemic steroids are needed to control the disease, the BP patients respond well to low dose steroids (20-40 mg daily). In resistant and recurrent cases we preferred to add adjuvants rather than increasing the dose of steroids, keeping in mind the age and underlying medical status of the patients and to avoid the steroids related complications.

A mortality of 39% among BP patients during a 3 year follow-up was comparable to earlier reports from elsewhere.[10-12] As observed earlier the old age with poor general conditions and extensive disease, hypoalbuminemia and eosinophilia were observed to be bad prognostic factors in these patients.

To conclude, we present the first series of BP from our region with 93% of the patients being of Arab ethnicity. Although many of the features in our patients were similar to those described earlier, the reasons for some differences including lower incidence, and a striking female preponderance need to be settled.

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