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Original Article

Epidemiologic evaluation of patients with blistering lesions in Sari: A retrospective study

Massoud Golpour, Ghasem Rahmatpour Rokni, Mohammad Rahmani*, Bahareh Golpour*, Ali Morad Heidari Gorji**

Department of Dermatology, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran
* Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran
** Members Faculty (EDC), Mazandaran University of Medical Sciences, Sari, Iran

Abstract

Objective To evaluate the histopathological and demographical features of patients with blistering lesions from the medical records in the pathology unit of Buali hospital in Sari.

Methods This descriptive retrospective study included medical records of 87 patients with bullous lesions during years 2003-2013 which were archived in the pathology unit of the hospital, were reviewed and evaluated. Biopsies were taken by dermatologist after sterilizing of the bullous lesion with betadine and applying local anesthesia with lidocaine 1%. After appropriate tissue slicing, fixation and hematoxylin and eosin staining, slides were examined under microscope by two pathologists. Histopathological and demographic data (such as age, sex, area of involvement, diagnosis) were recorded. The gathered information was analyzed by SPSS16 in terms of central and peripheral statistic distribution.

Results Of 87 patients with bullous lesions, the most common diagnosis was pemphigus vulgaris with 36 (41.4%) patients, followed by bullous pemphigoid with 22 (25.3%) patients, dermatitis herpetiformis with 8 (9.2%) patients, pemphigus foliaceus with 6 (6.9%) patients, epidermolysis bullosa with 4 (4.6%) patients, pemphigus erythematosus with 3 (3.4%) patients and subcorneal pustular dermatosis with 1 (1.1%) patient and 7 cases had uncertain diagnoses. The ratio of female to male was 1.17:1.

Conclusion Our study demonstrated that the frequency of diagnosis of skin bullous lesions in city of Sari is almost similar to other related studies and the most common diagnoses are pemphigus vulgaris, bullous pemphigoid, dermatitis herpetiformis and pemphigus foliaceus.

Key words
Skin bullous disease, pemphigus vulgaris, bullous pemphigoid, pemphigus foliaceus.

Introduction

Blistering diseases of skin are characterized by presence of lesions containing watery liquids. There is a wide variety of blistering diseases, some of which can be extremely debilitating and even fatal. Many of these diseases are autoimmune in nature and may be associated with certain human leukocyte antigen types. Some bullous diseases have serious sequelae, necessitating early treatment and intervention to prevent further morbidity or mortality. Auto-immune blistering diseases include pemphigus vulgaris, paraneoplastic pemphigus, bullous pemphigoid, cicatricial pemphigoid, dermatitis herpetiformis, and linear IgA dermatosis.[1] Pemphigus encompasses a group of autoimmune blistering diseases of the skin and mucous

Address for correspondence
Dr. Ghasem Rahmatpour Rokni
Department of Dermatology,
Bouali Sina Hospital, Pasdaran Boulevard, Sari,
Mazandaran Province, Iran
Email: seyedmd@yahoo.com

membranes. Included in this group is pemphigus vulgaris (PV), a bullous disease involving the skin and mucous membranes, which may be fatal if not treated with appropriate immunosuppressive agents. According to several retrospective studies, the prevalence of PV is equal in men and women. Although it may be seen in children and the elderly, the mean age of onset is between 40 and 60 years. PV is also more common in persons of Jewish and Mediterranean descent.[2] The incidence of PV varies from 0.5 to 3.2 per 100000 individuals and in Iran this rate is known to be 1 per 100000.[3] Bullous pemphigoid (BP) is an autoimmune skin disorder characterized by subepidermal blistering that results in large, tense bullae. It occurs mainly in the elderly and rarely in children. Onset is typically between 60 and 80 years of age. There is equal incidence in men and women, and there are no known racial or ethnic predilections. In France and Germany, the incidence is estimated at seven per 1 million per year. Dermatitis herpetiformis (DH) is an intensely pruritic, chronic skin disease characterized by papulovesicular lesions and urticarial wheals located on the extensor surfaces in a symmetric distribution. The disease persists indefinitely, and is associated with a gluten-sensitive enteropathy in most patients. The incidence of DH is 10 to 39 cases per 100,000 persons. Onset tends to be between 20 and 40 years of age but may occur at any age, including childhood, and there is a 2:1 preponderance for men.[4] Pemphigus foliaceus (PF) is generally a benign variety of pemphigus. It is an autoimmune skin disorder characterized by the loss of intercellular adhesion of keratinocytes in the upper parts of the epidermis (acantholysis), resulting in the formation of superficial blisters. It is typified by clinical involvement of healthy-appearing skin that blisters when rubbed (the Nikolsky sign; commonly but incorrectly spelled Nicholsky), a finding named after Dr. Piotr Nikolsky, who first described this sign in 1896.[5] The incidence of PF varies depending on the population studied. PF is rare and sporadic worldwide. In contrast to PV, no predominance of PF is found in Jews and in people of Mediterranean descent. An increased incidence of PF was noted in Tunisian women (6.6 cases per million per year), whereas, in Western Europe, the incidence of pemphigus foliaceus is about 0.5-1 case per million per year.[6] Epidermolysis bullosa (EB) is a group of inherited bullous disorders characterized by blister formation in response to mechanical trauma. Historically, EB subtypes have been classified according skin morphology.[7,8] According to National Epidermolysis Bullosa Registry, number of EB cases in Norway is 54 cases per million live births, in Japan is 7.8 cases per million live births, and in Croatia is 9.6 cases per million live births.[9] Pemphigus erythematosus (PE), also known as Senear-Usher syndrome, is an overlap syndrome with features of lupus erythematosus (LE) and PF. Pemphigus is demonstrated by acantholysis and immunoglobulin deposits in the interkeratinocyte substance.[10] The incidence of pemphigus is 0.5-3.2 cases per 100,000 population per year. Patients with PE comprise only a small subgroup of those with pemphigus. Kumar from India, reported a high prevalence (4.4 cases per million population).[11] Subcorneal pustular dermatosis (SPD) is a rare, benign, chronic relapsing sterile pustular eruption typically involving the flexural sites of the trunk and proximal extremities. It most commonly affects woman aged 40 years or older. The etiology of this entity is unknown, and its exact nosologic classification is still controversial. Studies also suggest that some cases of SPD represent a variant of pustular psoriasis. These cases have been reported to evolve clinically from initially presenting as SPD to lesions that are more typical of pustular or plaque psoriasis.[12,13]

Given the importance of these diseases and lack of previous researches and information in province of Mazanadaran we tried to gather statistical data of mentioned diseases and demographic data of the patients. Therefore, we evaluated the recorded data of the patients in the archive of pathology unit of hospital during 1994-2013 years.

Methods

It was a retrospective descriptive study conducted in Buali hospital of Sari, Iran. In this study, medical records of 87 patients with bullous lesions from the archive of pathology laboratory of the hospital were selected and evaluated. Dermatologist took biopsies after sterilizing the bullous lesion with betadine and applying local anesthesia with lidocaine 1%. Depending on the lesion type, different biopsy methods such as excisional, incisional or punch biopsy were applied and samples in formalin 10% container were sent to the pathology laboratory. After appropriate tissue slicing, fixation and hematoxylin-eosin staining, the slides were examined under microscope by two pathologists. The pathology reports were attached to the patients' medical records. Histopathological and demographic data (such as age, sex, area of involvement, diagnosis) were recorded. The gathered information was analyzed by SPSS 16.

Results

The population of our study was 87 patients and all of them had bullous lesions. Pathologic biopsies were taken from them and their data were recorded in the pathology unit archive of Buali hospital of Sari. 40 (46%) patients were males and 47 (54%) patients were females. Female to male ratio was 1.17:1. The mean age of the patients in this study was 53.1±18.3. Minimum age was 1 and maximum was 95 years. In evaluating the side of involvement, lesions were divided to three general sides: left, right and midline. The most common side of involvement was midline with 52 (59.9%) patients, then left side with 18 (20.6%) patients and right side with 17 (19.5%) patients.

In evaluation of the side of involvement based on the patient gender, the most common side of involvement in males was midline with 24 (60%) patients then left side with 10 (25%) patients and right side with 6 (15%) patients. In females, the most common side of involvement was midline with 28 (59.6%) patients then left side with 8 (17%) patients and right side with 11 (23.4%) patients (**Table 1**).

In terms of area of involvement, the most common area was upper limb with 21 (24.1%) patients, then head and face with 15 (17.2%) patients, lower limb with 14 (16%) patients, abdomen with 9 (10.3%) patients, flanks with 8 (9.2%) patients, back of the trunk with 7 (8%)

Table 1 Evaluation of the side of involvement based on the patient sex (n=87).

	Right side N (%)	*Left side N (%)*	*Midline N (%)*
Male	6 (15)	10 (25)	24 (60)
Female	11 (23.4)	8 (17)	28 (59.6)
Total	17 (19.5)	18(20.6)	52 (59.9)

Table 2 Evaluation of the area of involvement based on patient sex (n=87).

	Male	*Female*	*Total*
Upper limb	14	7	21
Head and face	7	8	15
Lower limb	3	11	14
Abdomen	2	7	9
Flanks	5	3	8
Back of trunk	6	1	7
Chest	1	5	6
Neck	2	2	4
Axillary region	0	3	3
Total	40	47	87

Table 3 Evaluation of the involved areas of body in different blistering diseases.

	Upper limb	*Head and face*	*Lower limb*	*Abdomen*	*Flank*	*Back*	*Chest*	*Neck*	*Axilla*	*Total N (%)*
PV	6	13	7	3	1	2	3	0	1	36 (41.4)
BP	6	1	4	2	3	2	2	3	0	22 (25.3)
DH	4	1	1	1	0	0	1	0	0	8 (9.2)
PF	0	0	0	1	2	2	1	0	0	6 (6.9)
EB	1	0	2	0	1	0	0	0	0	4 (4.6)
PE	2	0	1	0	0	0	0	0	0	3 (3.4)
SPD	1	0	0	0	0	0	0	0	0	1 (1.1)
Uncertain	2	0	0	2	1	1	0	0	1	7 (8)
Total	21	15	14	9	8	7	6	4	3	87 (100)

BP: bullous pemphigoid, DH: dermatitis herpetiformis, EB: epidermolysis bullosa, PE: pemphigus erythematosus
PF: pemphigus foliaceus, PV: pemphigus vulgaris, SPD: subcorneal pustular dermatosis

Table 4 Variation of types of diseases by patient sex (n=87).

Diagnosed bullous disease	*Male*	*Female*	*Total*
Pemphigus vulgaris	13	23	36
Bullous pemphigoid	12	10	22
Dermatitis herpetiformis	4	4	8
Pemphigus foliaceus	3	3	6
Epidermolysis bullosa	2	2	4
Pemphigus erythematosus	1	2	3
Subcorneal pustular dermatosis	1	0	1
Uncertain	4	3	7

patients, chest with 6 (6.9%) patients, neck with 4 (4.6%) patients and axillary region with 3 (3.4%) patients (**Table 2**).

In terms of pathological diagnosis, in 7 cases (8%) the diagnosis was uncertain. But in this aspect, the most common diagnosis was PV with 36 (41.4%) patients, then BP with 22 (25.3%) patients, DH with 8 (9.2%) patients, PF with 6 (6.9%) patients, EB with 4 (4.6%) patients, PE with 3 (3.4%) patients and SPD with 1 (1.1%) patient, **(Table 3).**

Considering the gender distribution of different bullous diseases, in patients with PV, 13 were males and 23 were females. However, the gender ratio was almost equal in case of BP (12 males vs. 10 females), DH (4 males and 4 females), PF (3 males and 3 females), EB (2 males and 2 females) and PE (1 male and 2 females). The only case of SPD was male (**Table 4**).

Discussion

The bullous skin diseases are being divided in two categories based on whether the skin is affected within the epidermis or at the epidermal-dermal interphase. The first category is referred to as pemphigus and entails 4 disease entities: pemphigus vulgaris, pemphigus foliaceus, paraneoplastic pemphigus, and IgA pemphigus. Altogether, the yearly incidence of this category is about 0.3/100,000 and the age of onset of these diseases is primarily in the fifties and sixties. The second category comprises multiple disease entities. The overall yearly incidence of the second category is about 1.0/100,000. These diseases typically become manifest at an age >65 years.[14-16] There were 87 participants in our study and the ratio of female

to male patients was 1.7:1. The mean age of the patients was 53.1 ± 18.3. The most common diagnosed blistering disease was PV seen in 36 (41.4%) cases, followed by BP in 22 (25.3%) cases, DH in 8 (9.2%) cases and PF in 6 (6.9%) cases. Other diseases were relatively uncommon.

In 2013, Arundhathi *et al*.[17] designed a study to evaluate vesiculobulbar lesions. 68 patients participated in the study and the eldest one was 83-year-old. Also similar to our study, the ratio of female to male in their study was 1.27:1. The most common diagnoses for these lesions were pemphigus vulgaris in 16 (38.2%) cases, bullous pemphigoid in 11 (16.2%) cases and pemphigus fuliaceus in 4 (5.8%) cases. But there was no case of dermatitis herpetiformis.[17]

In 2004, Nanda *et al*.[18] in Kuwait evaluated the autoimmune bullous diseases. The ratio of female to male was 2.05:1, higher than our study ratio. The mean age was 42±19.57 years, which indicates that the participants were younger than ours were. The most common diagnoses were pemphigus vulgaris in 48 (37.5%) cases, pemphigoid gestationis in 24 (18.75%) cases and pemphigus foliaceus in 11 (9%) case, which, except one disease, were similar to our results.[18]

In a study conducted by Jowkar *et al*.[19] in 2014 in Shiraz during 10 years, the most common diagnoses, like our study, were pemphigus vulgaris and bullous pemphigoid. However, the frequencies were different in comparison to our study for example pemphigus vulgaris had involved most of their patients (82.9%), then bullous pemphigoid (8.5%) and pemphigus foliaceus (4.7%).[19]

Also in a study by Daneshpazhoohet *et al*.[20] in 2012 in Tehran for evaluating the autoimmune bullous lesions, as our study and the study of Jowkar *et al*.[19], the most common diagnoses were pemphigus vulgaris (81.2%) then bullous pemphigoid (11.6%) and pemphigus foliaceus (4.4%).[20]

Conclusion

Our study demonstrated that the frequency of diagnosis of skin bullous lesions in city of Sari was almost similar to other related studies and the most common diagnoses were pemphigus vulgaris, bullous pemphigoid, dermatitis herpetiformis and pemphigus foliaceus.

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