AMJ Australasian Medical Journal [AMJ 2021;14(10):244-247]

Bullous pemphigoid patients and associated malignancies: Retrospective study; Riyadh – Saudi Arabia

Alanoud S. Alsuhibani[1]*, Gadah M. AlQurashi[1], Raghad M. Alharthi[2], Hanadi M. Almutairi[3], Mohammad Almohideb[2]

1 College of Medicine, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia
2 King Abdulaziz Medical City, NGHA, Riyadh, Saudi Arabia
3 King Khalid University Hospital, Riyadh, Saudi Arabia

RESEARCH

Please cite this paper as: Alsuhibani AS, AlQurashi GM, Alharthi RM, Almutairi HM, Almohideb M. Bullous pemphigoid patients and associated malignancies: Retrospective study; Riyadh – Saudi Arabia. AMJ 2021;14(10):244-247.

Corresponding Author:
Alanoud S. Alsuhibani
College of Medicine,
King Saud bin Abdulaziz University for Health Sciences,
Riyadh, Saudi Arabia.
Alanoud.alsuhibani@gmail.com

ABSTRACT

Objectives

The purpose of this study is to describe the prevalence of bullous pemphigoid (BP) and to determine the associated malignancies with BP in Saudi Arabia.

Methods

Data on patients aged more than 18 years old, who were diagnosed with BP, were retrospectively reviewed. Patients' sociodemographic, clinical symptoms and associated medical conditions were collected. Data were analyzed using the statistical package for social sciences, version 21 (SPSS, Armonk, NY: IBM Corp.).

Results

Our sample was composed of 83 patients who were diagnosed with bullous pemphigoid; their mean age was 80.3 years. 3.6 per cent of our patients had drug-induced BP. 97.6 per cent of our patients had comorbidities, such diabetes, hypertension, and dementia. The most commonly encountered co-morbidities were hypertension in 79.51 per cent patients (n=66) followed by diabetes in 51.80 per cent patients (n=43), and heart disease in 33.73 per cent patients (n=28). None of the patients had malignancies, except for 2.4 per cent patients (n=2) who had lymphoma.

Conclusion

No clear association between BP and malignancies, age group, gender, or other comorbidities was identified. We recommend larger prospective studies to investigate the association between BP and malignancies.

Key Words

Skin, Blisters, Autoimmune, Pemphigus, Autoimmune blistering skin disease

Introduction

Bullous pemphigoid (BP) is a rare chronic, relapsing, blistering disorder that predominantly affects elderly.[1] It is the most common autoimmune bullous disease.[2] According to M. Persson et al. the incidence of BP in England between 1998 to 2017 was 7.63 per 100 000 person-years, with an annual increase of 0.9 per cent. The prevalence approximately doubled over the observation period, reaching 47.99 per 100 000 persons.[3] BP classically presents with intense pruritus and tense blisters over urticaria-like or eczematous lesions on the trunk and the flexor surfaces of the extremities.[4] The blisters are usually filled with a clear fluid or blood.[4] The blisters heal without scarring; however hyperpigmentation is common.[4] Mucosal involvement is infrequent, but if present, it is usually limited to the oral mucosa.[1,4]

The pathogenesis is driven by antibodies against the hemi-desmosomal proteins BP180 and BP230 at the dermal-epidermal junction.[1] Both antigens are crucial components of the hemi-desmosomes, since they are responsible for the adhesion between the dermis and epidermis.[1] Binding of antibodies to the antigens leads to the disruption of the basement membrane zone (BMZ) and blister formation.[4] The diagnosis is based on clinical evaluation, histopathological evaluation demonstrating eosinophilic infiltration, the presence of IgG antibodies or C3 deposition at the BMZ using immunofluorescence assays and measuring circulating antibodies against BP180 and BP230.[1] The current mainstay of therapy is high potency topical

steroids and systemic steroids.[1]

The association between BP and malignancies is unclear and remains controversial, as some studies suggested that patients with BP had higher rates of malignancy.[5,6] In some cases, remission of BP was observed after the removal of the solid tumour or the effective treatment of the hematologic malignancy.[7] On the contrary, other studies found no difference between BP patients and the control group.[8,9]

To the limit of our knowledge, there are no studies conducted in Saudi Arabia describing the prevalence of BP or the link between BP and malignancy. This study aims to determine the associated malignancies with BP among the Saudi population.

Material and Methods

The study was an observational, retrospective chart-review study conducted in King Abdul-Aziz Medical City, a tertiary care centre, in National Guard Health Affairs, Riyadh, Saudi Arabia. The computer databases were searched for all patients, of both genders, aged more than 18 years old, who were diagnosed with Bullous Pemphigoid. Patients diagnosed with malignancies before developing BP were excluded.

Consecutive non-probability sampling technique was used to approach all affected patients or review the files of patients. The collected data from the patients' files, which was entered into Microsoft Excel, included sociodemographic, clinical symptoms and associated medical conditions.

Statistical Analysis

Descriptive statistics were presented using numbers and percentages. Between comparisons, Fischer Exact tests were applied. *p-value*<0.05 was considered statistically significant. All data analyses were performed using the statistical package for social sciences, version 21 (SPSS, Armonk, NY: IBM Corp.).

Results

We analyzed 83 Saudi patients with bullous pemphigoid. As seen in table 1, the mean age of the patients was 80.3 (SD 12.7) years old with more than a half (54.2 per cent) were in the older age group (>80 years) and 55.4 per cent were females. 3.6 per cent of our patients had drug-induced BP. In addition, the proportion of patients with associated comorbidities was 97.6 per cent.

Table 1: Baseline characteristics of the patients (n=83).

Type of malignancy	N (%)
Age in years (mean ± SD)	80.3±12.7
≤80 years	38 (45.8%)
>80 years	45 (54.2%)
Gender	
Male	37 (44.6%)
Female	46 (55.4%)
Diagnosis	
BP	80 (96.4%)
Drug induced BP	03 (03.6%)
Other comorbidities	
Yes	81 (97.6%)
No	2 (2.4%)

Also, we observed that the most commonly mentioned comorbidities were diabetes (12 per cent), followed by hypertension (10.8 per cent) and dementia (6 per cent).

As shown in table 2, No cases were observed for any type of malignancies except for lymphoma, which was the only type of malignancy documented in our sample (2.4 per cent; n=2).

Table 2: Associated Malignancies (n=83).

Type of malignancy	N (%)
Thyroid malignancy	
Yes	0
No	83 (100%)
Lymphoma	
Yes	02 (02.4%)
No	81 (97.6%)
Leukaemia	
Yes	0
No	83 (100%)
Breast cancer	
Yes	0
No	83 (100%)
Lung cancer	
Yes	0
No	83 (100%)
Multiple myeloma	
Yes	0
No	83 (100%)

We used Fischer Exact at table 3 to evaluate the relationship between BP and the baseline characteristics of the patients. Based on the results, factors such as age group (p=0.690), gender (p=0.690), lymphoma (p=0.782) and other

comorbidities (p=0.247) did not show significant relationship with BP.

Table 3: Relationship between BP and the baseline characteristics of the patients (n=83).

Factor	BP N (%) (n=80)	Drug Induced BP N (%) (n=3)	P-value §
Age in years			
≤80 years	36 (45.0%)	01 (33.3%)	0.690
>80 years	44 (55.0%)	02 (66.7%)	
Gender			
Male	36 (45.0%)	01 (33.3%)	0.690
Female	44 (55.0%)	02 (66.7%)	
Lymphoma			
Yes	02 (02.5%)	0	0.782
No	78 (97.5%)	03 (100%)	
Other comorbidities			
Yes	25 (31.3%)	0	0.247
No	55 (68.8%)	03 (100%)	
§ P-value has been calculated using Fischer Exact test.			

Discussion

BP is a rare and most common autoimmune blistering diseases characterized by antibodies to the BP180 and BP230 at the dermal–epidermal junction. Our main goal is to investigate the association between BP and different types of malignancies. One of the published studies was done in two different hospitals (Keck Hospital and Los Angeles Country/University of Southern California Hospital) included 99 patients were diagnosed with BP found that 26 had malignancies and concluded no significant relationship between BP and Malignancies.[2]

Another study was done in Japan 1995 to evaluate the incidence between internal malignancies and BP in 1113 cases diagnosed with BP.[6] The study concluded that: there was association between internal malignancies and BP observed in 64 cases, the association between neoplasms and BP increased by aging, gastric cancer was the most common neoplasm associated with BP, and they recommended oncologic screening in patients with BP.

Although the relationship between BP and malignancies remains controversial, several studies were published to explain the theories of pathogenesis of tumour formation. One of these theories was that because the antibodies directed against tumour-specific antigens of malignant cells cross-react with BP antigens in the BMZ leading to the formation of blisters.[7] 40 cases were collected of patients with BP and malignancy, 7 cases associated with haematological malignancy and 33 associated with solid tumours. This study showed there is significant risk of BP patients to develop malignancies.

A systematic review and meta-analysis was done in 2017 using different databases and included 8 studies that showed no significant relationship between BP and malignancies except one study that found association between BP and lymphoid leukaemia with larynx and kidney cancer.[8]

The association between BP and different types of malignancies remains controversy and approved by multiple published studies that BP not associated with solid malignancies.[10]

The association between BP and malignancy is debatable and no consensus reached regarding this theory.[11] A case report of 64 years old patient had squamous cell carcinoma associated with BP reported in 2014. This study concluded that BP can be associated with different types of malignancies.

Study limitations and recommendations

Our limitations are: the small sample size and the study were done in one centre in the capital city. We recommend for future studies to overcome our limitations.

Conclusion

To conclude, no clear association between BP and malignancies was identified. In addition, there was no significant association between BP and age group, gender, or other comorbidities. We recommend larger prospective studies to investigate the association between BP and malignancies.

References

1. Miyamoto D, Santi CG, Aoki V, et al. Bullous pemphigoid. An Bras Dermatol. 2019;94(2):133-46. doi: 10.1590/abd1806-4841.20199007.
2. Wright B, Halper K, Worswick S. Bullous pemphigoid and malignancy in two different hospital populations: A retrospective cohort review. Oncology. 2020;98(5):318-20. doi: 10.1159/000506055.
3. Persson MSM, Harman KE, Vinogradova Y, et al. Incidence, prevalence and mortality of bullous pemphigoid in England 1998-2017: A population-based cohort study. Br J Dermatol. 2021;184(1):68-77. doi: 10.1111/bjd.19022.
4. Fuertes de Vega I, Iranzo-Fernández P, Mascaró-Galy JM. Bullous pemphigoid: Clinical practice guidelines. Actas Dermosifiliogr. 2014;105(4):328-46. doi: 10.1016/j.ad.2012.10.022.

5. Lucariello RJ, Villablanca SE, Mascaró JM Jr, et al. Association between bullous pemphigoid and malignancy: A meta-analysis. Australas J Dermatol. 2018;59(4):253-60. doi: 10.1111/ajd.12764.
6. Ogawa H, Sakuma M, Morioka S, et al. The incidence of internal malignancies in autoimmune blistering diseases: Pemphigus and bullous pemphigoid in Japan. Dermatology. 1994;189(Suppl 1):82-4. doi: 10.1159/000246937.
7. Balestri R, Magnano M, La Placa M, et al. Malignancies in bullous pemphigoid: A controversial association. J Dermatol. 2016;43(2):125-33. doi: 10.1111/1346-8138.13079.
8. Atzmony L, Mimouni I, Reiter O, et al. Association of bullous pemphigoid with malignancy: A systematic review and meta-analysis. J Am Acad Dermatol. 2017;77(4):691-9. doi: 10.1016/j.jaad.2017.05.006.
9. Ong E, Goldacre R, Hoang U, et al. Associations between bullous pemphigoid and primary malignant cancers: An English national record linkage study, 1999-2011. Arch Dermatol Res. 2014;306(1):75-80. doi: 10.1007/s00403-013-1399-5.
10. Kridin K, Hammers CM, Ludwig RJ, et al. Risk of solid malignancies in bullous pemphigoid: A large-scale population-based cohort study. J Dermatol. 2021;48(3):317-23. doi: 10.1111/1346-8138.15685.
11. Fernandes J, Barad P, Shukla P. Association of bullous pemphigoid with malignancy: a myth or reality? Indian J Dermatol. 2014;59(4):390-3. doi: 10.4103/0019-5154.135493.