CASE SERIES

A clinic-epidemiological study of 148 patients of pemphigus at Lady Reading Hospital, Peshawar: a case series

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Abstract

A seven-year retrospective study was held at the Department of Dermatology, Lady Reading Hospital, Peshawar, between 2013 to 2020 to determine the demography and clinical features of pemphigus. Among 148 patients included in this study 88 (58%) were females and 60 (40%) were males with a female to male ratio of 1.46:1. Average age at onset of the disease was 38±12 years (range 14-75 years). On the basis of Autoimmune Bullous Skin Disorder Score (ABSIS), 14 (9.3%) patients had mild disease, 58 (38.7%) had moderate disease, and 76 (50.7%) patients had severe disease. In total, 144 (96%) patients had pemphigus vulgaris, 3 (2%) patients had pemphigus foliaceous and 1 (0.7%) patient had paraneoplastic pemphigus. Severe pemphigus was more frequently associated with multiple relapses (p=0.00). This study shows poor prognostic factors like severe pemphigus vulgaris associated with multiple relapses. Five years of follow-up shows that complete remission on minimal therapy was achieved more in patients who received Rituximab.

Keywords: Pemphigus, Autoimmune, Relapse, Remission, Epidemiology.

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Introduction

Pemphigus is a chronic blistering disease of the mucous membrane and skin. Two major types are pemphigus vulgaris (PV) and pemphigus foliaceus (PF), due to IgG autoantibodies against desmoglein 3 and 1. It presents with oral lesions in 50-70% patients. These may precede cutaneous lesions by months or be the only manifestation of disease. Flaccid blisters mostly appear on the scalp, neck and trunk. Blisters rupture to produce painful erosions that heal without scarring.[1]

Pemphigus vulgaris (PV) accounts for approximately 80% of cases worldwide. The annual prevalence rates of the disease range between 0.76 and 16.1 cases per million.[2] This varies depending on the geographic and ethnic populations. Women are affected more than men and mean age of onset is between the fourth and sixth decades of life. Systemic corticosteroids, immunosuppressive drugs, and biologics are the mainstay of therapy.[3,4]

The aim of this study was to establish the demography and clinical features of pemphigus, such as age at onset, gender, severity, phenotype of pemphigus, treatment received, relapses, and remission rates in patients admitted to the Department of Dermatology, Lady Reading Hospital, Peshawar. This is the first study conducted in KP, Peshawar. Its other advantage is that it has evaluated this disease over a period of seven years.

Case Series

A retrospective study was conducted by reviewing the charts of 148 pemphigus patients admitted to the Dermatology Department of Lady Reading Hospital, Peshawar, from 2013 to 2020 over a period of seven years, after ethical approval from the Institutional Review Board of Lady Reading Hospital, Peshawar (Ref no.115-A/LRH/MTI). Data was collected in May and June 2021. In accordance with the hospital practices, all newly-diagnosed pemphigus patients of either gender were admitted to the Department of Dermatology where they underwent medical history and physical examination. Skin biopsy for histopathology and direct immunofluorescence was done to confirm the diagnosis when diagnosis was clinically not confirmed. Clinical characteristics, including demographic variables (age at onset of disease and gender), and disease characteristics (phenotype of disease, type of pemphigus, severity, treatment received and its adverse effects, relapses and remission rates) were studied. The Autoimmune Bullous Skin Disorder Intensity Score (ABSIS) was used to determine the disease severity.[5] The total score ranges from 0 to 206, which includes oral involvement (0–11), cutaneous involvement (0–150), and subjective discomfort during eating and drinking (0–45). This score classifies pemphigus cases into three categories: mild pemphigus (scores from 1 to 10), moderate pemphigus

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(scores from 11 to 40), and severe pemphigus (scores from 41 to 206). Disease relapse was defined as the appearance of at least three new lesions in a month, which did not heal spontaneously over a week in a patient who had achieved disease control. Consent of patients/guardians was taken prior to the writing of the manuscript.

Statistical Analysis: The findings were recorded in a predesigned proforma. Results were analysed using SPSS version 26. Frequencies and percentages were calculated for all the categorical variables. Mean ± standard deviation was calculated for continuous variable. One sample T test was utilised to compare the means. Chi-square test was utilised for categorical variables. P-value of <0.05 was considered significant.

Results

Among the 148 patients included in this study, 88 (58%) were females and 60 (40%) males, with a female to male ratio of 1.46:1. Average age at onset of the disease was 38±12 years (range 14-75 years). Ninety (60%) patients were less than 40 years of age and 58 (38.7%) patients were aged more than 41 years. The average age at onset of the disease was 39.8 ± 12 years in male patients and 37.2 ± 11.4 years in female patients. The difference in the average age between the two genders was not statistically significant (p = 0.19).

Assessment of disease severity on the basis of ABSIS showed that 14 (9.3%) patients had mild disease, 58 (38.7%), had moderate disease, and 76 (50.7%) patients had severe disease.

Disease phenotype showed that 134 (89.3%) patients had mucocutaneous disease, 9 (6%) patients had only mucosal involvement, and 5 (3.3%) patients had only cutaneous disease.

Among the 148 patients,144 (96%) patients had pemphigus vulgaris, 3 (2%) had pemphigus foliaceous, and 1 (0.7%) patient had paraneoplastic pemphigus. Among the 144 patients of pemphigus vulgaris, 130 (87.8%) patients had mucocutaneous disease, 9 (6.1%) had mucosal disease, and 5 (3.4%) patients had cutaneous disease.

All 3 patients of pemphigus foliaceous and 1 patient of paraneoplastic pemphigus had mucocutaneous disease. Highest frequency of mucocutaneous involvement i.e. (51.4%) was seen in the age group ranging from 30 to 50 years. The most common initial site of the disease was the oral cavity. It was involved in 116 (77.5%) patients.

Mean duration of the disease was 2±1.8 years. Duration was less than 3 years in 114 (76%) patients, 3-6 years in 32 (21%) patients, and more than 6 years in 2 (1.3%) patients.

Systemic corticosteroid therapy was used in all patients initially at a dose of 1–1.5 mg/kg in combination with adjuvants i.e., Azathioprine. Second line of treatment was Rituximab, used in 24 (16%) patients who showed no response to conventional therapy. Methylprednisolone and Cyclophosphamide pulse was also used in 21 (14%) patients who were non-responsive to conventional therapy.

Three or more relapses were documented in 83 (55.3%) patients, and one or two relapses were documented in 41 (27.3%) patients during the first five years of follow-up. No relapse was seen in 13 (8.7%) patients, while 11 (7.3%) patients were lost to follow-up.

Multiple relapses were more frequently associated with severe pemphigus than in patients with moderate pemphigus (47.3% vs 8.8%; p = 0.001). No relapse was seen in patients with mild pemphigus. In 47 (31.3%) patients the cause of relapse was steroid tapering, especially at 30mg per day of Prednisolone, 35 (23.3%) patients relapsed due to use of over-the-counter medications, 34 (22.7%) patients had poor compliance to medications and in 32 (21.3%) patients no cause was observed. On follow-up, corticosteroid side-effects were seen in 116 (78.3%) patients. Most common side-effects were diabetes in 23 (15.3%) patients, hypertension and weight gain in 20 (13.3%), candidiasis in 8 (5.3%), cataract in 5 (3.3%), fracture in 2 (1.3%), and combination of side effects in 38 (25.3%).

Figure: Case of severe pemphigus vulgaris treated with Rituximab, inset shows post-treatment image

Table-1: Clinical data of pemphigus.

Variable	PV	PF	PP
No. of Cases (%)	144 (96)	3 (2)	1 (0.7)
Age Group Most	Less than 40	Less than 40	More than 41
Common (%)	88 cases (61.1)	2 cases (66.7)	1 case (100)
Gender (%)			
Male	57(39.6)	2 (66.7)	1 (100)
Female	87 (60.4)	1 (33.3)	0
Duration of Disease	Less than 3 years (111 cases)	Less than 3 years (2 cases)	Less than 3 years (1 case)
Initial site (%)			
Oral mucosa	113 (78.5)	2 (66.7)	1 (100)
Skin	31 (21.5)	1 (33.3)	0
Induction (%)			
Rituximab	24 (16.7)	0	0
Azathioprine	99 (68.8)	3 (100)	1 (100)
Cyclophosphamide	21 (14.6)	0	0
Remission (%)			
Complete remission	35 (24.3)	1 (33.3)	1 (100)
Partial Remission	98 (68.1)	2 (66.7)	0
Lost to follow-up	10 (7.6)	0	1
Relapse (%)			
No relapse	13 (9.0)	0	0
1-2 relapse	40 (27.8)	1 (33.3)	0
3 or more relapse	80 (55.6)	2 (66.7)	1 (100)

PV= pemphigus vulgaris PF= pemphigus foliaceous PP= paraneoplastic pemphigus

One (0.7%) patient died following a cardiovascular problem and 2 (1.3%) patients following severe sepsis.

Follow-up of patients showed that 37 (24.7%) patients were in complete remission on minimal therapy, 100 (66.7%) patients were in partial remission, and 11 (7.3%) patients were lost to follow up. Complete remission on minimal therapy was seen more in patients who received Rituximab (14.2%) followed by patients who received Azathioprine (8.8%). Figure shows a patient of severe pemphigus vulgaris treated with Rituximab, inset shows post-treatment images.

Table shows a summary of results given separately for different types of pemphigus.

Discussion

Our study showed that the average age of onset of pemphigus was 38± 12 years which is lower than in other countries.[2,6] The difference in average age of onset was statistically significant (P<0.001 with 95% confidence interval -8.6–-4.7).

Several studies[6,7] have mentioned female dominance which is similar to the present study with 58% females.

Both the skin and mucosal involvement was observed in 89% of our patients. This is much higher as compared to previous reports.[8,9] In 6% of patients in the current study, exclusive mucosal involvement was observed. This is comparable to reports from other countries. In 3.3% of patients in the current study there was exclusive skin involvement. This is lower than reports from other countries.

Pemphigus commonly presents initially with oral lesions. Most patients eventually develop cutaneous lesions. The present study showed a higher frequency of initial mucosal involvement (77%) as compared to the reported average figure of 50–70%.[1]

Corticosteroids along with Azathioprine were used as the first-line of therapy in many studies.[10] In our study, the same protocol was followed. Rituximab and Cyclophosphamide/Methylprednisolone pulse were used as a second-line therapy in 24 (16%) and 21 (14%) patients, respectively, who were non-responsive to conventional therapy. In the present study, adverse effects of steroids were observed in 116 (78.3%) patients, which is similar to previous studies.[10]

The results of the present study noted a statistically significant association between the severity of pemphigus and number of relapses. Multiple relapses were more frequently observed in patients with severe pemphigus than in patients with moderate pemphigus (47.3% vs 8.8%; p = 0.00). A study by Mignard C. et al showed that PDAI (Pemphigus Disease Area Index) score for patients with relapsing disease was higher than that of patients with non-relapsing disease (54 [33%] vs 28 [24%]; P = .03).[11]

In 47 (31.3%) patients, the cause of relapse was tapering dose of steroids, especially at 30mg per day of Prednisolone, 35 (23.3%) patients relapsed due to the use of over-the-counter medications, 34 (22.7%) patients due to poor compliance to medications, and in 32 (21.3%) patients no cause was discovered. Similar results were reported in previous cohorts.[10]

In the present study, after five years of follow up, 37 (24.7%) patients were in complete remission on minimal therapy, 100 (66.7%) patients were in partial remission and 11 (7.3%) patients were lost to follow-up. A study done by Hicham T. et al 2 showed complete remission on minimal therapy in 45% patients after five years of follow-up, which is higher than our study. Low percentage of complete remission in the present study can be explained due to poor drug compliance and low socioeconomic status. Complete remission on minimal therapy was seen more in patients who received Rituximab (14.2%) than in patients who received Azathioprine (8.8%).

Conclusion

The present study reveals poor prognostic factor such as the severe type of pemphigus vulgaris associated with multiple relapses. This study also reveals that after five years of follow-up complete remission on minimal therapy was seen more in patients who received Rituximab. It was also observed that in patients who achieved remission with Rituximab, steroid tapering was rapid and adverse effects of steroids were less commonly seen as compared to the patients in whom steroids were tapered slowly. Although there were minor differences, the results of the present study are in relatively good agreement with the literature.

Limitation: This study is its retrospective character.

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