CLINICAL FEATURES OF PEMPHIGUS AT NATIONAL HOSPITAL OF DERMATOLOGY AND VENEREOLOGY FROM 2015 TO 2021

Pham Thi Minh Phuong¹; Pham Thi Thao¹; Trinh Minh Trang¹, *

SUMMARY

Pemphigus is a group of autoimmune disease with several types different in clinical features and histopathology.

Objectives: To investigate clinical features of pemphigus in out-patients at National Hospital of Dermatology and Venereology (NHDV).

Method: We analyzed retrospectively 279 medical records of out-patients with pemphigus at NHDV from 2015 to 2020.

Results: Female accounted for 62.7%. The mean age was 48.3 years old, the youngest was 14 years old and the oldest was 88 years old. The mean age of onset was 46.3 years old, the earliest onset was at 10 and the latest onset was at 88. The mean disease duration was 23.9 months, the shortest was one month and the longest was 20 years. The average hospitalization was 1.54, there was a case hospitalized 10 times. Pemphigus vulgaris accounted for the highest rate of 85.3%, the following was pemphigus erythema (10%). Pemphigus vegetans took the lowest rate of 0.4%. 83.4% of cases having lesions on both normal and seborrheic skin. 56.1% of cases were not affected at mucous membranes while only 4.4% of them free from lesions on the skin. Pemphigus vulgaris was highly developed lesions at mucosal areas more than other types. Moderate pemphigus accounted for the major cases of 68.4%. 14.1% was severe pemphigus. Mono-therapy with corticoid was the most common of (65.1%). A combination regime of corticoid and azathioprine took 12.9%. Notably, there was 3.3% having traditional treatments with herbs.

Conclusions: Female accounted for 62.7%. The mean age was 48 years old; the mean age of onset was 46 years olds. Pemphigus vulgaris was the most common type and highly developed lesions at mucous membranes more than other types. Two-third suffered from moderate pemphigus. Mono-therapy with corticoid was seen the most.

Key words: Pemphigus; Blister; Acantholytic…

¹: National Hospital of Dermatology and Venereology
*: Corresponding author: Trinh Minh Trang
1. INTRODUCTION

Pemphigus is a group of chronic bullous autoimmune diseases, endured by the auto-antibodies against auto-antigens in desmosomes of keratinocytes. This leads to the destruction of the desmosomes resulting in acantholytic at the affected epidermis. The typical clinical features of pemphigus are painful blisters and erosions on the skin and mucous membranes due to the acantholytic.\(^1,2\) Based on clinical features and histopathology characteristics, pemphigus is categorized into types including pemphigus vulgaris (PV), pemphigus erythema (PE), pemphigus foliace (PF), pemphigus vegetans, Hailey Hailey disease and some others rare types. Pemphigus has a chronic process with flare-ups and remissions causing extremely harmful impacts to patients’ health and quality of life. The disease even can lead to death if there is no relevant management was brought.\(^3,4\)

Pemphigus has variety prevalence between regions. Countries at low latitudes highly possess a higher prevalence. Besides, the distribution of genders, age, onset and types of pemphigus is also different between areas all over the world. In Vietnam, surveys on pemphigus were often carried out with a restricted sample size and in a short period of time. Most of them focused on subclinical issues. This study aims to describe clinical features and regimes for the treatment of patients with pemphigus at the NHDV during a 5-years-period from 2015 to 2020.

2. MATERIALS AND METHOD

2.1. Materials: Files and medical records of out-patients with pemphigus at the NHDV

2.2. Sample size: Standardized medical records and files of 279 patients were included

2.3. Method: descriptive study (retrospective)

Patients were diagnosed as pemphigus based on the following criteria: (1) chronic condition with flares up and remissions, (2) mono-morphology blisters and erosions on the skin and mucous membranes, (3) appearance of acantholytic squamous cells in Tzanck test, (4) bullous formation at the epidermis on histopathology and (5) direct fluorescein staining shows IgG in fish-net pattern surrounding keratinocytes. Medical records of the eligible pemphigus patients were enrolled.

Pemphigus severity was divided based on Pemphigus Disease Area Index - PDAI (0-263 points) into mild (0-15 points), moderate (16-45 points) and severe (>45 points) pemphigus. Pemphigus was categorized into (1) PV: the most severe type of pemphigus with painful blisters and erosions on the skin and mucous membranes most commonly inside the mouth, (2) PF: a benign form characterized by blisters on trunk and limbs commonly without mucous membrane involvement, (2) PE: a subtype of PF with skin lesions localized mainly on seborrheic skin, (4) pemphigus vegetans: a localized form of PV and (5) Hailey disease: benign familial pemphigus characterized by hereditary blisters appear in early adulthood.
2.4. **Study variables include:** Mean age, mean age of onset, gender, occupation, pemphigus types, duration of the disease, and number of hospitalization, extension of lesions based on Body surface area - BSA, pemphigus severity and treatment regime.

2.5. **Time and place:** This study was conducted in 2021 at the Department of Consultation, NHDV.

2.6. **Data analysis using SPSS 20.0**

2.7. **Ethnic’s approval:** Data confidentiality was ensured according to Good Clinical Practices regulations.

3. **RESULTS**

3.1. **Characteristics of the subjects**

*Table 1: Age, age of onset, disease duration and hospitalization number (n = 279)*

<table>
<thead>
<tr>
<th></th>
<th>Mean age (year)(min-max)</th>
<th>Mean age of onset (year)(min-max)</th>
<th>Mean disease duration (month)(min-max)</th>
<th>Mean hospitalization (min-max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PV</td>
<td>238</td>
<td>48.5 ± 13.6 (14 - 88)</td>
<td>46.7 ± 13.6 (13 - 88)</td>
<td>21.5 ± 29.7 (1 - 168)</td>
</tr>
<tr>
<td>PE</td>
<td>28</td>
<td>47.4 ± 13.9 (15 - 75)</td>
<td>44.4 ± 15.5 (10 - 75)</td>
<td>35.3 ± 41.9 (2 - 180)</td>
</tr>
<tr>
<td>PF</td>
<td>9</td>
<td>47.8 ± 16.5 (22 - 74)</td>
<td>45.9 ± 16.6 (19 - 73)</td>
<td>21.4 ± 19.6 (3 - 60)</td>
</tr>
<tr>
<td>P.vegetans</td>
<td>1</td>
<td>28</td>
<td>25</td>
<td>36</td>
</tr>
<tr>
<td>Hailey- Hailey disease</td>
<td>3</td>
<td>50.7 ± 14.0 (35 - 62)</td>
<td>41.0 ± 13.5 (27 - 54)</td>
<td>116.0 ± 115.3 (12 - 240)</td>
</tr>
<tr>
<td>Total</td>
<td>n = 279</td>
<td>48.3 ± 13.7 (14 - 88)</td>
<td>46.3 ± 13.9 (10 - 88)</td>
<td>23.9 ± 33.8 (1 - 240)</td>
</tr>
</tbody>
</table>

- Mean age was 48.3 years old, the youngest was 14 and the oldest was 88.
- Mean age of onset was 46.3 years old, the earliest was 10 and the latest was 88.
- Mean disease duration was 23.9 months, the shortest was 01 months, and the longest was 240 months.
- Mean of hospitalization was 1.54 times, the maximum was 10 times.

*Figure 1: Distribution of gender (n = 279)*
There were 175 females and 104 males accounted for 62.7% and 37.3% consecutively.

3.2. Clinical features of pemphigus

Pemphigus vulgaris accounted for the highest rate of 85.3%, the following was pemphigus erythema of 10%. Pemphigus vegetans took the lowest rate of 0.4%.

**Figure 2: Distribution of pemphigus types (n = 279)**

Pemphigus vulgaris accounted for the highest rate of 85.3%, the following was pemphigus erythema of 10%. Pemphigus vegetans took the lowest rate of 0.4%.

**Table 2: Duration of pemphigus types (n = 279)**

<table>
<thead>
<tr>
<th></th>
<th>PV</th>
<th>Other types</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean disease duration (month)</td>
<td>21.5 ± 29.9</td>
<td>38.1 ± 49.5</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Mean disease duration of PV was shorter than other types (p<0.05).

**Table 3: Extension of pemphigus lesions (n = 271)**

<table>
<thead>
<tr>
<th></th>
<th>BSA &lt; 10</th>
<th>BSA ≥ 10</th>
<th>Total</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PV</td>
<td>192 (83.5)</td>
<td>38 (16.5)</td>
<td>230 (100)</td>
<td>0.763</td>
</tr>
<tr>
<td>Others</td>
<td>35 (85.4)</td>
<td>6 (14.6)</td>
<td>41 (100)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>227</td>
<td>44</td>
<td>271</td>
<td></td>
</tr>
</tbody>
</table>

There was no difference between pemphigus types on the extension of lesions.
There was 4.4% of cases have pemphigus affected mucous membranes only. 83.4% of cases have lesions on both normal and seborrheic skin. Lesions localized on seborrheic skin took 10% while lesions localized on skin folds were 1.5%.

56.1% of cases were not affected at mucous membranes. 42.4% had lesions on mouth only. Only 1.5% of them had lesions on mouth, eye and genital mucosa.

### Figure 3: Distribution of skin lesions (n = 271)

![Distribution of skin lesions](image)

### Figure 4: Distribution of mucous membrane lesions (n = 271)

![Distribution of mucous membrane lesions](image)

### Table 4: Mucous membrane lesions of pemphigus types (n = 271)

<table>
<thead>
<tr>
<th></th>
<th>Not affected n (%)</th>
<th>Having lesions on mucous membrane n (%)</th>
<th>Total</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PV</td>
<td>112 (48.7)</td>
<td>118 (51.3)</td>
<td>230 (100)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Others</td>
<td>40 (97.6)</td>
<td>1 (2.4)</td>
<td>41 (100)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Total</td>
<td>152</td>
<td>119</td>
<td>271</td>
<td></td>
</tr>
</tbody>
</table>
PV had a higher rate of lesions on mucous membranes than other types ($p < 0.05$).

\[\text{Figure 5: Distribution of pemphigus severity}\]

Moderate pemphigus accounted for 68.4%. There were only 14.1% of cases severe.

\[\text{Figure 6: Distribution of treatment regimens (n = 272)}\]

Mono-therapy with corticoid took the highest rate of 65.1%, the combination treatment with corticoid and azathioprine was 12.9%. Notably, there were 3.3% of cases treated with traditional drugs.

4. DISCUSSION

The rates of female and male in our study were 62.7% and 37.3%, consecutively (Fig.1). Literature review shows some studies on pemphigus reported a higher rate of female than male but some of them reported an opposite trend.\textsuperscript{5, 6} Table 1 showed the mean age of cases was 48.3 years old. This finding was suitable with reports in Asia however our number was lower than numbers in Japan where the published mean age of pemphigus patients was 52.8 years old.\textsuperscript{7, 8, 9} Mean age of onset this study was 46.3 years old, the earliest onset was at 10 years old and the latest onset was at 88 years old. These results consistent to findings in Asia while Europe reported later onset at 60 - 70 years old.\textsuperscript{5, 10, 11, 12}
The ratio of PV and other pemphigus types was 5.8:1. This was relevant to the results of Kumar (India) and Ljubojevic (Croatia).\textsuperscript{11, 13} Kanokvaila reported the ratio of PV and PF was 5.3:1.\textsuperscript{14} PE is a subtype of PF that is less severe with lesions localized mostly at seborrheic skin. Our results showed that PE was more common than PF (Fig.2). This may be due to the patients tended to seek medical help at the early stage of their pemphigus, particularly in the group of PF and PE. Pemphigus duration was defined as a period from the appearance of skin lesions to the study enrollment. Our study found that the mean disease duration of PV was shorter than others types (Tab.2). This was supported by a study of Kanokvaila et al. The authors reported the mean duration of PV was 5.7 months in comparison to PF of 6.6 months. The duration of pemphigus has multiple influences of some different factors such as the age of onset, the natural process of pemphigus and the efficacy of treatments. Different from other types, PV is a severe condition with significant proportion of mortality. However, there was no strong evidence to prove that PV has a shorter natural process rather than other pemphigus types.

There was 4.4% of cases had their pemphigus affecting mucous membranes only. Most of them had lesions on both normal and seborrheic skin (Fig.3). A major of patients had no mucous membranes affected (Fig.4). Our patients with PV developed lesions at mucous membranes more likely than others groups (Tab.4). The result was relevant to the results of Kanokvaila in 2010 that noted 37.8% had onset with lesions on mucous membranes in PV while there was no case of PF develops mucosa lesions.\textsuperscript{14} These findings were suitable with the natural characteristics of PV.

There were most the cases suffering from moderate pemphigus that was relevant to the study of Kanokvaila reporting this rate was two-third.\textsuperscript{14} However, the author did not detect any mild case while this number in our study was 17.5%. The difference may be due to the application of several of scales on pemphigus severity assessment. We used PDAI for the categorization of pemphigus severity while Kanokvaila applied the classification of Herbst and Bystryn based on both the extension of lesions and the effectiveness of treatment.

This study found mono-therapy with corticoid was the most popular treatment. The following choice was the combination therapy with corticoid and an immunosuppressive agent (Fig.6). Other studies show that treatment with corticoid in combination with at least one of immunosuppressive agent has been used the most, particularly in the PV group. Choosing immunosuppressive agents was also various. Kanokvaila reported cyclophosphamide and dapsone were the privilege choices while methotrexate and azathioprine were used more common in the NHDV.\textsuperscript{14} Unfortunately, there was 3.3% of the patients had their pemphigus treated with unknown traditional drugs. This is due to the restricted awareness of the community on pemphigus. Hence, patients should be provided more education on the disease.

There were some drawbacks in our study that we could not able to determine the average dose and the cumulative dose of corticoid treatment to compare with others results. This could help
to bring useful recommendation. Besides, we assumed that if treatment outcome could be assessed through monitoring the remission, relapse rates and side effects... that would bring a more comprehensive insight on pemphigus.

5. CONCLUSIONS

Analyzing 279 standardized medical records and files of pemphigus out-patients at NHDV from 2015-2020, we brought some conclusions: Female accounted for 62.7%, the mean age of the patients was 48 years old, the mean age of onset was 46 years old. Pemphigus vulgaris was the major group that more likely had lesions on mucous membranes than other types. Less than half of the patients had their mucous membranes affected, commonly in the mouth. Two-third of the patients had moderate pemphigus. Monotherapy with corticoid was the most popular treatment.

REFERENCES


