

# Pemphigus Vulgaris Management in Elderly Patient: A Case Report

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## ABSTRACT

Pemphigus vulgaris is an autoimmune disease characterized by mucocutaneous involvement in the form of loose bullae on the skin and mucous membranes. This disorder is typically associated with the poor general condition and can be life-threatening. Furthermore, it has a rare incidence among elders. Pemphigus vulgaris was reported in a 73-year-old female patient. The diagnosis was performed clinically according to the history of the disease course and its typical lesions with a predilection for location. The patient's clinical condition improved after receiving systemic corticosteroids and additional supportivetherapy.

**Keywords:** *corticosteroid; elderly; management; pemphigus vulgaris*

## INTRODUCTION

Pemphigus vulgaris is an autoimmune disease that manifests as loose as well as thin-walled bullae on the skin and mucous membranes<sup>1,2</sup>. The severity of the disease is based on its progressive course which is accompanied by an increased body catabolism with loss of body fluids and proteins and secondary bacterial and viral infections which may lead to sepsis and cardiac failure. Before the advent of systemic corticosteroids, pemphigus was almost always fatal within two years after making the diagnosis<sup>3</sup>. The patient's general condition is typically poor and can be life-threatening, with a mortality rate of approximately 5-15%<sup>4</sup>. The incidence of pemphigus varies from 0.5 to 34 cases/million inhabitants/ year, with the highest incidence rates in Brazil<sup>5</sup>. The prevalence of pemphigus vulgaris in the United States exceeds 30,000 cases per year, with an incidence of 1-10 new cases per million people each year<sup>4</sup>. Wardhana et al<sup>6</sup>. conducted a retrospective study in 2013

at Sanglah Hospital in Bali, Indonesia, and reported that this disease has a 5.8% prevalence. Its annual incidence rates in Japan and France are between 3.5 and 1.7 cases per million people<sup>7</sup>. The peak onset of this disease occurs in the middle-age group of around 40-60 years<sup>4,7</sup>. Pemphigus vulgaris is uncommon among elders,<sup>8,9</sup> but has been documented in some previous studies<sup>10-12</sup>. Despite the unknown disease pathogenesis in this age group, it is thought to be related to immune system dysfunction caused by ageing<sup>13,14</sup>. The first-line treatment is a systemic corticosteroid with immunosuppressive effects. The use of corticosteroids in treating pemphigus vulgaris is well established. Reported rates of remission vary but occur, on average, in approximately 25% of patients treated with corticosteroids alone<sup>15</sup>. Once the condition is under control and exhibits remission, the corticosteroid doses will be tapered<sup>16-18</sup>. Furthermore, this therapy improves the patient's pemphigus vulgaris prognosis<sup>18-20</sup>. The disease was diagnosed in a 73-year-old female patient that received

systemic corticosteroid treatment and showed significant clinical improvement.

### CASE ILLUSTRATION

A 73-year-old female patient with COVID-19 status was negatively detected by PCR and presented a chief complaint of blistering all over the body for three days before hospital admission and skin erosions for ten days. The blister appeared on the left side of the back area and then ruptured. They also developed into erosions in various locations, including the chest, abdomen, limbs, buttocks, and genitals. The patient reported mouth ulcers and intermittent fevers for four days before admission, drastically decreasing oral intake. Also, there was a history of well-controlled diabetes mellitus. Eventually, the patient was admitted with slightly reactive hyperglycemia (221 mg/dL), hypertension, cancer, autoimmune disease, allergy, drug use before the complaint, smoking, alcohol consumption, herbal medication, and contact with specific chemicals or cosmetics. Furthermore, the person was admitted and treated for six days in the hospital. There was improvement based on clinical condition and blood glucose control. Three months after the treatment, there were no recurrent symptoms. Afterwards, the follow-up mechanism continued for a year.

#### General Status:

The following vital signs were observed upon physical examination: blood

pressure of 130/80 mmHg, palpable, strong and regular pulse at 87 times/min, respiratory rate of 20 times/min, an axillary temperature of 36.9°C, O<sub>2</sub> saturation of 99%. Based on Asia-Pacific criteria, the anthropometric state was grade II obesity (body weight of 80 kg, height of 160 cm, and BMI of 31.25 kg/m<sup>2</sup>). Ophthalmic examination showed no erosional lesions or conjunctival injection. Furthermore, examination of the heart, lungs, abdomen, and extremities was within normal limits.

#### Dermatological Status:

1. Chest, abdomen, back, bilateral upper arms, legs, and buttocks: multiple erosions-excoriations, nummular-plaque, circumscribed, discrete-confluent, with red-yellowish and black-yellowish crusts, hyper-pigmented macules, discrete-confluent, circumscribed, nummular-plaque.
2. Chest, abdomen, back, bilateral upper arms, right leg, and bilateral feet: multiple serous-hemorrhagic bullae, sagging walls, Nikolsky sign (+), discrete-confluent nummular-plaque, circumscribed.
3. Oral region: multiple miliary erosions on the right and left sides of the tongue.
4. Genital region (mons pubis): multiple erosions-excoriations, lenticular-nummular, circumscribed, red-yellowish crusts.
5. Epidermolysis >30% Body Surface Area (BSA)



Figure 1. Bullous lesions and erosions in the trunk region



Figure 2. Bullous lesions and erosions in the superior and inferior extremity regions

The laboratory data of hematological examination on the initial admission of a patient to the hospital showed normal hemoglobin, normal hematocrit, an increased white blood cell count, average platelets count, a random glucose level, normal sodium concentration, slightly hyperkalemia, and normal chloride serum of 11.5 g/dL, 38.1%, 15.900/uL, 286.000/uL, 165 mg/dL, 138 mmol/L, 5.6 mmol/L, and 101 mmol/L, respectively. During the hospital treatment, the patient had the variability of blood glucose ranging from 67 to 289 mg/dL, and also a chronic kidney disease based on the function test (70 mg/dL of serum urea, 1.24 mg/dL of serum creatinine, and 45.0 mL/min/1.73 m<sup>2</sup> of glomerular filtration rate). The HIV test has not yet been conducted.

The diagnosis of pemphigus vulgaris was based on the patient's history of disease progression and dermatologic examination, which revealed skin and mucosal lesions. Toxic Epidermal Necrolysis (TEN) and Bullous Pemphigoid were considered differential diagnoses for this patient. Meanwhile, immunofluorescence and histological examinations were not conducted due to a lack of facilities.

The systemic dosage consisted of intravenous methylprednisolone 62.5 mg/day, corresponding to 1 mg/kg BW/day prednisone, administered in divided doses of 31.25 mg b.i.d. After two weeks of treatment, the methylprednisolone dose was tapered to 48 mg q.d. orally for seven days, gradually decreased to 40 mg q.d., and finally to 16 mg q.d. The following were the additional systematic treatment: 0.9% of 500 ml saline every 12 hours, antibiotic IV cefoperazone 1 gram b.i.d., IV paracetamol 500 gram b.i.d as an analgesic, and Lantus 10 IU subcutaneously. Furthermore, the topical management prescribed includes 0.25% desoximetasone cream b.i.d, topical antibiotic 2% mupirocin cream twice a day and 0.9% saline compresses every four hours for 15 minutes/day. The patient had clinical improvement, as evidenced by the absence and healing of new and old lesions, respectively.

## DISCUSSION

Pemphigus vulgaris is an autoimmune disease defined by the presence of autoantibodies directed against one or both of the desmosome junction components (desmoglein-1 and-3) of epithelial tissue in the skin and mucous membranes.<sup>2</sup> It can manifest

clinically as the involvement of the mucous membranes, both skin and mucous membranes involvement, or rarely as skin manifestation<sup>19</sup>. Pain predominates over pruritus as the primary symptom. Generally, the patient is in poor condition<sup>2,7,18</sup>. Oral mucosal lesions are the most common manifestation of pemphigus vulgaris, affecting the mucous membranes of approximately 90% of patients<sup>8,19</sup>. The primary skin lesion is a loose, thin-walled bulla with a positive Nikolsky sign that occurs on any skin surface except the palms and soles. Bullae that are too loose and easily ruptured could cause severe erosions on the skin<sup>2,7,16,19</sup>. Therefore, additional examination rules out possible diagnoses and confirms pemphigus vulgaris. The Tzanck staining revealed suprabasal bullae with acantholysis and a typical "row of tombstones" appearance.

Immunofluorescence examination is the gold standard for diagnosing pemphigus vulgaris because it detects the presence of IgG and C3 autoantibodies on the surface of keratinocyte cells<sup>2,4,7</sup>.

The patient in the presented case was clinically diagnosed with pemphigus vulgaris. A positive Nikolsky sign and loose bullae containing serous-hemorrhagic fluid indicated an acantholytic in the suprabasal layer<sup>2,4</sup>. Ruptured bullous lesions create erosions, excoriations, and crusts in many sites, with epidermolysis affecting over 30% of the body surface area. The lesions manifest in practically every part except the palms and soles. Furthermore, the erosive lesions of the oral mucosa indicate mucocutaneous tissue involvement. There was no history of allergies or drug use in the patient before the appearance of the lesion. The authors considered TEN and bullous pemphigoid differential diagnosis based on the patient's medical history and clinical symptoms. In TEN cases, lesions can develop everywhere over the body, including the palms and soles. Bullae could initially show as erythematous macules, purpura, target lesions, or vesicles, eventually developing

severe necrosis. The mucous membrane lesions occur in at least two places. The most prevalent are the oral, vaginal, and conjunctival mucosa<sup>21,22</sup>. TEN is a hypersensitivity reaction to drugs<sup>22</sup>, but the patient denied any history of drug allergy or potential medication use. Furthermore, it could be clinically ruled out as a differential diagnosis. Bullous pemphigoid typically manifests after 70 years of age, preferring the axilla, flexor arms, inguinal, and medial legs<sup>23</sup>, with no or uncommon mucosal involvement<sup>24</sup>. Due to sub-epidermal acantholysis, characterized by a negative Nikolsky sign, the walls of the bullae are tense and thick<sup>23</sup>.

Pemphigus vulgaris is uncommon in the elders. The cases peak epidemiologically between the age of 40 to 60<sup>4,7</sup> and have been documented in elders by several studies. The disease was also identified in male patients aged 73 to 79 in Syria<sup>10</sup> and Iran.<sup>9</sup> Studies conducted by Suryawati et al<sup>11</sup> and Prihanti et al<sup>12</sup>. reported female patients aged 70 and 75 with pemphigus vulgaris. Additionally, Gonzales et al<sup>8</sup>. reported an oral pemphigus vulgaris case in a 70-year-old female patient. Meanwhile, the pathophysiology of this disease in geriatric patients is unknown. Several studies have confirmed the relationship between the ageing process and autoimmune diseases<sup>11</sup>. The innate and adaptive immune systems decline and become dysfunctional with age. Age-related immune system deterioration results in an inability to tolerate self-antigens (antigens produced by the body), which increases the chance of developing autoimmune disease. Lymphopenia occurs due to ageing, leading to the aberrant proliferation of homeostatic lymphocytes. The accumulation of differentiated effector T cells is associated with a low threshold for signaling and production of self-antigen molecules. This is triggered by the release of pro-inflammatory cytokines and the cells' excessive cytotoxic activity. The process plays a role in developing autoimmune disorders among elders<sup>10,11,13,14,25</sup>.

Masjedi et al<sup>9</sup> showed contradictory results that the immune system is suppressed in elders, implying that immunological diseases will improve with ageing.

The primary aim of treating pemphigus vulgaris is disease control and remission by managing bullous lesions on the skin and mucosa<sup>19,20</sup>. The first-line therapy in the management of this disease is corticosteroids<sup>6,17,26</sup>. Its mechanism involves interaction with receptors in the cell cytoplasm, increasing and decreasing pro and anti-inflammatory protein expression, respectively. Additionally, corticosteroids can stimulate the production of desmoglein or other cell adhesion molecules<sup>2,20</sup>. Prednisolone is frequently used at an initial dose of 0.5-1 mg/kg BW/day, as recommended by the European Dermatology Forum (EDF)<sup>16</sup>, or 1 mg/kg BW/day recommended by the British Association of Dermatologists (BAD)<sup>17</sup>. The dose may be increased to 2 mg/kg BW/day when the patient shows no clinical improvement within 1-2 weeks<sup>20</sup>. BAD suggests increasing the dose by 50%–100% when new lesions are formed within 5–7 days<sup>17</sup>. Clinical remission is the absence of new bullae and the presence of 80% healing in skin and mucosal erosional lesions after two weeks<sup>16,17</sup>. Using corticosteroids for 3-4 weeks prevents the body from overcoming a variety of stress responses due to adrenal cortex suppression. The dose is gradually reduced (tapering) to avoid disease exacerbations and restore the hypothalamic-pituitary-adrenal axis (HPA-axis)<sup>2,26</sup>. Furthermore, its doses are tapered by 25% every two weeks in patients with pemphigus vulgaris<sup>2,16,18,20</sup>. Tapering should be done gradually when the corticosteroid dose is increased to 20 mg/day of prednisolone by decreasing it to 5-10 mg every 2-4 weeks. It is recommended to taper every 2-4 weeks when the corticosteroid dose is equivalent to 10 mg/day of prednisolone<sup>16-18</sup>. This continues until the dose reaches 10 mg or less, hence, maintaining disease

remission<sup>16,17,20</sup>. Long-term use (more than four weeks) of this therapy causes side effects that affect almost all organ systems, including hypertension, diabetes mellitus, infections, glaucoma, peptic ulcers, and osteoporosis<sup>19,20,26</sup>. In the first 6 - 12 months of therapy, corticosteroids could also stimulate osteoclast activity, followed by a decrease in the function of osteoblasts and osteocytes. Monitoring bone mineral density and fracture risk prevention should be prioritized, particularly in the elder age group receiving long-term treatment<sup>26</sup>. Systemic corticosteroids can be combined with adjuvant therapy, such as immunosuppressive or cytostatic agents, especially in long-term usage. The adjuvant therapy is prescribed when disease activity cannot be controlled with high-dose corticosteroids. Furthermore, its commonly used treatment for pemphigus vulgaris cases is azathioprine, mycophenolate mofetil (MMF), rituximab, cyclophosphamide, methotrexate, intravenous immunoglobulin, and plasmapheresis<sup>17,19,20</sup>. Tarakji et al<sup>10</sup>. reported that a 73-year-old patient received 80 mg/day of prednisolone followed by a 40 mg/day tapered dose, which was gradually reduced by 5 mg every three weeks. The patient received 5 mg/day of prednisolone and 100 mg/day of azathioprine as maintenance doses. Masjedi et al<sup>9</sup>. reported pemphigus vulgaris in a 79-year-old patient showing clinical improvement with prednisolone treatment of 70 mg/day, a tapered dose of 50 mg/day, and a 5 mg gradual reduction every two weeks. The maintenance dose was 10 mg/day of prednisolone and 100 mg/day of azathioprine. The patient also received calcium supplementation of 1000 mg/day and vitamin D3 of 400 IU/day to manage the osteoporosis complications, which are common among elders.

The patient received systemic corticosteroids as initial treatment and also had diabetes mellitus that was controlled using insulin. Methylprednisolone was selected for

its minimal mineralocorticoid and glucocorticoid effects, with relatively short onset and biologic time<sup>26</sup>. IV methylprednisolone of 62.5 mg/day, equivalent to 1 mg/kg BW/day prednisone, was administered in divided doses of 31.25 mg b.i.d. Intravenous methylprednisolone was converted to oral methylprednisolone within 14 days. The methylprednisolone was tapered to 25% of the previously used dose. Furthermore, oral methylprednisolone was administered at a 48 mg/day for seven days, then gradually reduced to 40 mg/day (a decrease of 10 mg equivalent to prednisolone equivalent) until the maintenance dose reached 16 mg/day. The patient showed clinical improvement with gradual dose tapering during systemic methylprednisolone therapy.

Topical management in pemphigus vulgaris cases during reduction aims at relieving pain and preventing secondary infection. Corticosteroid creams and antibiotics are the most commonly used topical treatments<sup>2</sup>. Those for the current patient were 0.25% desoximetasone cream, a class of highly-potent topical corticosteroids (class II). The mechanism includes inhibiting DNA synthesis, cell mitosis, and reducing cell mitosis keratinocyte proliferation and vasoconstriction<sup>2</sup>. Antibiotics are also needed because extensive erosional lesions can cause *Staphylococcus aureus* (*S. aureus*) and other pathogens colonization, leading to secondary infection and sepsis<sup>20,27</sup>. Additionally, in cases of extensive and severe pemphigus vulgaris, vital signs and correction fluids and electrolytes should be monitored appropriately to improve the patient's general condition.

This patient received subcutaneous insulin treatment from the internal medicine department to regulate her blood sugar levels and prevent corticosteroid-induced hyperglycemia<sup>11,20</sup>. Corticosteroids can cause hyperglycemia by increasing hepatic gluconeogenesis and peripheral insulin resistance<sup>20,26</sup>. The vital signs and laboratory

results were within normal limits during its treatment. The current patient was not administered adjuvant drugs but only received a corticosteroid dose of less than 1 mg/kg BW/day and achieved controlled disease status while serial laboratory monitoring was always standard.

There is no consensus about the optimal management of pemphigus vulgaris cases in elders. The treatment of these cases needs to be extensive, vigorous, and multidisciplinary. Most of the elderly are diagnosed with additional comorbidities, making them prone to complications, either from the disease itself or drug side effects. Porro et al.<sup>19</sup> stated that the adverse effects of corticosteroid treatment contribute to the disease's morbidity and mortality<sup>20</sup>. To assist patients' clinical improvement, early detection, close monitoring, supportive care, and education should also be implemented.

Blistering autoimmune diseases such as pemphigus vulgaris can affect the patient's quality of life (QoL). Symptoms such as pain, itch, blistering, and scarring can reduce the functional capacity, thereby imposing disability and emotional condition. Patients with skin lesions experience the emotional alteration caused by shame, low self-esteem, and poor self-image. The poor self-esteem affects the patient's psychosocial aspect, such as coping mechanisms with their disease, ways to act in the environment (such as how to choose the clothes), compliance with the treatment, and social functioning<sup>28</sup>. These factors can induce loneliness and depression among elders. Low self-esteem can affect the desire to socialize with the neighbor. This is a factor of patient immobilization, which can affect the general condition and worsen the disease. Therefore, the psychosocial aspect needs to be assessed and intervened<sup>29</sup>.

## CONCLUSION

Pemphigus vulgaris is an autoimmune disease characterized by loose-walled bullae on the skin and mucous membranes. There is a rare incidence of this disease among elders. Dysfunction of the immune system due to ageing is thought to cause pemphigus vulgaris. Therefore, a good prognosis can be provided in elderly patients using systemic corticosteroid therapy.

## CONFLICTS OF INTEREST

The authors declare that there were no conflicts of interest in this study.

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## AUTHOR CONTRIBUTION

The authors equally contributed to the study.

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