

Case Study**EXPLORING THE CLINICAL SPECTRUM AND INDIVIDUALIZED DRUG THERAPY IN PEMPHIGUS VULGARIS: A CASE SERIES**EVANGELINE GLADWIN^{1*}, PRIYANSHI SHAH², HIMANI SHAH³, KRUNAL TRALSAWALA⁴^{1,2}Department of Pharmacy Practice, Parul Institute of Pharmacy, Parul University, Vadodara, Gujarat, India. ³Department of Pharmacy Practice, Indubhai Patel College of Pharmacy and Research Centre, Anand, Gujarat, India. ⁴Department of Dermatology, Parul Sevashram Hospital, Vadodara, Gujarat, India

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ABSTRACT

Pemphigus Vulgaris (PV) is a rare, chronic, life-threatening immunopathogenic disease that is characterized by flaccid, easily ruptured intraepithelial bullae, mostly found on the skin and mucous membranes. Attempting to keep the treatment plan of this potentially deadly disorder in primary focus, we have observed five patients with Pemphigus vulgaris. All patients have been presented with oral lesions or ulcers resulting in difficulty in swallowing. Patient one had a family history of the disease, while the other patients did not present any family history. All five patients had diverse ways of dealing with the disease before getting hospitalized. Microcytic anaemia and hypoalbuminemia have been found in all of them. Patients 1 and 3 had leucocytosis, while patient three had platelets in clumps with Hypercobalaminemia and the presence of ketone bodies in urine analysis. The Desmoglein I and Desmoglein III Antibody along with Punch biopsy results, confirmed the diagnosis. All patients were given systemic corticosteroids on hospitalization, but the case series observed variations in the dosages emphasizing individualized drug therapy. Some developed psychological impairment, some had generalized headaches or cardiac impairment, while ophthalmic involvement was seen in the other patients. Healthcare providers should do close monitoring while providing individualized drug therapy to prevent any systemic involvement and further complications.

Keywords: Pemphigus, Blister, Oral ulcer, Skin diseases, Mucous membrane

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INTRODUCTION

Pemphigus Vulgaris (PV), a chronic, life-threatening immunopathogenic dermatologic disease, is derived from the Greek word pemphix, translating to bubble or blister, which generally appears on the skin and mucous membrane [1]. It is a rare intraepidermal bullous disease with a mean incidence being two cases in 100,000 people per year [2]. It is more prevalent in females and usually occurs between the age of 50-60 [3]. It is characterized by flaccid, easily ruptured intraepithelial bullae, mostly found on the skin and mucous membranes. Blisters primarily appear in the mouth and scalp, spreading to face, back, chest, umbilicus, and groin region. Among these, the most common type is PV accounting for over 80 % of cases [4]. PV occurs due to the separation of keratinocytes in the epidermis, known as acantholysis, leading to blister formation, which ruptures, leading to the crusting and oozing of fluid with a foul smell, usually indicated as a Nikolsky positive sign. This results in antibodies attacking different desmosomes especially. Desmoglein III, further resulting in lesions on different layers of epithelium which is classified as a type-II hypersensitivity reaction [5]. This condition can also lead to sepsis and further causes death [6]. In this article, the following cases are briefly described along with reviewing the results of investigations and the plan of treatment.

CASE REPORTS**Case 1**

A 23 y old female patient developed fluid-filled lesions over leg, abdomen, back, scalp and mouth (fig. 1). She took ayurvedic treatment before 1.5 y ago for the same. The patient had tiny erosions over hard palate of buccal cavity, resulting in Dysphagia and Dysphonia. 15 d back, the patient presented with fluid-filled lesions over nipple region, gradually increased in size and number and aggravated lesions over the body trunk, extremities, genitalia, and oral cavity resulting in Dysphagia. It was found that patient's maternal aunty passed away due to PV before one year. Patient had

an unhealthy diet pattern. High Desmoglein I and III Antibody and Punch Biopsy confirmed Pemphigus Vulgaris. Pus C/S showed Streptococcus Pyrogen was found.

Initially, treatment started with dexamethasone to reduce inflammation as it is the Drug of choice for PV. On 1st and 2nd d, she developed 2-3 episodes of anxiety, pruritis, irritation and fever so, clonazepam and escitalopram were given. Symptomatic treatment involving antihistamines and topical antibiotics were prescribed. Cetrimide solution and triamcinolone acetonide gel were applied over scalp and oral ulcers, respectively. The patient was discharged with oral prednisolone 30 mg for a week.

**Fig. 1: Pemphigus vulgaris lesions developed on back**

Case 2

A 39 y old female patient started developing raw, painful oral lesions 6 months ago, with clear fluid-filled lesions over back and abdomen gradually extended to lower extremities (fig. 2). She was given oral prednisolone. She presented with painful oral ulcers with Dysphagia since 5 d, multiple crusted areas over back and flanks since 15 d and fluid-filled lesions over upper limbs. Patient also experienced generalized, occasional headache for 6 months. The patient had anorexia due to raw mouth lesions. Punch Biopsy was suggestive of Pemphigus vulgaris. Treatment was started with systemic corticosteroid and was tapered gradually. New vesicles and bullae appeared over back so the dose was again increased. Immunosuppressive steroid-sparing adjuvant cyclophosphamide tablet was also given. Multivitamins, antihistamines, H2-receptor blocker, topical corticosteroid, and antibiotics were given for symptomatic relief. Amitriptyline with NSAIDs were given for chronic headache. On discharge, patient was prescribed with oral prednisolone 10 mg, cyclophosphamide and amitriptyline for 20 d.



Fig. 3: Multiple crusted areas of pemphigus vulgaris over back



Fig. 2: A. Crusted area of Pemphigus Vulgaris over neck, B. Crusted area of Pemphigus Vulgaris over right forearm, C. Healed lesion of Pemphigus Vulgaris on index finger of right hand, D. Healed patches of Pemphigus Vulgaris on left forearm

Case 3

A 34 y old female patient developed fluid-filled lesion for 12 months with aggravated fluid-filled lesion over back, flank, oral ulcers for 15 d, crusted areas over body since 12 d and Dysphagia since 6 d (fig. 3). She had history of lesions over back and took over the counter (OTC) medication but was not treated. With a history of recurring oral ulcers and hospitalization due to non-compliance, the lesions aggravated. Punch biopsy confirmed Pemphigus Vulgaris. From eighth day, pedal and hand oedema started. Dexamethasone was given with low dose overnight to treat new facial lesions since fourth day. Cyclophosphamide was given as a steroid-sparing agent. During hospitalization, new vesicles appeared over body so, acyclovir was given. Alleviative therapy was given. Analgesics were given to relieve body ache. Calamine lotion for miliaria, benzydamine mouth wash for oral ulcers, antibiotic creams for infection and ciprofloxacin eye drops for crusting around eyes. Prednisolone 30 mg, cyclophosphamide, betamethasone lotion was advised for 7 d.

Case 4

A 50 y old female patient experienced painful oral ulcers, dysphagia, skin lesions over body trunk extending to all extremities, anorexia, diffuse hair fall and disturbed sleep. Punch Biopsy diagnosed Pemphigus vulgaris. Paracetamol IV was given to reduce fever which occurred during hospitalization. Dexamethasone alone was given with symptomatic treatment. 40 mg prednisolone and liquid paraffin cream was given for 7 d.

Case 5

A 45 y old male patient presented plaques with crusting over the oral cavity, face, neck, abdomen, back and limbs. Patient developed itching with lesions 2 Y back and is a case of PV but was non-adherent to prednisolone for 1.5 months. During hospitalization, dexamethasone was prescribed with supportive care. Patient had a fever, so paracetamol was given. On the second day, Ophthalmic examination was done due to red eyes, which diagnosed Grade-III Nasal Pterygium. Prednisolone 30 mg with antibiotics, topical corticosteroid was prescribed on discharge.

DISCUSSION

Pemphigus is a group of rare autoimmune blistering diseases of which PV is the common type [7]. PV is an immunopathogenic dermatologic disease characterized by cutaneous or mucosal blister formations that, when remain untreated, may lead to life-threatening condition. These are more prevalent in females than males with the age of 50-60 Y being mostly affected [3]. Eighty percent patients in our series are females and 20% are males, which aligns with the study by Ljubojević *et al.*, (2002) [8]. The people exposed to organophosphates, allergens, diet, and stress are predisposed to this disease [9]. PV primarily involves the production of autoantibodies against desmogleins, especially Desmoglein III, causing acantholysis and blister formation (Cholera and Chainani-Wu, 2016) [10]. The characteristic lesions and blisters are caused by the separation of keratinocytes in the epidermis, and if they are not well controlled, they can result in considerable morbidity and mortality (Sadeghzadeh-Bazargan *et al.*, 2023) [11]. The lesions are found in the oral mucosa and areas with frictional trauma (cheek mucosa, oesophagus, and genital mucosa) [4]. The symptoms primarily affect the oral health and thus, this disease should be symptomatically managed as soon as possible. It is diagnosed by taking 4 mm punch biopsy and detection of desmoglein antibodies. Standard treatment involves systemic and topical corticosteroids as it controls disease progression [12]. Additionally, studies by Tsuruta *et al.*, (2012) and Hashimoto *et al.*, (2012) states that cyclophosphamide and mizoribine have been used as adjuvant therapies because it gives steroid-sparing effect, which aligns with our series. They also stated about the use of antihistamines, analgesics, and topical antibiotics for symptomatic relief [13, 14]. If untreated, it has a high fatality rate due to substantial skin involvement.

Table 1: Comparison between five patients of pemphigus vulgaris

Parameter	Case one	Case two	Case three	Case four	Case five
Period of primary manifestation	1.5 y back	6 mo back	1 y back	20 d back	2 Y back
Regions with lesions	Mouth, leg, abdomen, Chest, back, scalp and mouth, Nipple, genitalia	Mouth, Back, flanks, upper limbs, thighs	Mouth, Back, flanks, chest, buttocks, thighs, legs, arm, eyes, genitals	Mouth, Back, chest, abdomen	Mouth, Chest, abdomen, back, all limbs, neck
Medical history	K/C/O PV	K/C/O PV	K/C/O PV	-	K/C/O PV
Medication history	Ayurvedic treatment	Oral prednisolone 10 mg	Over-the-counter medication	-	Prednisolone 40 mg
Family history	Maternal aunty C/O PV	-	-	-	-
Diet	Unhealthy	Reduced	Reduced	Reduced	Low
Abnormal relevant laboratory investigation	1) WBC-18190/cmm(↑) 2) MCV-62.9 fl(↓) 3) S. Albumin-3.4 g/dl(↓)	1) MCV-61.1 fl(↓) 2) S. Albumin-3.30 g/dl(↓) 3) Neutrophil-72% (↑)	1) WBC-12420/cmm (↑) 2) MCV-70.6 fl(↓) 3) S. Albumin-2.9 g/dl(↓) 4) Neutrophil-83% (↑)	1) MCV-61.3 fl(↓) 2) S. Albumin-2.9 g/dl(↓)	1) WBC-13180/cmm(↑) 2) MCV-60 fl(↓) 3) S. Albumin-1.4 g/dl(↓)
Desmoglein Antibody	Desmoglein I-97.50 RU/ml Desmoglein III-143.41 RU/ml	-	-	-	-
Punch Biopsy	Suggestive of PV	Suggestive of PV	Suggestive of PV	Suggestive of PV	Suggestive of PV
Treatment plan	Dexamethasone IV 2cc→1 cc(after 5 d) Ceftriaxone IV 1g Ranitidine IV 25 mg Pheniramine maleate IV 25 mg Clonazepam PO 0.5 mg Escitalopram PO 10 mg Triamcinolone gel	Dexamethasone IV 2cc→1 cc(after 5 d) Ceftriaxone IV 1g Ranitidine IV 25 mg Pheniramine maleate IV 25 mg Cyclophosphamide PO 50 mg Amitriptyline PO 25 mg Triamcinolone gel, Benzocaine gel, Fusidic acid cream	Dexamethasone IV 1.5cc→1cc(from day22) Ceftriaxone IV 1g Ranitidine IV 25 mg Pheniramine maleate IV 25 mg Cyclophosphamide PO 50 mg Acyclovir PO 400 mg Triamcinolone gel, Clobetasol cream, Mometasone cream, Calamine lotion, Neosporin powder, Ciprofloxacin eyedrops, Carmellose eyedrops	Dexamethasone IV 1.5cc Paracetamol IV 150 mg Ceftriaxone IV 1g Pheniramine maleate IV 25 mg Triamcinolone gel, Clobetasol cream	Dexamethasone IV 1.5 cc→1 cc (after 7 d) Ceftriaxone IV 1g Ranitidine IV 25 mg Neosporin powder Pheniramine maleate IV 25 mg Triamcinolone gel, Benzocaine gel, Fusidic acid cream
Notable follow-up complaints	Anxiety, Irritation, and fever	Headache Day10-New vesicles and bullae over back Day11-New bullae on back	Day8-Pedal and hand oedema Day6-Fresh lesions over face, back and arms. Day8-Vesicle over face, chest and back Day13-New bulla over right forearm, back and left leg. Day14-Neck pain, erosions over face. Day17-Increased pain Day21-New bulla over back of right shoulder and back Day23-Throat pain Day24-New bulla over legs Day29-Neck stiffness	Fever	Nasal Pterygium
Discharge medication	Prednisolone PO 30 mg Linezolid PO 600 mg Rabeprazole PO 50 mg Triamcinolone gel, Fusidic acid cream	Prednisolone 10 mg Cyclophosphamide 50 mg Amitriptyline 25 mg Triamcinolone gel, Benzocaine gel	Prednisolone 30 mg Cyclophosphamide 50 mg Mometasone cream Triamcinolone gel, Clobetasol cream, Betamethasone lotion	Prednisolone 40 mg Liquid paraffin cream	Prednisolone 30 mg Amoxicillin 625 mg Ranitidine 150 mg Triamcinolone gel, Benzocaine gel, Fusidic acid

Legend: ↑-Raised levels than normal. ↓-Decreased levels than normal.

The summary of the five cases is elaborated in table 1. We observed complaints of oral ulcerations causing dysphagia, anorexia, paraesthesia resulting in sleep disturbance which are classic symptoms of PV. It further progressed to fluid-filled lesions over back, abdomen, scalp, flank extending to groin and all limbs. Patient-1 had a family history of PV, unlike other patients in this series. During the primary manifestation of PV, patient-1 took ayurvedic medication, patient-2 and patient-5 had non-compliance to the treatment, patient-3 had OTC medication, while patient-4 was newly diagnosed. Patient-1 developed anxiety, patient-2 had generalized headache, patient-4 had atrial abnormality while patient-5 had Nasal Pterygium. Patient-3 had crusting involving eyes and peripheral oedema. All cases had laboratory findings of Microcytic anaemia and Hypoalbuminemia. Upon admission, all patients received different dosages of corticosteroid according to their condition. Case-2 and 3 experienced worsened manifestation so, Cyclophosphamide was given to reduce disease progression. The different treatment strategies emphasize the need for Individualization of drug therapy to achieve disease control and prevent complications.

This series highlighted the worsening of illness due to non-adherence. According to Ljubojević *et al.* (2002), non-adherence to prescribed medications results in PV flares, underscoring the difficulties in managing PV, thus highlighting the crucialness of patient education and adherence to treatment plans. The correlation of PV with other illnesses including nasal pterygium, focal segmental glomerulosclerosis, and sepsis emphasizes the systemic nature and the demand for all-encompassing treatment approaches (Sadeghzadeh-Bazargan *et al.*, 2023; lan, 2024) [11, 15]. Given that some patients experienced anxiety and depression in relation to their condition, it is essential to address the psychosocial aspects of this disease.

CONCLUSION

PV is a rare autoimmune dermatological disease which leads to formation of lesions primarily affecting oral mucosal membranes. It is life threatening if untreated. Treatment for PV usually involves the use of corticosteroids and immunosuppressive medications to reduce inflammation preventing further damage to the skin and mucous membranes. Close monitoring by a healthcare provider is important for managing the condition, giving symptomatic relief, and preventing complications.

ABBREVIATIONS

PV-Pemphigus vulgaris, OTC-Over the counter, C/S-Culture-sensitivity, NSAID-Non-steroidal anti-inflammatory drug.

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AUTHORS CONTRIBUTIONS

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Evangeline Gladwin, Priyanshi Shah and Himani Shah. The first draft of the manuscript was written by Evangeline Gladwin, Priyanshi Shah and Himani Shah and all authors commented on previous versions of the manuscript. Krunal Tralsawalacritically revised the manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTERESTS

Declared none

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