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Case Report

Autoimmune Unraveling: Phenobarbital-Associated Pemphigus Vulgaris Case Report

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ABSTRACT

This case report presents the clinical scenario of a 22 years old female patient with decade long history of seizure disorder and is on chronic anti-seizure management therapy. The patient's initial symptoms manifested as lesions over the oral cavity, over the period of time the lesions progressed to scalp, chest and buttocks. Pemphigus is a rare heterogeneous group of autoimmune disease that affects the skin and the mucous membrane. A combination of inappropriate activation of host B lymphocytes producing intracellular ImmunoglobulinG antibodies and biochemical interactions results in the drug-induced pemphigus. Acantholypsia is the term for the process by which these auto antibodies target the desmogleins and split the cells in the epidermis. This case emphasizes the requisite for further research on understanding the effect of anti-seizure therapy.

Keywords: Barbiturates, Blister, Desmosomes, Epidermis, Lymphocytes.

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INTRODUCTION

Pemphigus Vulgaris (PV) is an autoimmune disease with common symptoms of blisters on mucosal and cutaneous surfaces.[1] Their origin stems from the synthesis of pathogenic auto antibodies, primarily of the IgG class, which are targeted against distinct desmosome proteins, or desmogleins. The combination of these auto antibodies with the desmosome components weakens intraepidermal adhesion, resulting in vesicles, blisters and erosions on the skin and/or mucous membrane.[2] Based on clinical and histopathological features, as well as the particular antigens that the auto antibodies are produced against, several forms of pemphigus have been identified.[3] PV is the predominant clinical form of pemphigus, making up about 70% of cases; it is also thought to be the most severe kind of the illness.[4] One can diagnose drug-induced pemphigus when a medication has caused a form of the disease. After starting the medication, pemphigus may appear days, weeks, or even up to six months later. Drug-induced pemphigus can be difficult to diagnose, particularly in patients taking multiple medications because symptoms may take longer to appear after ingesting the causative drug. The presence of typical antibodies on direct immunofluorescence and the characteristic intra epidermal blistering observed on skin biopsy histology confirm the diagnosis of pemphigus.[5]

CASE REPORT

A 22-year-old female patient weighs 56 kg got admitted in dermatology department in tertiary care teaching hospital, with chief complaints of painful fluid filled lesions over the oral cavity (Figure 1), scalp (Figure 2), trunk (Figure 3), chest (Figure 4), genital and buttocks since 1.5 months. History revealed that lesions initially started over the oral cavity 1.5 months back, which gradually increased in size and number over scalp, chest and buttocks over a period of 15 days. She was the third child of second-degree consanguineous marriage with no history of similar complaints in the family. She developed epilepsy at the age of 9 years and was treated with the Tab. Phenobarbital 60 mg (0-0-1) for 13 years, she developed lesions which were associated with itching moderate to severe in nature and insomnia since 15 days. The patient underwent chest X-ray, 2-D ECHO and ECG (Figure 5) which showed sinus rhythm with poor R wave progression. Her Peripheral smear report revealed normocytic, normochromic blood picture with neutrophilia. Direct immunofluorescence in which C3 was negative, IgG showed 2+ fish net pattern positive in epidermis, IgA and IgM was negative. Skin biopsy was done in which section study showed the structure of skin with the epidermis showing suprabasal bullae consisting of plenty of neutrophils few eosinophils and acantholytic cells. Sub epithelium showed chronic inflammatory cell infiltrates, adnexal structures

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and few blood vessels and features were suggestive of Pemphigus Vulgaris. The current treatment comprises of Cap. Amoxiclav 625 mg (1-0-1), Tab. Pantoprazole 40 mg (1-0-0), Tab. Paracetamol 500 mg (1-0-1), Tab. Phenobarbital 60 mg (0-0-1), Tab. Levetiracetam 500 mg (1-0-1), Mucopain gel(1-1-1), Triamcinolone gel (0-0-1), Chlorhexidine mouth wash (1-0-1), Tab. CTZ (1-0-0), Tab.

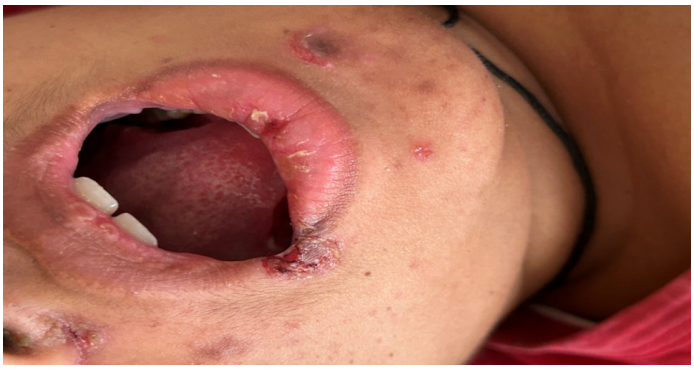

Figure 1: Oral Cavity Blister.

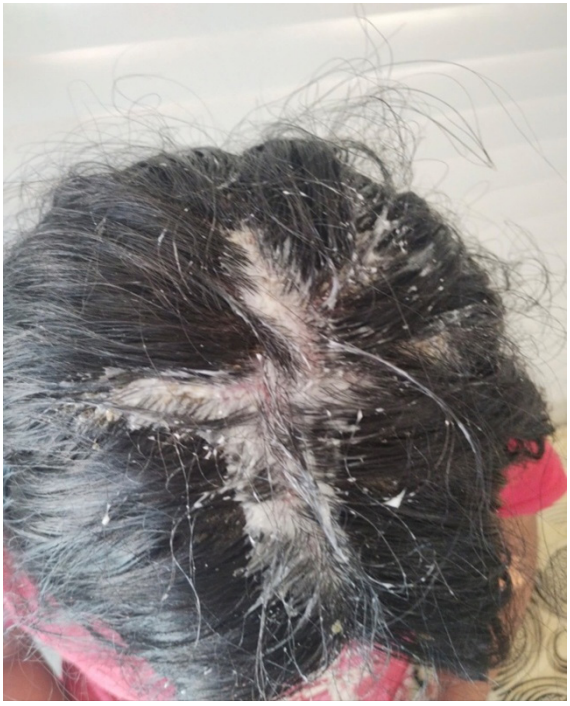

Figure 2: Lesions on Scalp.

Vitamin B-complex (0-1-0), saline compression (1-1-1-1), Soframycin skin cream (1-0-1), Inj. Dexamethasone 2cc IV (1-0-0), Tab. CPM (0-0-1), Tab. Azathioprine 50 mg (1-0-1), Clobetasol cream (0-0-1), Flucinolone shampoo. The treatment was given for 15 days and discharged with the medications Tab prednisolone 40 mg 1-0-0X 6 days, Tab prednisolone 30 mg 1-0-0X 10 days, Tab prednisolone 20 mg 1-0-0 X10 days, Tab levitiracetam 500 mg 1-0-1, Tab clobazam 10 mg 0-0-1, Tab pan 40 mg 1-0-0, Tab FS/BC/Ca 0-1-0, Tab CPM 0-0-1, Tab CTZ 1-0-0, Tab PCT 500 mg sos and Soframycin ointment L/A 1-0-1. painful fluid filled lesions over the oral cavity, scalp, back and chest was found to be gradually decreased. Overall, there is a lack of well controlled clinical studies on the proper treatment of drug-induced pemphigus, but the mainstay of the therapy

Figure 3: Lesions on Trunk.

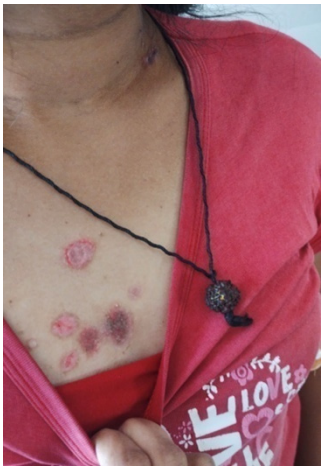

Figure 4: Lesions on Chest.

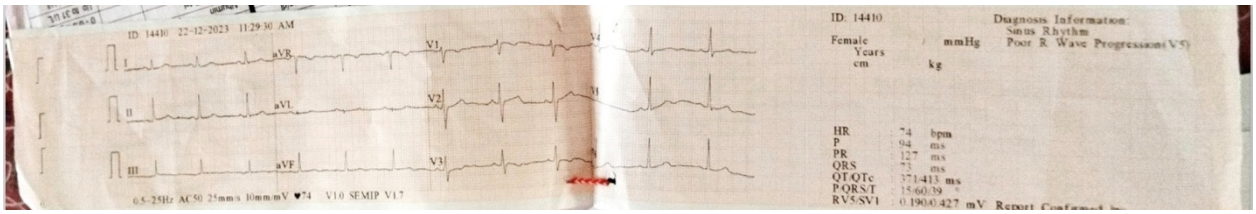

Figure 5: ECG Report.

continues to consist of a combination of corticosteroids and an immunosuppressive agent such as Azathioprine.

DISCUSSION

Pemphigus is a potentially fatal inflammatory disease of the skin and mucous membranes that is defined histologically by acantholysis and clinically by blisters and erosions.[6]

Acantholysis is a morph functional alteration of malpighian epithelia that causes the keratinization process to stop and intercellular cohesiveness to disappear. Piqued by circulating and skin-fixed auto antibodies directed against the intercellular desmosomes of epidermal keratinocytes-that is, two sets of transmembrane glycoproteins known as Desmoglein (Dsg) and Desmocollin (Dsc)-it is thought to be the primary patho-genetic event in pemphigus. Both proteins are members of the family of cadherin genes. Dsg-1 and Dsg-3 are the desmogleins most commonly implicated in the pathophysiology of pemphigus. While Dsg-3 is significantly expressed in mucosa and poorly expressed in the epidermis, Dsg-1 is mostly expressed in the upper layers of the epidermis and weakly in the squamous mucosa. Accordingly, pemphigus foliaceus typically has high amounts of anti-Dsg-1 antibodies, whereas pemphigus vulgaris typically has high levels of anti-Dsg-3 antibodies.[7]

Phenobarbital is classified as a barbiturate medicine. Barbiturates are primarily employed as oral anticonvulsants or intravenously as anesthetics these days. To inhibit the activity of excitable tissue, they mainly work on the Central Nervous System's (CNS) Gamma Amino Butyric Acid (GABA) channels.[8] With a half-life of up to 12 hr after intake; phenobarbital is a long-acting barbiturate with the lowest abuse potential. Apart from central nervous system depression, barbiturate overdoses can cause acute cognitive impairment, which typically results in delirium, irritability, combativeness and paranoia. Much fewer cases involve dermatological findings. In actuality, they happen about 6% of the time in barbiturate poisonings. However, after fatal phenobarbital toxicities, 50% of patients with dermatological abnormalities would present with obvious, bullous skin lesions that are tense and uncertain in their genesis. According to one of the first case reports, numerous bullous lesions on the surface and conjunctivae of the eyes are a sign of severe barbiturate poisoning.[9]

The absence of new lesions during the patient's close surveillance by the medical staff points to a recent history of topical chemical exposure. It's probable that handling the phenobarbital pills by hand exposed the patient topically to the drug's active components. In the same vein, it is possible that the patient was topically exposed to a toxin or substance other than phenobarbital. The clinical significance of this case is that lesions can result from oral intake of doses of phenobarbital similar to those that are recommended, assuming that her dermatologic lesions were in fact entirely or partially caused by phenobarbital oral ingestion. According to all prior case reports, phenobarbital only causes lesions when injected in the area around the injection site or after sufficiently high dosages to cause coma. This could indicate increased concentrations in the veins close to the injection site prior to systemic dilution, or it could indicate subcutaneous leaking.

CONCLUSION

Beyond therapy, there is no need for continued care since the lesions self-regulate. For the purpose of preventing secondary infection of burst bullous lesions, a broad-spectrum antifungal ointment, like Soframycin topical cream, is adequate. Within two weeks, most bullous lesions disappear and are replaced by clinically normal, intact skin. Based only on this one case report, conclusions on the mechanism of bullous lesion formation cannot be drawn. However, medical professionals should be aware of this possible side effect if phenobarbital is still taken orally. Healthcare practitioners on phenobarbital should be on the lookout for skin manifestations in their patients, stressing the importance of careful observation and interdisciplinary teamwork in handling such cases. To clarify the precise processes behind this fascinating relationship, more investigation is necessary.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

CNS: Central Nervous System; **CPM:** Chlorpheniramine; **CTZ:** Cetirizine; **Dsg:** Desmoglein; **Dsc:** Desmocollin; **ECG:** Electrocardiogram; **2D ECHO:** 2 - Dimensional Echocardiogram; **GABA:** Gamma Amino Butyric Acid; **HCT:** Hematocrit; **HGB:** Hemoglobin; **Ig:** Immunoglobulin; **MCV:** Mean Cell Volume; **PV:** Pemphigus Vulgaris; **RBC:** Red Blood Cell; **WBC:** White Blood Cell.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The consent to participate has been provided as supplementary file.

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