Case Report

Drug-induced Pemphigus Vulgaris of the Gingiva: An Unusual Case Report

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Abstract

Pemphigus vulgaris (PV) is a rare autoimmune blistering disease that frequently affects the oral mucosa and is characterized by painful mucocutaneous blisters and erosions. In this particular case report, a 26-year-old woman reported desquamative gingivitis and gingival overgrowth, underscoring the difficulty in detecting and treating oral disorders that could have systemic effects. Given the patient's history of phenytoin use, drug-induced gingival enlargement, which resembled PV was suspected. Clinical, histopathological, and immunological evidence were used to make the diagnosis, and ELISA testing confirmed the existence of autoantibodies against Desmoglein 3. Immunosuppressive medications, such as corticosteroids and immunosuppressive drugs, were commonly used in the treatment, while newer options like Rituximab presented hopeful alternative with less adverse effects. This example highlights how PV management is changing, with targeted medicines being investigated more and more to enhance patient's outcome and quality of life, underscoring the significance of a comprehensive approach to diagnosis and treatment.

Keywords: Autoimmune disorder, Drug-induced gingival enlargement, Pemphigus vulgaris, Phenytoin.

Introduction

Pemphigus vulgaris (PV), a rare and disabling autoimmune blistering illness, mostly affects the skin and mucous membranes, producing uncomfortable intraepithelial blisters and erosions. PV is a well-known disease, but when it only affects the gingiva, it takes on a special and extremely unusual form. This presentation, which is frequently brought on by particular drugs, poses a unique clinical challenge and necessitates a thorough comprehension of its origin, pathophysiology, clinical aspects, and key characteristics. This introduction gives a summary of drug-induced PV and emphasizes the molecular element involving the Desmoglein 1 and 3 genes, drawing on knowledge from pivotal studies.[1-7]

Onset and pathogenesis

Ramoa *et al*. (2000),[1] revealed that PV can happen at any age, including adolescent. Desmogleins are adhesion molecules crucial for tissue integrity, and autoantibodies, usually IgG, that target them are the pathogens that cause it. These autoantibodies attach to Desmogleins, which causes acantholysis and blister development. Drug-induced PV is a distinct type brought on or aggravated by specific drugs, such as angiotensin-converting enzyme inhibitors, as reviewed by Trackman and Kantarci in 2015.[4] These medications may alter immune function by triggering the creation of autoantibodies or escalating already present autoimmune conditions.

Molecular aspect: Desmoglein 1 and 3 genes

The molecular element involving Desmoglein genes is crucial to comprehend PV, particularly drug-induced variations. The desmosomal cadherin family includes Desmogleins, such as Desmoglein 1 and 3. The epidermis and mucous membranes depend on these transmembrane glycoproteins for cell-cell adhesion.[4] Desmoglein 3, which is expressed in the basal and suprabasal layers of stratified squamous epithelia, is the main target of autoantibodies in PV. Desmoglein 1 can also be targeted; it is located in the top epidermal layers.[4] Desmosomal adhesion is broken down as a result of autoantibody binding to these proteins, which ultimately results in blister formation.

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Clinical features

Clinical signs of PV include painful mucocutaneous blisters and erosions, which frequently impact the gingiva and cause severe swelling and ulceration along with discomfort and poor oral hygiene. Along with the distinctive Nikolsky's sign, PV can also present as skin lesions, mouth ulcers, and involvement of other mucosal surfaces. Drug-induced PV differs from conventional PV in that it exclusively or predominately affects the gingiva and is frequently linked to particular drugs, making diagnosis more difficult. For a proper diagnosis and course of treatment, a thorough review of the clinical, histological, and immunological findings is essential.[3,5,6]

Principal features of drug-induced PV[2,3,4,6]

1. Gingival Predominance: Drug-induced PV differs from conventional PV in that it exclusively or predominately involves the gingiva.
2. Drug-Triggered: This variety emphasizes the importance of drug history in diagnosis by being closely related with particular medications.
3. Immunological alterations: Medication-induced immunological alterations might aggravate or trigger the formation of autoantibodies against Desmogleins, especially Desmoglein 3.

Therefore, among the variety of PV, drug-induced PV of the gingiva poses a special therapeutic problem. It differs from typical PV in terms of its onset, etiology, clinical symptoms, and primary characteristics. Understanding the underlying molecular mechanisms of the Desmoglein genes, particularly Desmoglein 1 and 3, is essential for understanding the disease. To lessen the potential severity of this illness, early detection and management are crucial. This case report lays the groundwork for a more in-depth investigation of drug-induced PV, using cited literature to explain this fascinating dermatological condition.

Patient presentation

A 26-year-old female patient reported to the department with the chief complaint of desquamative gingivitis, gingival overgrowth, and bleeding on light probing (Figure 1a-c). The patient was receiving phenytoin, an antiepileptic medication. Routine oral prophylaxis was done and oral hygiene instructions were given. The following drugs were recommended like candid mouth paint to be used twice daily, an antioxidant tablet to be taken once daily for 30 days, and Kanacort 0.1% ointment (triamcinolone) for topical treatment. The patient was referred to the Neuromedicine in state general hospital for possible replacement of the said drug in the antiepileptic medication since it was thought that the medication might have caused desquamative gingivitis.

Primary diagnosis

Based on clinical symptoms and the patient's medication history, the primary diagnosis of drug-induced gingival enlargement (DIGE) with PV was made.

Investigations

To confirm the diagnosis, the patient was advised for ELISA testing to show Desmoglein 1 and 3. The autoantibodies against Desmoglein 3 were found in the test findings, supporting the PV diagnosis (Figure 2). Lesions of the skin were also seen on the upper and lower limbs.

Referral to dermatology

The appearance of skin lesions and the confirmation of PV led to the patient's referral to the dermatology department at the National Medical College in Kolkata for additional assessment and care. Prednisolone 10 for 2 weeks, Azathioprine 50 twice daily, and ongoing calcium and Vitamin D3 supplementation were all part of the patient's dermatological treatment plan. For oral hygiene maintenance, chlorhexidine mouthwash (0.2%) was recommended. Levatiracetam 500 mg twice daily was used in place of the probable condition-triggering drug phenytoin.

Monoclonal antibody administration and follow-up

The patient was instructed to administer a monoclonal antibody (Rituximab) as part of the therapy strategy, with a 1-year follow-up period anticipated.

This case study demonstrates the intricate relationship between PV and drug-induced gingival hypertrophy. In the diagnosis

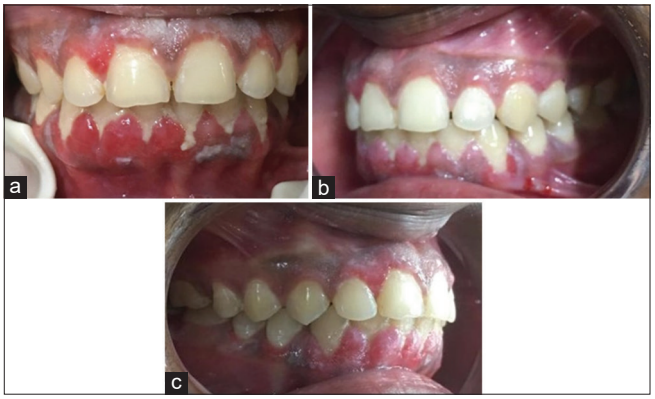

Figure 1: (a-c) Desquamative gingivitis, gingival overgrowth, and bleeding on light probing

Test Report

Test Name	Results	Units	Bio. Ref. Interval
DESMOGLEIN (DSG) 1 AND 3 ANTIBODY (IFA)			
Desmoglien 1	Negative		
Desmoglein 3	**Positive**		
Titer	1:10		

Note

1. Auto Immune reactivity are not by themselves diagnostic and must be correlated with other laboratory and clinical findings.
2. Test conducted on Serum.

Interpretation

PEMPHIGUS DISEASES	TARGET ANTIGEN
Pemphigus vulgaris	DSG 3
Pemphigus foliaceus	DSG 1
IgA pemphigus	DSG 1 or DSG 3 & Desmocollin 1

Figure 2: Autoantibodies against Desmoglein 3 were found positive by ELISA test

and treatment of such situations, it emphasizes the value of interdisciplinary cooperation between the dental, neurological, and dermatological departments. To improve the patient's overall health and quality of life, early detection, effective medication management, and specialist treatments such monoclonal antibody therapy are crucial.

Discussion

PV is a rare autoimmune blistering disease that frequently affects the oral mucosa and causes painful mucocutaneous blisters and erosions. Oral ulcers, skin lesions, and mucosal involvement are some of the traditional clinical signs of PV (Malik *et al*., 2021; Lim *et al*., 2022).[7,8] This case illustrates the difficulty in detecting and treating oral disorders with potential systemic effects by presenting a 26-year-old girl with gingival overgrowth, desquamative gingivitis, and a history of antiepileptic drug usage (phenytoin).

In clinical practice, gingival hypertrophy is a frequent oral finding, and its causes might be complex. Differentiating between illnesses, such as DIGE and autoimmune blistering disorders like PV that might present with identical clinical characteristics is one of the difficulties in diagnosing gingival enlargement. The patient in the present case report was on phenytoin, an antiepileptic medication, and research has linked it to DIGE previously (Trackman and Kantarci, 2015; Kim and Lee, 2020).[4,6]

Understanding PV's pathogenesis requires an understanding of its immunological components. Autoantibodies, mostly IgG, are produced in PV and are directed against Desmogleins, specifically Desmoglein 1 and 3 (Malik *et al*., 2021; Lim *et al*., 2022).[7,8] According to Holmstrup *et al*. (2018),[9] these desmosomal cadherin proteins are essential for preserving cell-cell attachment in the epidermis and mucous membranes. Desmoglein autoantibodies damage epithelial cell layers, causing intraepithelial blister development, a defining characteristic of PV.

A combination of clinical, histological, and immunological results is used to make the diagnosis of PV. In this instance, autoantibodies against Desmoglein 3 were found by ELISA testing, validating the diagnosis of PV which could be related to previous cases as reported by Moshe, 2020; Lim *et al*., 2022; Ramesh *et al*., 2021.[8,10,11] This diagnostic phase is essential because it offers a thorough evaluation of the underlying autoimmune process.

When assessing individuals with desquamative gingivitis and gingival hypertrophy, differential diagnosis is crucial. Lichen planus and other autoimmune blistering illnesses can mimic PV at times (Holmstrup *et al*., 2018; Ramesh *et al*., 2021).[9,10] To determine the best course of treatment, it is crucial to rule out certain illnesses and make an accurate diagnosis.

Immunosuppressive treatments are frequently used to treat PV to reduce disease activity and stop new blister development. Prednisolone and other corticosteroids are frequently used as the first-line therapy, particularly when the condition is severe (Pettini *et al*., 2015; Kim and Lee, 2020; Lim *et al*., 2022).[5,6,8] To lessen the dependence on corticosteroids and their accompanying negative effects, immunosuppressive medications such Azathioprine may also be administered (Pettini *et al*. 2015).[5]

The scheduled injection of monoclonal antibody therapy, namely, Rituximab, as part of the treatment plan is one noteworthy feature of this instance. Rituximab, which targets B cells and lowers the formation of autoantibodies against Desmogleins, has proven to be an effective therapeutic option for PV (Malik *et al*., 2021; Lim *et al*., 2022; Moshe, 2020).[7,8,11] This highlights the changing PV therapeutic landscape and the promise for more focused and immunosuppressive-free methods of treating the illness.

In situations like these, when oral symptoms may be a sign of underlying systemic problems, interdisciplinary teamwork is essential. The fact that the patient in this case was referred to several specialties, including dermatology, dentistry, and neurology, emphasizes the value of a comprehensive approach to diagnosis and care (Moshe, 2020; Ferreira *et al*., 2013).[11,12] Immunosuppressive medications are used in combination to treat PV, with recently developed drugs like Rituximab giving intriguing alternatives. To ensure an accurate diagnosis and improve patient treatment, interdisciplinary collaboration is essential. This case serves as an example of how the PV treatment landscape is changing, with more and more focused medicines being investigated to enhance patient outcomes and quality of life.[1-3,6,7,12]

The complexity of detecting and treating oral illnesses with potential systemic ramifications is demonstrated by this example, especially when they manifest with similar clinical characteristics. Through ELISA testing, which identified autoantibodies directed against Desmoglein 3, the diagnosis of PV was confirmed, proving the illness's autoimmune etiology. Differential diagnosis is essential in excluding disorders that can resemble PV, highlighting the necessity of a thorough assessment of clinical, histological, and immunological findings.

Conclusion

This case report highlights the critical need of accurate diagnosis in PV, a complicated autoimmune blistering condition. PV must be distinguished from other disorders with similar clinical manifestations, such as DIGE, using immunological testing, particularly ELISA for autoantibodies against Desmoglein 3. A thorough diagnosis and individualized treatment strategies require interdisciplinary cooperation between the dental, neurological, and dermatological departments, highlighting the importance of a comprehensive patient care strategy. The use of cutting-edge treatments like Rituximab emphasizes how the PV treatment landscape is changing. These targeted medicines have the potential to boost patient outcomes while lowering the need for conventional immunosuppressive drugs.

In conclusion, this case report serves as a succinct reminder of the complexity of autoimmune diseases, the significance of accurate diagnosis, and the promise for cutting-edge treatments to improve the lives of PV-affected people. Knowing about recent medical developments is essential to provide patients with therapeutic options that are both successful and minimally intrusive.

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