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Case Report

Concurrent oral and genital herpes simplex virus infection leading to diagnosis of pemphigus vulgaris: A case report

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Abstract

A 39-year-old woman presented with a one-month history of painful oral ulcers involving the inner lip, buccal mucosa, and pharynx, followed by fever and the appearance of multiple tender purulent genital ulcers. Tzanck smear from both oral and genital ulcers was positive for multinucleated giant cells, and HSV serology showed IgG positivity for HSV-1 and HSV-2. She was treated with oral aciclovir and co-amoxiclav, resulting in complete resolution of genital ulcers and partial improvement of oral lesions. Two weeks later, she developed new erosive skin and lip lesions. This case highlights the diagnostic challenge of differentiating herpes simplex virus (HSV) infection from early pemphigus vulgaris, as HSV may either trigger or mimic pemphigus lesions, underscoring the need for histological evaluation in atypical or persistent mucocutaneous ulcers. In this patient, the dermatology referral for skin biopsy, histologically confirmed the diagnosis of pemphigus vulgaris.

Key words: genital herpes, oral herpes, pemphigus vulgaris, Tzanck smear, autoimmune disease

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Introduction

Herpes simplex virus (HSV) infections are common worldwide, with HSV-1 typically causing orolabial infections and HSV-2 primarily causing genital herpes (1). Typical lesions are painful vesicles or ulcers, but atypical presentations can occur, complicating diagnosis (2). Additionally, HSV infection may trigger or exacerbate autoimmune diseases such as pemphigus vulgaris (PV), a rare blistering disorder (3). This report describes a case of rare concurrent oral and atypical genital HSV infection complicated by subsequent PV diagnosis.

Case presentation

A 39-year-old married woman from Kalutara, Sri Lanka, presented to the STD clinic, Colombo, Sri Lanka with painful oral ulcers over the inner lips,

buccal mucosa, and pharynx for one month, preceded by low-grade fever. Two weeks later, she developed multiple tender nodular genital

ulcers (0.25 cm diameter) on the labia majora, minora, mons pubis, and perineal commissures. She also complained of dysuria and mild vaginal discharge.

Examination showed multiple superficial, non-indurated oral ulcers and multiple tender nodular genital ulcers with serous discharge (Figures 1-3).

Figure 1. Superficial, well-defined, non-indurated mucosal ulcers noted over the inner right side of upper lip.

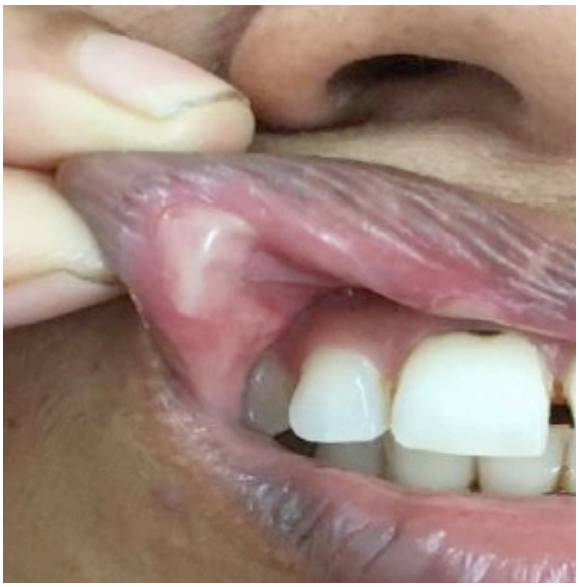


Figure 2. Superficial, well-defined, non-indurated mucosal ulcers noted over the inner side of the lower lip.

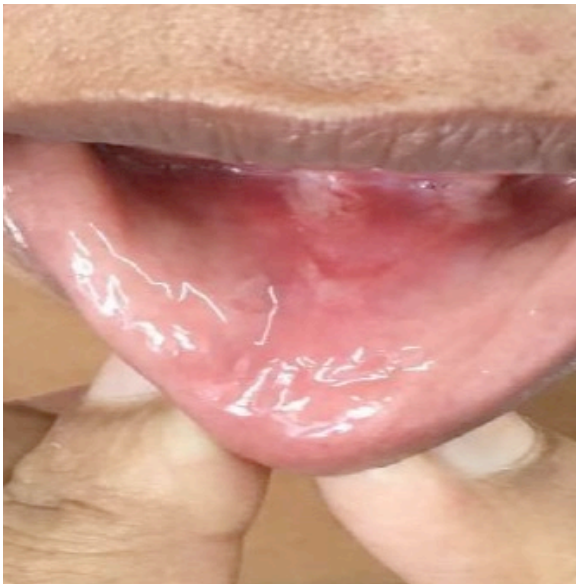
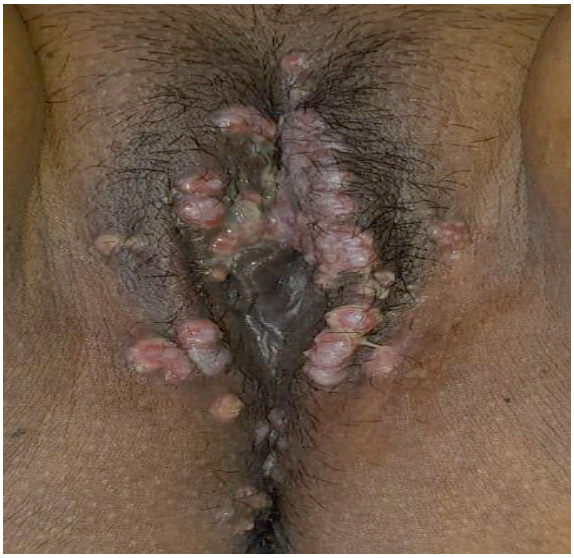


Figure 3. Multiple nodular ulcers seen over the anterior and posterior commissure, labia majora, minora and mons pubis



Investigations revealed a positive Tzanck smear showing multinucleated giant cells from both oral and genital ulcer sites, supporting a diagnosis of herpes simplex virus (HSV) infection. Dark ground microscopy for *Treponema pallidum* was negative, and syphilis serology, including VDRL and TPPA remained negative at both baseline and follow-up. HIV testing was also negative. HSV serology performed at three weeks demonstrated IgG positivity for both HSV-1 and HSV-2, further supporting prior exposure to the virus. HSV PCR was not available.

She was treated with oral aciclovir 400 mg eight hourly and oral co-amoxiclav 625mg eight hourly for one week for concurrent oral and genital herpes simplex virus infection, with complete resolution of genital ulcers and partial response to oral ulcers. Following 2 weeks of treatment, she developed new multiple superficial non-indurated oral ulcers as well as multiple tender nodular skin lesions over the chest and face. Skin biopsy of new oral and skin lesions showed suprabasal acantholysis and intraepidermal blistering consistent with pemphigus vulgaris.

Following corticosteroids and immunosuppressive therapy, patient reported complete healing of genital ulcers and gradual improvement of PV lesions. No systemic complications were reported during follow-up.

Discussion

HSV-1 and HSV-2 cause lifelong infections with latent phases in sensory neurons. Primary infection typically causes painful vesicular mucocutaneous ulcers. HSV-1 commonly causes orolabial infections; HSV-2 causes genital herpes via sexual transmission (1,2).

This patient's presentation with simultaneous oral and nodular genital ulcers was atypical and complicated by delayed healing and the development of new lesions in the skin following successful treatment with aciclovir.

In settings with limited resources, diagnosis relies on Tzanck smear detection of multinucleated giant cells, which has a sensitivity between 80-90% but limited specificity (4). PCR-based molecular diagnostics have higher specificity but the unavailability of the investigation warrants the diagnostic limitation in resource-limited settings. Hence, serological assays detecting type-specific antibodies (gG1 and gG2) support the diagnosis of HSV infection (5).

Syphilis, chancroid, and Behçet's disease are the other possible differential diagnoses (6–8), but they were excluded based on clinical findings and laboratory results. Irritant dermatitis was unlikely due to the absence of exposure history (9).

HSV infection can trigger or worsen autoimmune diseases such as pemphigus vulgaris by immune cross-reactivity (3). The patient's new oral lesions responsive to immunosuppressive therapy support the HSV-triggered Pemphigus vulgaris diagnosis.

PV is a potentially life-threatening autoimmune blistering disorder that primarily affects the mucous membranes and skin. The circulating autoantibodies targeting desmogleins—desmosomal cadherins critical for keratinocyte adhesion in the epidermis cause the disease. The binding of these autoantibodies leads to intraepithelial acantholysis and the characteristic blistering lesions of PV. Even though the disease has a well-established autoimmune basis, various environmental triggers, including medications, malignancies, and infections, are thought to influence its onset and exacerbation (3). Among the infectious agents, herpes simplex virus (HSV) has been increasingly implicated in the initiation and aggravation of PV.

The evidence to support an association between HSV and PV viral reactivation may serve as an environmental stimulus capable of breaking immune tolerance in genetically predisposed individuals is growing. HSV-induced epithelial damage may expose hidden antigens, triggering an autoimmune response. The molecular mimicry between viral components and desmosomal proteins may play a role in autoantibody production, alternatively. As HSV and PV can share overlapping manifestations—especially in mucocutaneous regions—leading to diagnostic confusion or delayed identification of dual pathology, this association is particularly relevant clinically.

With a global incidence ranging from 0.1 to 0.5 cases per 100,000 individuals annually, PV remains a rare disorder, epidemiologically. However, higher prevalence rates have been reported in specific ethnic and geographic populations. For instance, PV is more common among Ashkenazi Jews and individuals from India, the Middle East, and Southeast Europe. The typical age of onset is between 40 and 60 years, although cases outside this range have been documented. Gender distribution is generally equal, though regional variations exist. In Tunisia, for example, a female predominance has been reported, with a female-to-male ratio of 4:1 (10).

Clinically, PV often begins with oral involvement, with approximately 80% of patients presenting initially with painful erosions following the rupture of fragile mucosal blisters. These oral lesions may significantly impair nutritional intake and quality of life. The skin involvement typically follows the disease progression. Cutaneous lesions present as flaccid bullae or erosions on normal or erythematous skin and can appear anywhere but characteristically spare the palms and soles. The Nikolsky sign—blistering with gentle pressure—is a hallmark finding. Involvement of additional mucosal sites is common and may include the conjunctiva, nasal mucosa, larynx, esophagus, and anogenital areas (Table 1). Cervical PV can pose a diagnostic

challenge due to atypical Pap smear findings, potentially mimicking dysplasia or malignancy (10).

Table 1. Features of HSV and PV

HSV	PV
Usually, painful vesicular mucocutaneous ulcers	Blistering disorder that primarily affects the mucous membranes and skin, sparing the palms and soles
Orolabial herpes infections, usually caused by HSV-1 type	Often begins with oral involvement - painful erosions
Genital herpes infections, usually caused by the HSV-2 type	Mucosal sites - the conjunctiva, nasal mucosa, larynx, esophagus, and anogenital areas
	The Nikolsky sign—blistering with gentle pressure—is a hallmark

The interplay between HSV and PV has important clinical implications. In cases where HSV coexists with or mimics PV, misdiagnosis may occur if only one of the conditions is considered. Moreover, HSV infection may not only trigger the onset of PV but also contribute to disease flares in previously diagnosed patients (3). This dual pathology necessitates careful diagnostic workup, including histopathology, direct immunofluorescence, and appropriate viral testing. For HSV, the Tzanck smear remains a simple yet effective diagnostic tool, demonstrating multinucleated giant cells in active lesions. Meanwhile, PV diagnosis relies on identifying suprabasal acantholysis and intercellular IgG or C3 deposition in the epidermis (10).

Rarely, PV may present in atypical forms such as pemphigus herpetiformis, characterized by herpetiform or annular vesicles that can further complicate the diagnostic process by mimicking primary HSV infection. In such cases, the distinction relies heavily on histologic and immunopathological findings (3). Awareness of these rare presentations is critical to prevent misdiagnosis and to guide appropriate management.

In the case presented, the patient's clinical features included painful oral and genital erosions, with laboratory findings confirming both HSV infection and PV. The temporal relationship suggests a possible role of HSV in unmasking or exacerbating underlying autoimmune activity. This case highlights the importance of considering HSV not just as a differential diagnosis but also as a possible trigger in PV pathogenesis.

In conclusion, the potential link between HSV infection and PV underscores the need for a high index of suspicion and thorough diagnostic evaluation in patients presenting with mucocutaneous ulcerations. Managing HSV co-infection may play a role in controlling PV disease activity and improving outcomes.

Conclusion

Atypical HSV infections may mimic or precipitate autoimmune diseases such as pemphigus vulgaris. This case highlights the importance of early recognition of atypical presentations of genital/oral ulcers and referrals to relevant specialities for addressing both infectious and autoimmune aetiologies to minimize morbidity and psychological implications.

Therefore, persistent or atypical mucocutaneous ulcers warrant prompt histological evaluation. Hence, adequate knowledge, clinical vigilance, and multidisciplinary care are critical for optimal outcomes.

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