Dermatology Practical & Conceptual

Hand, Foot, and Mouth Disease As An Unusual Cutaneous Viral Infection Post-Rituximab: A Rare Observation

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Introduction

Pemphigus vulgaris is an IgG-mediated autoimmune blistering disorder caused by autoantibodies against desmosomal proteins, with genetic and environmental factors contributing to its pathogenesis. Rituximab, a CD20+ B-cell monoclonal antibody, is currently the first-line therapy but is associated with increased infection risk [1]. We report a case of pemphigus vulgaris complicated by Hand, Foot, and Mouth Disease (HFMD) following rituximab treatment.

Case Report

A 24-year-old female presented with multiple blisters over her face, thorax, and upper limbs and ulcerations of the oral mucosa for the preceding three weeks. Examination revealed flaccid blisters along with erosions over her face, upper thorax, abdomen, genitalia, and upper limbs; the palms and soles were spared (Figure 1). Oral mucosa showed extensive ulcers. Histopathological examination and direct immunofluorescence confirmed pemphigus vulgaris. She was initiated on oral prednisolone 40 mg once daily and supportive care.

She was scheduled for two doses of intravenous rituximab (1000 mg each, Day 0 and Day 14); The first dose was uneventful. At follow-up for the second dose, she had developed low-grade fever and new maculopapular-to-papulovesicular lesions over the palms and soles, alongside new painful oral ulcers. Lesions varied from 0.1 cm^2 on palms to 1 cm^2 on soles (Figure 2). Tzanck smear from new lesions showed no acantholytic cells or multinucleated giant cells.

Prior to the emergence of new lesions on palms and soles, pemphigus activity was relatively controlled, with no new vesicle on the body. The development of small oral ulcers and papulovesicular lesions on the palms and soles following low-grade fever, coupled with the absence of acantholytic cells and multinucleate giant cells on Tzanck smear, led to a diagnosis of adult HFMD. Corticosteroids were withheld, and the second rituximab dose deferred. After five days of symptomatic treatment with antihistamines and emollients,

palm and sole lesions resolved, but new flaccid bullae and erosions appeared. The second rituximab dose was later administered, leading to significant disease control during follow-up.

Rituximab has revolutionized pemphigus management by achieving higher remission rates than conventional therapies [1]. However, it increases infection susceptibility due to B cell depletion. Kridin et al. reported that rituximab-treated patients had higher rates of septicemia, pneumonia, cytomegalovirus, and herpes virus infections, particularly within the first six months. Chronic use also predisposes to neutropenia and hypogammaglobulinemia [2]. Cazzaniga et al. further identified pneumocystis pneumonia and viral reactivations as significant compli cations [3].

Figure 1. Multiple flaccid bullae and few vesicles, along with few bullae with overlying crust, present diffusely over the chest and abdomen.

Our patient developed HFMD following rituximab, with atypical acral and mucosal lesions. HFMD, caused mainly by Coxsackievirus A16 and Enterovirus 71, may present atypically in immunosuppressed individuals. Smail et al. described neurological complications following HFMD in a rituximab-treated patient [4].

Timely distinction between viral exanthem and pemphigus activity was crucial to avoiding exacerbating infection risks. Furthermore, infections may trigger autoimmune flares via molecular mimicry or epitope spreading [5].

Conclusion

This case highlights the need for vigilant infection surveillance in rituximab-treated pemphigus patients. Opportunistic infections can mimic or complicate underlying disease and must be promptly identified. Infection surveillance, pretreatment vaccination, and cautious scheduling of immunosuppressive therapy are essential to optimizing clinical outcomes and ensuring patient safety during rituximab-based treatment.

Figure 2. A: Multiple erythematous maculopapular to papulovesicular lesions present diffusely over bilateral palms ranging from 0.1 cm^2 to 1 cm^2. B: Multiple maculopapular lesions present all over bilateral soles.

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