Student's Journal of Health Research Africa
e-ISSN: 2709-9997, p-ISSN: 3006-1059
Vol. 6 No. 3 (2025): March 2025 Issue
https://doi.org/10.51168/sjhrafrica.v6i3.1570
Original Article

RECURRENT BULLOUS ERYTHEMA MULTIFORME SECONDARY TO HERPES SIMPLEX INFECTION IN AN 18-YEAR-OLD MALE: A CASE STUDY.

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ABSTRACT

Introduction
Erythema multiforme (EM) is an acute, immune-mediated mucocutaneous disorder characterized by characteristic targetoid lesions. The bullous subtype is rare and often triggered by infections such as herpes simplex Virus (HSV). Recurrent EM is strongly associated with HSV reactivation.

Case Presentation
We report an 18-year-old HIV-seronegative male with recurrent bullous erythema multiforme secondary to oral HSV infection. The patient had a two-year history of recurrent blistering episodes occurring every 2-3 months. Laboratory findings confirmed high HSV-1 IgG titers. Histological examination supported the diagnosis of bullous erythema multiforme. The patient was treated successfully with oral acyclovir suppression therapy, leading to a complete resolution of symptoms with no recurrences for six months.

Conclusion
This case highlights the importance of recognizing HSV as a potential trigger for recurrent bullous erythema multiforme and the effectiveness of antiviral suppression therapy in preventing recurrences.

Recommendation
Early identification of recurrent HSV-associated erythema multiforme is crucial for timely intervention. Long-term suppressive antiviral therapy should be considered in patients with frequent recurrences.

Keywords: *Bullous erythema multiforme, Recurrent erythema multiforme, Herpes simplex virus, Herpes Simplex Virus-associated erythema multiforme, Acyclovir suppression therapy*
Submitted: *2025-02-11* ***Accepted:*** *2025-03-09* ***Published:*** *2025-03-11*

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INTRODUCTION

Erythema multiforme (EM) is an acute, immune-mediated skin disorder characterized by distinctive targetoid lesions. It can be classified into minor and major forms based on the severity and the presence of mucosal involvement. Bullous erythema multiforme, a rarer subtype, features bullous lesions superimposed on typical target-like plaques.

Common triggers for EM include viral infections, particularly herpes simplex virus (HSV), medications, and, less frequently, bacterial infections such as *Mycoplasma pneumonia*. Recurrent erythema multiforme has a well-documented association with HSV, often linked to viral reactivation. In this case report, we present an HIV seronegative 18-year-old male with recurrent bullous erythema multiforme secondary to oral HSV infection, successfully managed with antiviral suppression therapy.

CASE PRESENTATION

An 18-year-old HIV seronegative male from Isingiro District, Western Uganda, presented to the skin clinic at Mbarara Regional Referral Hospital with a two-week history of generalized blistering. The patient reported a recurrent history of similar episodes over the past two years, occurring every 2–3 months. He described that each episode would begin with a burning and tingling sensation on the lower lip, followed by the development of a blistering rash in the same area. These lip blisters would typically dry up within a few days, after which a generalized blistering rash would appear, involving the trunk, limbs, palms, soles, and genitalia while sparing the oral cavity.

The patient had no history of chronic illness or allergies. He reported using Vaseline jelly as a moisturizer and worked as a farmer, spending much of his time outdoors herding

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animals under direct sun exposure. He denied using any medications.

Physical Examination

On examination, the patient was afebrile with a temperature of 36.4°C, respiratory rate of 17 breaths per minute, blood pressure of 125/87 mmHg, and oxygen saturation of 99-100% on room air. He appeared well, with no signs of distress.

A dermatological examination (figure 1, figure 2, and figure 3) revealed generalized targetoid plaques with mixed morphology. Some plaques had a dusky center, while others had bullous centers. These lesions involved the trunk, limbs, genitalia, palms, and soles but spared the oral mucosa. Atypical plaques with two zones were observed on the arms. Both Nickolsky and Asboe-Hansen's signs were negative on individual blisters, indicating the absence of epidermal detachment.

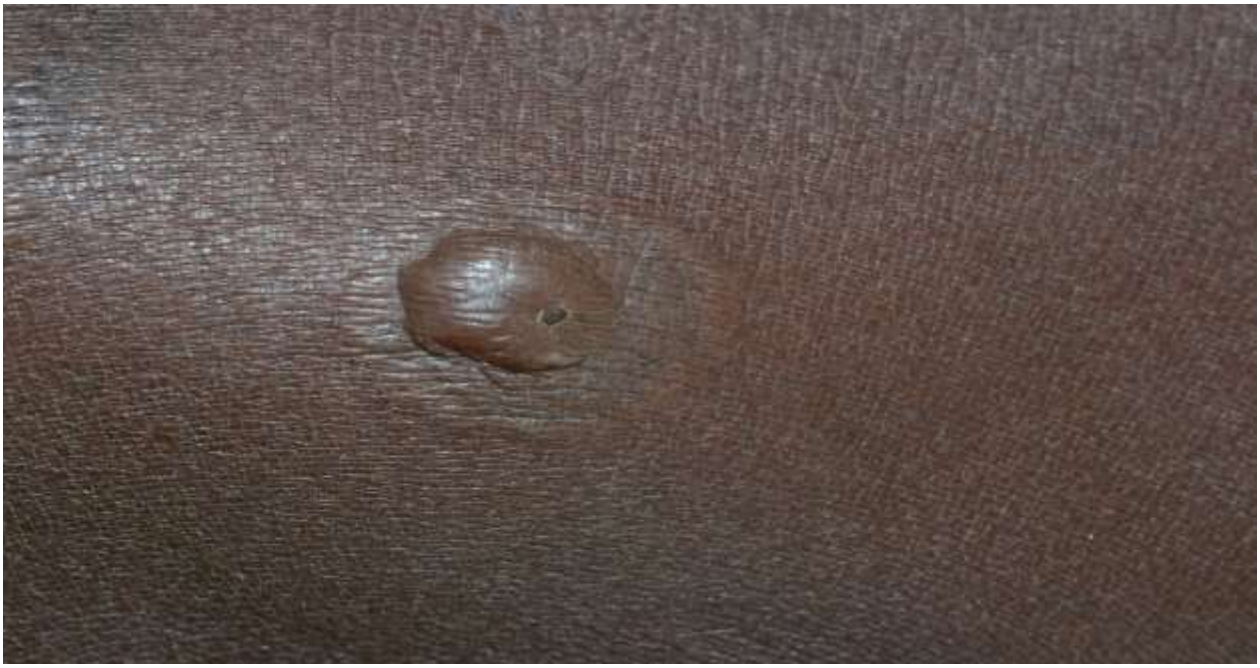

Figure 1. Bullous erythema multiforme: bullous lesion at the center of a targetoid plaque

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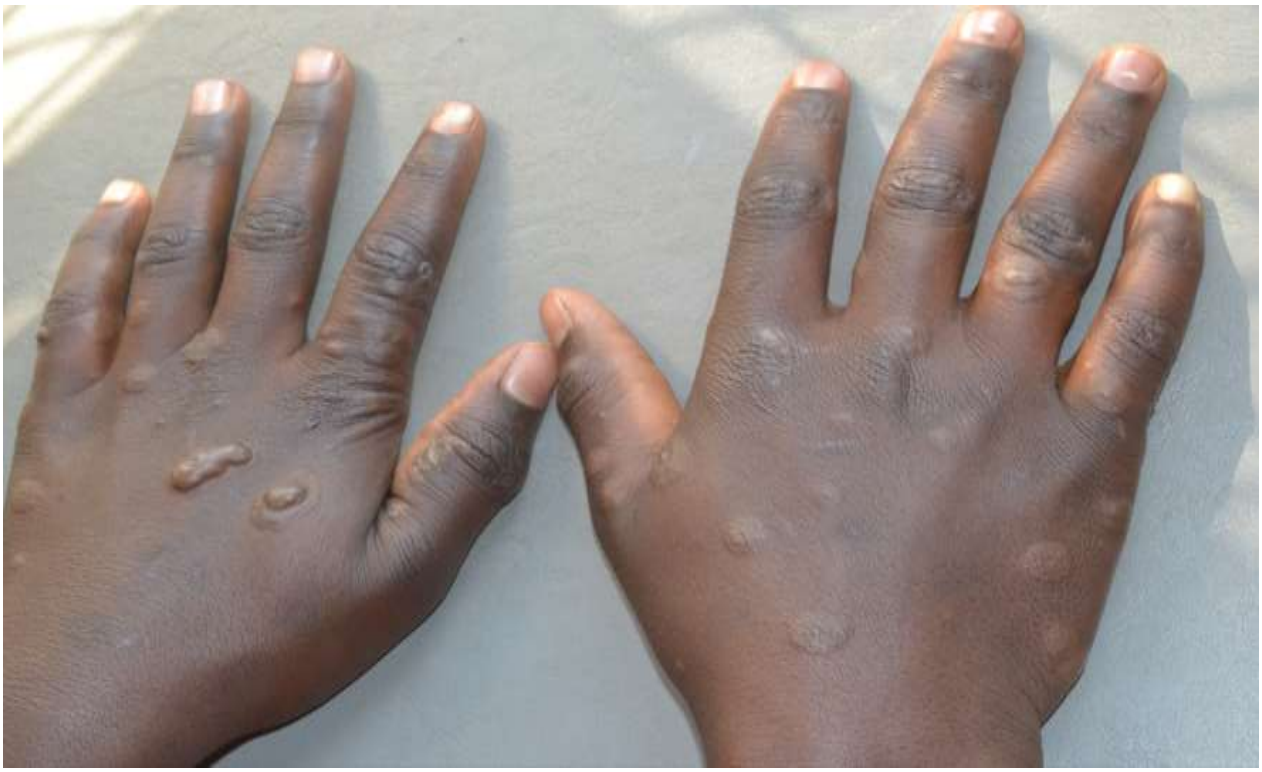

Figure 2. Mixed typical and atypical targetoid lesions on the hands

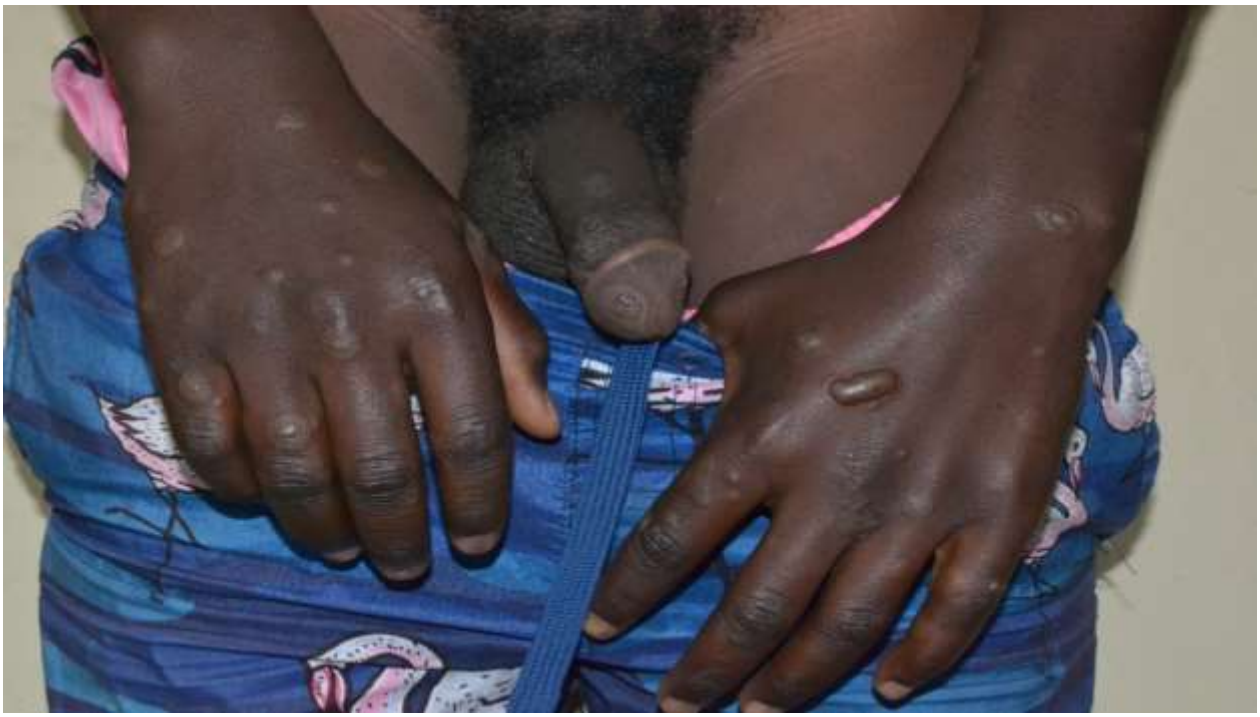

Figure 3. Targetoid lesions involving the genital

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Routine laboratory investigations, including tests for HIV, *Treponema pallidum* hemagglutination (TPHA), complete blood count (CBC), liver function tests (LFTs), and renal function tests (RFTs), were all within normal limits. HSV-1 IgG and IgM antibody titers revealed a positive HSV-1 IgG with high titers, indicating prior exposure or a chronic infection. HSV-1 IgM was negative, suggesting no evidence of an acute or recent infection. Histological examination of the skin section revealed focal intra-epidermal blisters, exocytosis, and a subdermal mixed inflammatory infiltrate composed of lymphocytes and plasma cells, as well as necrotic keratinocytes. (Figure 4)

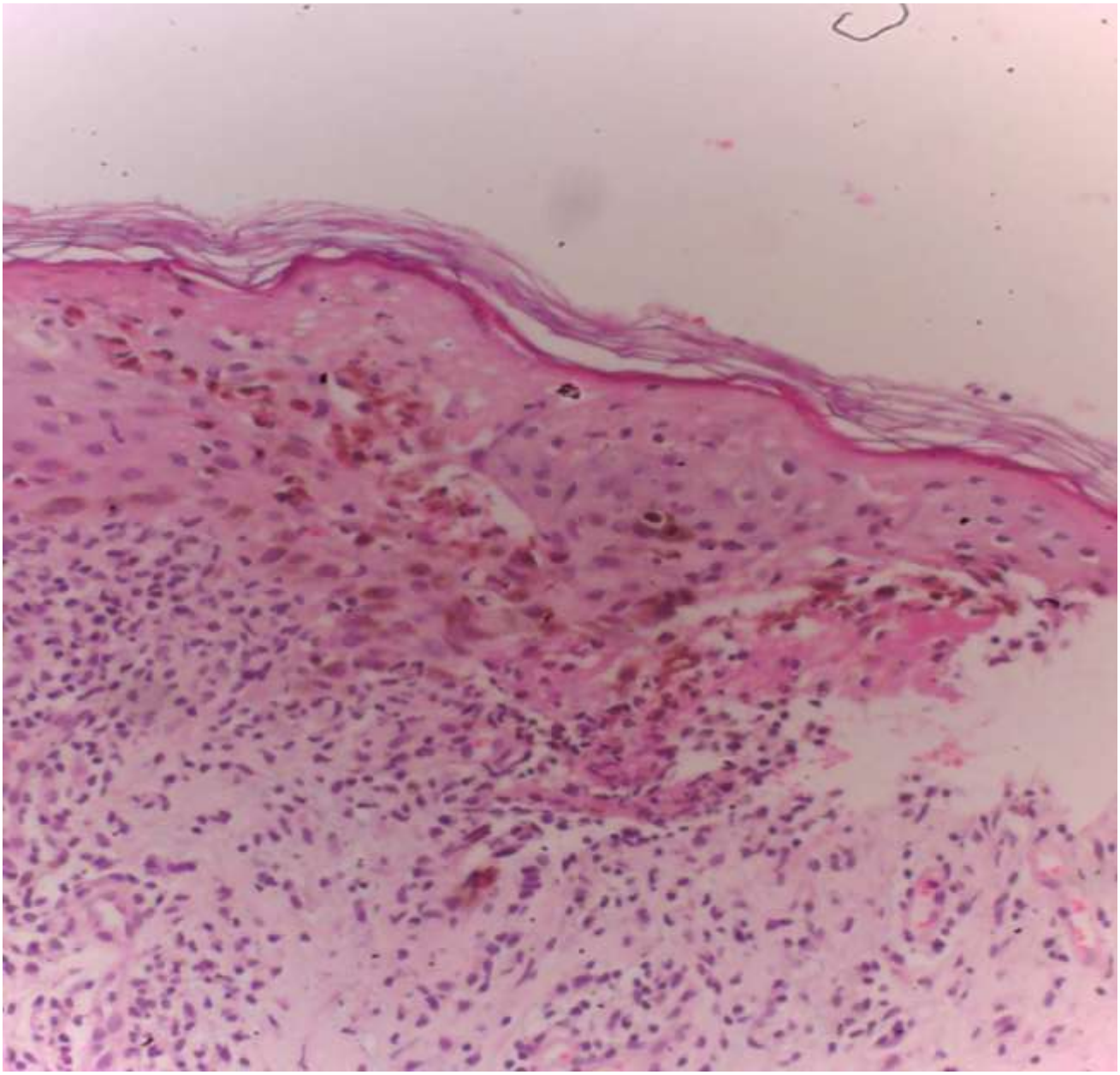

Figure 4. Histology Slide of bullous erythema multiforme showing intra-epidermal blister with mixed inflammatory infiltrate and necrotic keratinocytes. (Hematoxylin & Eosin X400)

Diagnosis

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The clinical presentation, history of recurrent bullous lesions with targetoid morphology, positive HSV-1 IgG titers indicating prior herpes simplex virus infection, and histological findings of focal intra-epidermal blisters and necrotic keratinocytes with mixed inflammatory infiltrate led to a diagnosis of recurrent bullous erythema multiforme, most likely triggered by herpes simplex virus reactivation.

Management

The patient was initially prescribed oral acyclovir 800 mg three times a day for two weeks to manage the acute outbreak. Following this, a maintenance dose of 400 mg twice daily was started for chronic suppression, planned for six months, to prevent recurrent episodes. The patient was closely monitored during follow-up for any changes in the frequency and severity of flare-ups. Additionally, he was advised to practice sun protection and to use lip balm with SPF 15+ to minimize the risk of sun exposure, which could act as a potential trigger for herpes simplex virus reactivation.

Follow-Up

At the six-month follow-up appointment, the patient reported no new generalized blistering episodes or flare-ups during this period. The lesions cleared within two weeks of starting treatment, and he did not have any outbreaks while on suppression therapy. He expressed relief at the positive outcome and stated that he tolerated the acyclovir well, with no adverse effects. Overall, he felt much better and was pleased with his progress.

DISCUSSION

Erythema multiforme (EM) is a complication of herpes simplex virus (HSV) infection, particularly in its recurrent forms(1, 2). While EM typically presents with targetoid lesions, the bullous variant is rare, characterized by central blistering superimposed on these classic plaques(3, 4). The early recognition of recurrent erythema multiforme and its association with HSV is crucial for effective management (1).

In this case, the patient's recurrent episodes of bullous erythema multiforme underscore the need to consider HSV as a potential trigger, particularly in younger patients(5). Antiviral suppression therapy with acyclovir significantly reduces recurrence rates, alleviates symptoms, and improves the quality of life for patients by decreasing the frequency and severity of flare-ups(6, 7).

Additionally, the management of EM requires a comprehensive approach that includes patient education on the condition and its triggers, such as sun exposure and stress. Implementing protective measures, such as sunblock and moisturizing agents, can help prevent exacerbations. This case highlights the importance of identifying the herpes simplex virus in recurrent bullous erythema multiforme and the option of antiviral suppression therapy in its management.

CONCLUSION

This case emphasizes the role of HSV reactivation in recurrent bullous erythema multiforme and highlights the effectiveness of suppressive antiviral therapy in reducing recurrences.

STUDY LIMITATIONS

This study is limited by the lack of direct viral PCR testing to confirm active HSV reactivation and direct immunofluorescence to rule out other blistering conditions. Additionally, long-term follow-up beyond six months was not conducted.

RECOMMENDATION

Early recognition of HSV-associated erythema multiforme is vital for appropriate treatment. For patients with frequent recurrences, long-term antiviral suppression should be considered. Further studies are needed to assess the optimal treatment duration.

ACKNOWLEDGMENT

The authors also recognize the patient for allowing this rare condition to be published.

The authors acknowledge the support of the Dermatology Department -Mbarara University of Science and Technology for providing the platform for this study.

LIST OF ABBREVIATIONS

EM: Erythema Multiforme
HSV: Herpes Simplex Virus
CBC: Complete Blood Count
LFTs: Liver Function Tests
RFTs: Renal Function Tests

FUNDING

The study had no funding.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

PATIENTS CONSENT

The authors obtained written consent from patients for their photographs and medical information to be published in print and online with the understanding that this information may be publicly available. Patient consent forms were not provided to the journal but were retained by the authors.

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AUTHOR CONTRIBUTIONS

Mukalazi Abraham was responsible for manuscript writing and study conception. Tumuhairwe Julian Katungi contributed to the discussion section.

DATA AVAILABILITY

The data used in this study are available upon reasonable request from the corresponding author.

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PUBLISHER DETAILS

Student's Journal of Health Research (SJHR)
(ISSN 2709-9997) Online
(ISSN 3006-1059) Print
Category: Non-Governmental & Non-profit Organization
Email: studentsjournal2020@gmail.com
WhatsApp: +256 775 434 261
Location: Scholar's Summit Nakigalala, P. O. Box 701432, Entebbe Uganda, East Africa