

Fulminant ulceronecrotic dermatosis: revisiting a classic diagnosis

Dermatose ulceronecrótica fulminante: revisitando um diagnóstico clássico

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Abstract

Malignant syphilis (lues maligna) is a rare and aggressive variant of secondary syphilis, predominantly affecting immunocompromised patients. We report a 56-year-old male with newly diagnosed human immunodeficiency virus (HIV)-1 infection (viral load 637,000 copies/mL; CD4+ 134 cells/ μ L) who presented with a 1-2-month history of constitutional symptoms followed by a fulminant, disseminated ulceronecrotic dermatosis involving the scalp, face, trunk and limbs. A vesicular eruption preceding the ulceronecrotic phase was initially misdiagnosed as varicella. Diagnosis was established on the integration of clinical findings, serological confirmation (rapid plasma reagin 1:16; positive *Treponema pallidum* antibody), positive DNA polymerase chain reaction for *T. pallidum* from a cutaneous ulcer exudate, and compatible skin biopsy histology. The patient was treated with three weekly doses of intramuscular benzathine penicillin G 2.4 million units, with complete healing and only atrophic scarring at 4-month follow-up. This case highlights that malignant syphilis can manifest as a rapidly progressive ulceronecrotic dermatosis, and underscores the importance of maintaining a broad differential diagnosis in the context of newly diagnosed HIV infection.

Keywords: Syphilis. Malignant syphilis. Lues maligna. Human immunodeficiency virus infections. Skin diseases. Infectious. Penicillin G benzathine.

Resumo

A sífilis maligna (lues maligna) é uma variante rara e agressiva da sífilis secundária, predominantemente associada a imunodepressão. Apresentamos o caso de um homem de 56 anos, com infeção por VIH-1 de novo diagnóstico (carga viral 637.000 cópias/mL; CD4+ 134 células/ μ L), com um quadro de 1-2 meses de sintomas constitucionais, seguido de uma dermatose ulceronecrótica fulminante, disseminada pelo couro cabeludo, face, tronco e membros. Um exantema vesicular precedente foi inicialmente interpretado como varicela. O diagnóstico foi estabelecido pela integração de dados clínicos, serológicos (RPR 1:16; anticorpo anti-*Treponema pallidum* positivo), PCR positivo para DNA de *Treponema pallidum* em exsudado de uma das lesões cutâneas e histologia de biópsia cutânea compatível. O doente foi tratado com três doses semanais de penicilina G benzatínica intramuscular 2,4 milhões de unidades, com cicatrização completa das lesões, apresentando apenas cicatrizes atróficas aos quatro meses de seguimento. Este caso ilustra como a sífilis maligna se pode manifestar como uma dermatose ulceronecrótica rapidamente progressiva, e sublinha a importância de manter um diagnóstico diferencial alargado no contexto de infeção por VIH de novo diagnóstico.

Palavras-chave: Sífilis. Sífilis maligna. Lues maligna. Infeção HIV. Dermatoses infecciosas. Penicilina G benzatínica.

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Introduction

Malignant syphilis, or lues maligna, is a rare and severe variant of secondary syphilis first described in the mid-19th century.¹ It is characterized by a prodrome of constitutional symptoms followed by the development of disseminated papulopustular lesions that rapidly evolve into painful ulceronodular plaques with necrotic bases and thick, rupioid crusts.² The condition predominantly affects immunocompromised patients, particularly those with human immunodeficiency virus (HIV) co-infection and low CD4⁺ T-cell counts, although cases in immunocompetent individuals have also been reported.³

Since the resurgence of syphilis across Europe, with a 100% increase in notifications between 2014 and 2023⁴, clinicians must maintain a high index of suspicion for atypical manifestations of this infection. The clinical heterogeneity of malignant syphilis, its tendency to mimic other dermatological conditions, and the recognized limitations of histological diagnosis render this entity a significant diagnostic challenge.⁵

We present a case of fulminant ulceronecrotic malignant syphilis as the inaugural manifestation of newly diagnosed HIV-1 infection, with an extensive diagnostic work-up that ultimately required the integration of clinical, serological, molecular, and histological data.

Clinical case

We present a 56-year-old Portuguese male, autonomous, and a resident in Angola between 2000 and 2015, with no known medical history and no regular medication, who had no documented prior sexually transmitted infections and a social history notable for occasional alcohol use. He had received the full childhood vaccination program. In January 2026, he presented with a 2-month history of unintentional weight loss (10 kg), marked asthenia, and night sweats, followed by a generalized vesicular eruption, initially pruriginous, which spread across the body, including the scalp. He attended a primary care facility, where a clinical diagnosis of varicella was made, and oral valaciclovir 1000 mg twice daily was prescribed for 10 days. Lesions partially resolved but subsequently recurred as painful vesiculopustular, then ulceronodular lesions, with copious exudation. On repeat assessment at the primary care facility, a rapid HIV-1/2 test was found to be positive, and given the deterioration of his overall status as well as a fulminant worsening of the dermatosis, the patient was referred to our emergency department.

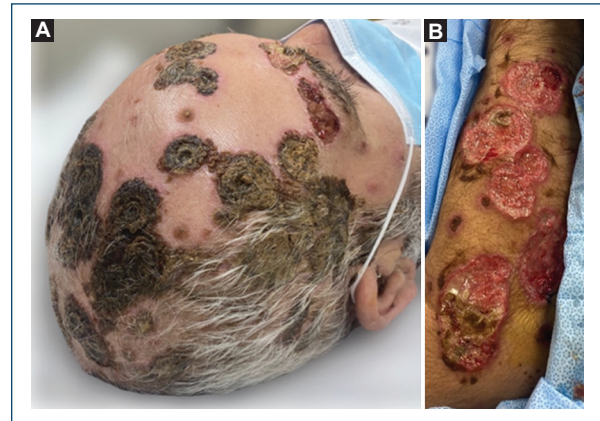


Figure 1. Malignant syphilis at presentation: disseminated ulceronodular lesions. **A** and **B**: malignant syphilis: clinical evolution. Disseminated ulceronodular plaques with necrotic bases and thick, adherent, rupioid crusts on the forearm and scalp at presentation.

On admission to the emergency department, clinical examination revealed an emaciated patient with multiple, disseminated ulceronodular lesions with well-demarcated borders, necrotic bases, thick, adherent, rupioid crusts distributed over the scalp, face, trunk, forearms, and lower limbs (Fig. 1A and B). Lesions were markedly tender on palpation, with significant functional impairment. Genital examination revealed a single, painful ulcer with a necrotic base, morphologically similar to the disseminated cutaneous lesions, and lacking the indurated, painless character typical of the classic syphilitic chancre. The patient reported sexual contact exclusively with his wife, who was referred for serological screening and treatment; however, as she currently resides in Angola, this has not been possible yet.

Admission laboratory work-up revealed hyponatremia (Na⁺ 123 mmol/L) in the context of significant dehydration from extensive exudative lesions and marked elevation of the inflammatory markers. Immunological work-up confirmed a newly diagnosed HIV-1 infection, with a plasma viral load of 637,000 copies/mL and a CD4⁺ count of 134 cells/ μ L (13%). The HIV-1 subtype was A1, and the resistance profile showed an L74I/L74M mutation associated with low potential resistance to cabotegravir only, but no mutations affecting protease or reverse transcriptase.

Given the broad differential of this disseminated ulceronecrotic dermatosis in a newly diagnosed HIV-positive patient, which included monkeypox virus (Mpox), deep fungal infection, cutaneous leishmaniasis, pityriasis lichenoides et varioliformis acuta, rupioid

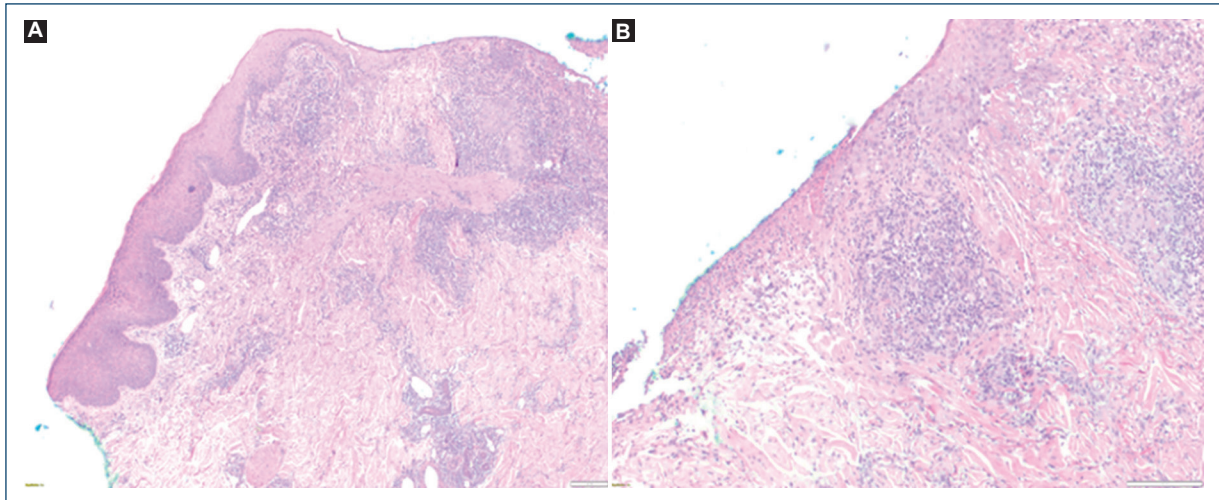


Figure 2. Skin biopsy findings. **A** and **B:** H&E, $\times 20$ and $\times 40$. Skin biopsy showing hyperplastic epidermis, areas of ulceration, and a lichenoid, periadnexal, and perivascular inflammatory infiltrate.

psoriasis, and malignant syphilis, a comprehensive microbiological and serological work-up was initiated. Serology confirmed active syphilis: antibody anti-*Treponema pallidum* positive (electrochemiluminescence immunoassay) and rapid plasma reagin (RPR) 1:16. Hepatitis C serology and cytomegalovirus (CMV) immunoglobulin M were negative. Serology also confirmed past hepatitis B exposure (Hepatitis B Surface Antigen negative; Hepatitis B Surface Antibody and Hepatitis B Core Antibody positive) and immunity to hepatitis A. Polymerase chain reaction (PCR) of a cutaneous ulcer exudate was positive for *T. pallidum* DNA and negative for mpox, herpes simplex virus type 1, herpes simplex virus type 2, varicella-zoster virus, CMV, *Haemophilus ducreyi*, and lymphogranuloma venereum.

A skin biopsy of a lesion on the right forearm showed ulcerated epidermal hyperplasia with a superficial and deep, perivascular and periadnexal lichenoid inflammatory infiltrate, rich in plasma cells, lymphocytes, and histiocytes, a pattern histologically compatible with malignant syphilis (Fig. 2A and B). Immunohistochemistry for *Treponema* was equivocal; the diagnosis of malignant syphilis was therefore established based on clinical, serological, and molecular correlation.

A reported childhood penicillin allergy was reassessed by the immunoallergy service during the hospitalization. Given the absence of any documented prior severe reaction and the low clinical pre-test probability, no contraindication to treatment was identified. The patient was started on antiretroviral therapy (3TC/DTG), and intramuscular benzathine penicillin G

2.4 million units was administered weekly for 3 consecutive weeks, given the severity of the presentation and the degree of immunosuppression. Trimethoprim/sulfamethoxazole (TMP-SMX) was added empirically for 10 days for *Pneumocystis jirovecii* prophylaxis; it was subsequently discontinued and replaced by atovaquone following a probable idiosyncratic cholestatic hepatitis, with progressive normalization of liver enzymes. Lumbar puncture to exclude neurosyphilis was not performed, as the extensive ulceronecrotic lesions involving the back precluded safe access to the puncture site; the patient was instead managed with close clinical surveillance, including serial, exhaustive neurological examinations that remained consistently unremarkable, together with rigorous serological follow-up, which showed a progressive decline in antibody titers. He completed 24 days of inpatient care with progressive improvement of the global status and the cutaneous lesions and was discharged after that on combination antiretroviral therapy and outpatient follow-up.

At dermatology review consultation, 4 months later, cutaneous examination showed complete resolution of all active lesions, with atrophic, centrally depressed scarring (Fig. 3A and B). The patient remained asymptomatic and was adherent to antiretroviral therapy. Serological and immunological follow-up demonstrated a marked treatment response, with RPR titer declining to 1:1, an HIV-1 viral load of 45.5 copies/mL, and a CD4+ count of 319 cells/ μ L.

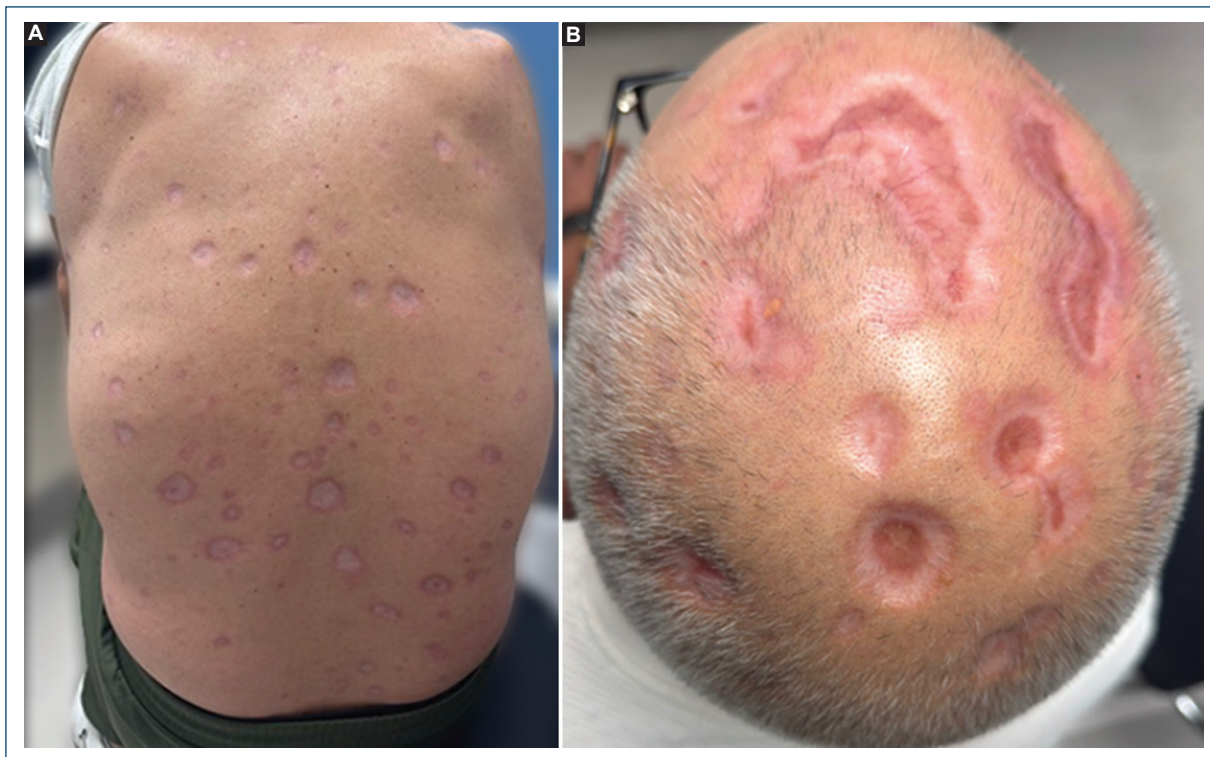


Figure 3. Clinical outcome at 4-month dermatology follow-up. **A** and **B**: complete resolution with atrophic, centrally depressed scarring at 4-month dermatology follow-up.

Discussion

This case illustrates several salient features of malignant syphilis. First, it demonstrates the potential for an initial vesicular phase that may be mistaken for varicella or other vesiculobullous dermatoses before the characteristic fulminant ulceronecrotic pattern emerges. This atypical early presentation has been reported in a minority of cases and may contribute to diagnostic delay, particularly in a primary care setting.² Second, the case highlights that the broad differential diagnosis of rapidly progressive ulceronecrotic lesions in newly diagnosed HIV infection, including mpox, deep fungal infection, and cutaneous pityriasis lichenoides et varioliformis acuta, among others, necessitates a structured multi-modal diagnostic approach, with no single modality being sufficient in isolation.⁵

The diagnosis of malignant syphilis was supported by the concordant positivity of PCR for *T. pallidum* DNA in a cutaneous ulcer, the high RPR titer, and the histological pattern. The equivocal immunohistochemical result for *Treponema* is a well-recognized limitation of this technique in everyday clinical practice and has been described in previous series.⁵ In this case, the combination of serological, molecular, and histological data was determinant.

Regarding treatment, the choice of three weekly doses of intramuscular benzathine penicillin G, rather than the single dose indicated for uncomplicated secondary syphilis, was guided by the severity of cutaneous involvement and the degree of immunosuppression. This approach is supported by clinical reports of malignant syphilis in HIV-positive patients.^{3,6} The reassessment and clearance of the penicillin allergy label by the immunoallergy service, a childhood attribution without any documented prior reaction, illustrates the importance of allergy delabeling as a clinical intervention that may have direct therapeutic consequences.⁷ The management of concurrent conditions during this admission, including the probable TMP-SMX-related cholestatic hepatitis and hyponatremia, further underscores the multisystem complexity of newly diagnosed advanced HIV disease.⁸

The favorable outcome (complete healing with only atrophic scarring within four months) confirms the responsiveness of malignant syphilis to appropriate penicillin-based therapy, even in the context of profound immunosuppression. As syphilis notifications continue to rise across Europe,⁴ this case reinforces the importance of including malignant syphilis in the differential diagnosis of severe, atypical, and rapidly progressive skin disease, particularly in newly diagnosed HIV-positive patients with relevant epidemiological risk factors.

Conclusion

Malignant syphilis is a rare but potentially fulminant presentation of secondary syphilis that should be considered in the differential diagnosis of any rapidly progressive ulceronecrotic dermatosis, particularly in patients with newly diagnosed HIV infection. An initial vesicular phase, which may mimic varicella, can contribute to diagnostic delay, and no single diagnostic method is sufficient on its own: the integration of clinical, serological, molecular (*T. pallidum* PCR) and histological data was decisive in this case. Treatment with benzathine penicillin G, together with the initiation of antiretroviral therapy, led to complete healing of the lesions, with atrophic scarring. With syphilis notifications rising across Europe, a high index of suspicion for atypical manifestations is essential.

Funding

None.

Conflicts of interest

None.

Ethical considerations

Protection of human subjects and animals. The authors declare that they have followed the ethical

standards of the relevant experimentation committee, according to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional ethics committee.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from all patients, and secured approval from the Ethics Committee. SAGER guidelines have been followed as applicable to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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