

## CASES FOR DIAGNOSIS

# Ulcers in a Patient With Chronic Lymphocytic Leukemia

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## Clinical History

A 45-year-old man reported the appearance of a painless, slow-growing, progressive ulcer on the left ear lobe. The lesion had appeared 1 month earlier, and there were 2 similar lesions, 1 on the penis and 1 on the palm of the left hand. The patient had stage IV chronic lymphocytic leukemia and, given the refractory nature of his disease, had received treatment with fludarabine monophosphate during the previous 6 months.

## Physical Examination

Physical examination revealed ulcerated lesions on the left ear lobe, the palm of the left hand, and dorsum of the penis. The lesions had poorly defined, edematous, erythematous-violaceous borders (Figures 1 and 2).

## Complementary Tests

An intense leukocytosis of  $28\,500$  white cells/ $\text{mm}^3$  (85% lymphocytes) was detected in the complete blood count; the other laboratory values and serological tests were normal. The Mantoux test and chest radiograph were negative.

## Histopathology

Skin biopsy from the lesion on the hand showed an ulcer with destruction of the full thickness of the epidermis, with multiple, multinucleated giant cells (Figure 3). Cultures of the biopsy for bacteria, fungi, and mycobacteria were negative.



Figure 1.



Figure 2.

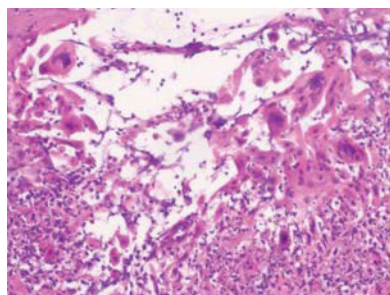


Figure 3.  
Hematoxylin-eosin,  
 $\times 400$ .

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What Was the Diagnosis?

## Diagnosis

Herpetic ulcers in a patient with chronic lymphocytic leukemia.

## Clinical Course and Treatment

Immunohistochemical staining for the herpes simplex group of viruses was positive.

Treatment was started with oral acyclovir at a dose of 800 mg/6 h for 15 days, achieving complete resolution of the lesions in 3 weeks. However, the patient has presented several recurrences after interruption of the treatment, and these have been controlled with further cycles of aciclovir.

## Discussion

Patients with hematological malignancies frequently present various types of infectious conditions, with a high morbidity and mortality.<sup>1</sup> One of the most common is infection due to herpes simplex virus.<sup>2,3</sup> Rarely, these patients present atypical lesions that are difficult to diagnose, with vesicular rashes on the fingers or palms, chronic ulcerated lesions, or even serious mucocutaneous or disseminated systemic infections, with an indolent, progressive course and frequent recurrences.<sup>4</sup>

Patients with insidious, resistant chronic lymphocytic leukemia are usually treated with multiple cycles of alkylating agents and fludarabine monophosphate,<sup>5</sup> which has a powerful immunosuppressive effect that could contribute to the appearance of unusual herpetic lesions. Patients on treatment with fludarabine sometimes present certain adverse effects, including fever, rigors, myelotoxicity, and the appearance of infections due to mycobacteria, candida, listeria, pneumocystis, aspergillus, and cytomegalovirus.<sup>5</sup> A significant increase in infections due to herpes simplex virus has also been reported in patients who receive this drug.<sup>6</sup> Its immunosuppressive effect can persist in some cases up to 1 year after finishing the cancer treatment, and some authors have therefore proposed prophylactic strategies with antibiotics and antiviral agents in patients with chronic lymphocytic leukemia treated with fludarabine.<sup>1</sup>

The diagnosis of atypical forms of herpes in immunosuppressed patients can sometimes be complicated

due to the appearance of lesions with unusual characteristics or at unusual sites, or due to the minimal information obtained in the histopathological study.<sup>4</sup> The differential diagnosis of ulcerated lesions in patients with lymphoproliferative diseases must include uncommon skin infections (tuberculosis or other mycobacteria, and deep mycoses), cutaneous infiltration by the hematological disease, primary skin tumors (squamous cell or basal cell carcinoma), and adverse effects of chemotherapy.

Aciclovir is the treatment of choice in immunocompromised patients. Higher doses are usually required and for longer periods, followed by continuous, low-dose prophylactic therapy to prevent the frequent recurrences that usually develop.<sup>4</sup> However, due to the possible onset of resistance, some authors recommend close follow-up in these cases, treating each episode of a possible herpes simplex virus infection with a short cycle of antiviral agents at the first signs or symptoms instead of maintaining continuous prophylactic treatment.

## Conflicts of Interest

The authors declare no conflicts of interest.

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