Clinical History

The patient was a 41-year-old man who was admitted for a 3-week history of fever, dysphagia, odynophagia, and painful ulcers in the oropharynx. The patient reported that 3 years earlier he suffered a similar condition that was less severe and resolved spontaneously. He had been diagnosed with human immunodeficiency virus (HIV) infection, category B3, and hepatitis C infection, and was on treatment with cotrimoxazole.

Physical Examination

The right anterior tonsillar pillar was affected by a large ulcer with a necrotic base and erythematous border and there were small satellite ulcers (Figure 1).

Complementary Tests

The important findings in the complementary studies were a CD4 lymphocyte count of 17 cells/mm$^3$, a viral load of 2600 copies/mL, and a negative result for cytomegalovirus antigenemia. Computed tomography of the neck showed bilateral small laterocervical lymph nodes, with no masses in the parapharyngeal spaces. A barium swallow performed after a failed attempt at endoscopy demonstrated the presence of an ulcer in the distal third of the esophagus (Figure 2).

Histopathology

Two biopsies of the ulcer were taken for histological and microbiological study. Histopathology revealed the presence of an ulcer surrounded by a chronic inflammatory infiltrate; stains and culture for fungi, mycobacteria, and viruses, the viral polymerase chain reaction, and immunohistochemistry for herpesvirus were all negative.
Diagnosis
HIV-associated recurrent aphthous stomatitis.

Clinical Course and Treatment
The possibility of recurrent aphthous stomatitis was considered based on the histological and microbiological findings and after having treated the patient with intravenous acyclovir, oral fluconazole, nystatin, and topical steroids. Treatment was started with systemic steroids and dapsone, with no improvement. After requesting thalidomide for compassionate use, the patient restarted antiretroviral therapy, this time with tenofovir, lamivudine, and efavirenz, with a good virological and immunological response and resolution of the ulcer in the following weeks, without having started the thalidomide.

Discussion
There is a high prevalence of oral lesions in HIV-infected patients and the most common conditions are herpetic infections, oral candidiasis, oral hairy leukoplakia, and recurrent aphthous stomatitis. This latter is a chronic disease of inflammatory nature, characterized by the appearance on the nonkeratinized oral mucosa of one or more painful ulcers that show nonspecific histological findings and that persist for days or weeks and recur after variable periods of remission.1,2 The 3 types of aphthous stomatitis are minor, major, and herpetiform. They are differentiated by the number, size, and duration of the lesions, though this is not always clear.3 The major form has very painful ulcers that can leave scars after their resolution. Similar lesions may be present in the esophagus, rectum, anus, and genitalia. Its etiology is unknown, and genetic, infectious, immunologic, and local factors have been proposed. The diagnosis is clinical, after exclusion of other disorders.

Severe episodes of recurrent aphthous stomatitis have been reported in patients with HIV infection; the lesions may correspond to any of the clinical forms, and the most common sites are the soft palate, tonsillar area, and tongue. The majority of infected patients do not recall having had episodes of recurrent aphthous stomatitis before acquiring HIV infection. An interesting aspect is that the number of lesions per episode is higher in patients with AIDS than in HIV-infected patients who have not developed AIDS; this may indicate a correlation between immune suppression and an increase in the severity of the disorder.4

Before highly active antiretroviral therapy, the treatment of HIV-associated recurrent adverse stomatitis was disappointing. Topical treatments with anesthetics and intralesional steroids were used, achieving symptomatic relief but without reducing the frequency, severity, or rate of recurrence. Systemic treatment with steroids or immune modulators such as thalidomide have been shown to be effective in a number of clinical trials,5 but they do not prevent recurrences and their use is limited by toxicity. At the present time, the treatment of choice is antiretroviral therapy, as immune recovery is a determining factor in resolution of the ulcers, as occurred in our patient, in whom the ulcers have not recurred after almost 2 years of follow-up.

Conflicts of Interest
The authors declare no conflicts of interest.

References