Infections caused by mycobacteria are the leading cause of morbidity and mortality in patients infected with the human immunodeficiency virus (HIV), especially in developing countries (Sterling et al., 2010).

Among nontuberculous mycobacteria (NTM), the species most frequently found are *M. avium*–*intracellulare* complex (MAC), *M. chelonae*, *M. abscessus*, *M. kansasii*, *M. xenopi*, and *M. fortuitum*.

Due to the low incidence of infections caused by other species such as *M. simiae*, such infections are often difficult to manage (Samra et al., 2005).

The introduction of highly active antiretroviral therapy (HAART) has changed dramatically the natural history of HIV infection since it resulted in a drastic reduction in the incidence of opportunistic infections and mortality from all causes. However, despite these benefits, HAART is also responsible for the occurrence of immune reconstitution inflammatory syndrome (IRIS) (Muller et al., 2010).

We report the second case in Europe and the first case in Spain of *M. simiae* pulmonary infection unmasked during immune reconstitution in an HIV-infected patient.

A 29-year-old woman, a native of Ghana living in Spain for a year, was admitted in our hospital after a 3-day history of fever accompanied by delirium. She had no other medical history of interest. Chest X-ray and routine blood test results were normal, and tuberculin skin test (TST) result was negative. During hospital admission, she was diagnosed with herpes encephalitis and advanced HIV infection (24 CD4/mm³ [1%] and HIV viral load [VL] 457,000 copies/mm³). She was treated with intravenous acyclovir (10 mg/kg per 8 h) for 21 days and started antiretroviral therapy with oral nevirapine 200 mg/12 h and emtricitabine/tenofovir 245/200 mg, associated with cotrimoxazole 800/160 mg every 48 h.

She was discharged 30 days after admission to continue outpatient follow-up. Two months later, she was readmitted for fever (39 °C), productive cough, and general malaise. Crackles on auscultation were detected in the upper third of the left lung. Chest X-ray and computed tomography (CT) confirmed the presence of a condensation in the upper left lobe (Fig. 1A and B). Blood analysis revealed the following: hemoglobin 10.3 mg/dL, hematocrit 31%, 4600 leukocytes/mm³. She had no history of diabetes, malignancy, or other chronic lung disease.

During hospital follow-up, she had an episode of fever, cough, and malaise. She was treated with intravenous acyclovir (10 mg/kg per 8 h) for 21 days and started antiretroviral therapy with oral nevirapine 200 mg/12 h and emtricitabine/tenofovir 245/200 mg, associated with cotrimoxazole 800/160 mg every 48 h.

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Positive culture results were obtained from 4 expectorated sputum samples on consecutive days. All samples were positive for acid-fast bacilli (AFB). She was treated with rifampicin 600 mg/24 h, isoniazid 300 mg/24 h, pyrazinamide 500 mg/8 h, and ethambutol 1200 mg/24 h. After 5 days, microbe growth was observed in liquid medium inoculated with sputum samples, and following Ziehl–Neelsen staining, AFB were detected. These bacilli did not present cording and were identified as *Mycobacterium* spp. by hybridization using the commercial probe GenoType Mycobacterium CM (Hain LifeScience, Nehren, Germany). New hybridization using GenoType Mycobacterium AS (Hain LifeScience) identified the specimen as *M. simiae*. Restriction fragment length polymorphism analysis of the gene encoding heat shock protein 65 kDa (*hsp65*) was performed corroborating the identification as *M. simiae* type 3.

Therapeutic regimen was modified, replacing pyrazinamide and isoniazid with clarithromycin 1000 mg/24 h and levofloxacin 500 mg/24 h. In 2 weeks, the new treatment achieved negative sputum smears in 3 consecutive controls.

After 6 months with the 4 drugs (rifampicin, ethambutol, clarithromycin, and levofloxacin), complete resolution of lung condensation was evidenced by X-ray and CT (Fig. 2), and all sputum cultures remained negative. Her immunovirologic situation had also improved (320 CD4/mm³ [16%] and VL <20 copies/mm³).

The suppression of CD4 “T cell” by HIV causes a decrease in the body’s normal response. HAART inhibits viral replication and raises the CD4 counts very quickly; this often results in IRIS as an adverse consequence of antigen-specific immune restoration. Pathogenic mycobacteria cause several long-term infections in their respective hosts, and persistently infected individuals can harbor bacteria for many years, and even throughout their life, with infected macrophages being the main reservoir of infection. The risk of conversion to a clinically active infection occurs most often in immunologically compromised individuals (Monack et al., 2004). Then, IRIS manifestations are due to excessive unregulated immune response against these infections. The frequency of IRIS ranges between 8% and 43% (Breton, 2010), and its risk factors are youth, a low body mass index, strong immunosuppression (CD4 lower than 50–100 CD4/mm³) and very high viral loads (Smith et al., 2009). When the treatment starts, it usually appears after the second month of treatment.

Among HIV patients with IRIS, *M. tuberculosis* and NTM are the most common infections, and since 1996, coinciding with the increasing power of antiretroviral drugs, the number of cases is growing (Berman et al., 2008; Griffith et al., 2007; Hibiya et al., 2011; Lawn et al., 2005; Leone et al., 2008). IRIS may occur as a paradox, which results in worsening of an infection already diagnosed during treatment or, as in the case of our patient, an unmasked IRIS manifested by florid symptoms of a disease yet asymptomatic (Pornprasert et al., 2010).

*M. simiae*, one of the NTM, was described in 1965 when it was isolated from a *Macacus rhesus* monkey (Karassova et al., 1965). Its presence in respiratory sample culture in patients with suspected pulmonary infectious disease must always be interpreted within the clinical context in response to American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) recommendations, which specifies that this diagnosis is based on clinical, radiological, and microbiological evidence; also, patients should have at least 3 sputum specimens collected on separate days (Griffith et al., 2007). Following

![Fig. 1. (A) Chest X-ray at the time of readmission. (B) Chest CT at readmission.](image)

![Fig. 2. Chest X-ray after 6 months of treatment.](image)
In our country and in relation to the HIV-infected immigrant population, we expect an increase in the diagnosis of mycobacterial infections associated with IRIS. Tools for early diagnosis, improvements in the screening of latent infections at the start of HAART, and a deeper knowledge of epidemiologic changes related with immigration are needed. Generally, chest X-ray or TST of asymptomatic immunosuppressed patients is not informative enough for these infections. We consider that systematically collecting respiratory specimens for culture are most cost-effective for diagnosis because a high percentage of asymptomatic patients are culture positive as we have observed in this case.

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