

Diagnosis at first sight

Papular lesions and pancytopenia in a patient with severe immunosuppression due to HIV



Lesiones papulares y pancitopenia en paciente con inmunosupresión severa por VIH

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Figure 1. Pigmented papular lesions on the trunk and limbs up to 5 mm in diameter.

Case report

This was a 28-year-old male who presented with a skin rash. He was originally from Ecuador and had lived in Spain for five years. He was a regular user of cannabis, cocaine and alcohol. He reported having unprotected heterosexual relations without a stable partner. He had no known previous illness.

He reported constitutional syndrome for the previous four months, with the addition of fever and night sweats for the last two months and the appearance of disseminated skin lesions on his trunk, limbs and face for the last two weeks.

On arrival in Accident and Emergency, the patient was haemodynamically stable with a slight temperature, general condition fair, with a malnourished and pale appearance. Oropharyngeal candidiasis was noted, plus lymphadenopathy of 3 × 2 cm in his left submandibular region and further smaller lymphadenopathies in his axillae and groin areas. An exanthem in the form of painless, purplish papules 5 mm in size was noted over his entire body, except the palms of his hands and soles of his feet (Fig. 1).

Blood tests showed pancytopenia (leucocytes $2.73 \times 10^9/l$, haemoglobin 9 g/dl, platelets $50 \times 10^9/l$), elevation of acute phase reactants with a C-reactive protein of 14 mg/dl, ferritin of over 200,000 ng/ml and LDH 2869 U/l, as well as abnormal liver function, with hypertransaminasaemia (AST 334 U/l, ALT 212 U/l) and elevated GGT (409 U/l), with alkaline phosphatase and bilirubin within normal ranges. Chest X-ray showed a diffuse micronodular pattern predominantly in the lung bases. Serology tests and cul-

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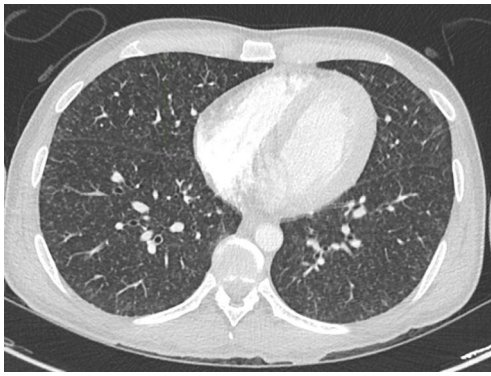


Figure 2. Micronodular, diffuse lung involvement with miliary pattern and mediastinal, bilateral perihilar and bilateral supraclavicular lymph nodes.

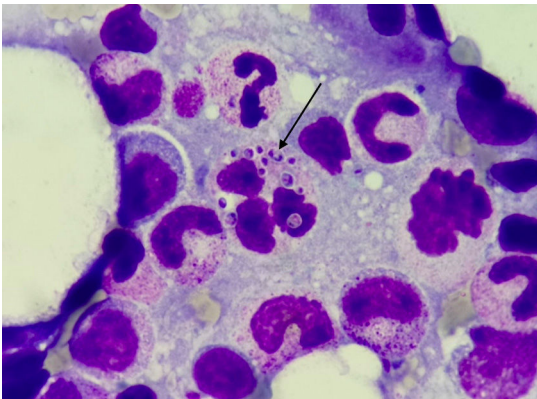


Figure 3. Neutrophils with rounded intracytoplasmic structures consistent with an endemic microorganism (arrow).

tures were performed, including HIV, and the patient was admitted to complete the investigations.

Clinical course and diagnosis

Intracytoplasmic forms consistent with *Histoplasma* sp. were detected in the blood smear, for which treatment was started with liposomal amphotericin B 5 mg/kg/day for two weeks as an induction treatment. HIV serology was positive, CD₄ 6 cells/mm³ and

viral load 1,300,000 copies/ml. He was started on antiretroviral therapy with bictegravir, emtricitabine and tenofovir alafenamide.

The study was completed with a computerised tomography scan of his chest and abdomen, which showed diffuse micronodular pulmonary involvement with a miliary pattern and mediastinal, bilateral perihilar and supraclavicular lymph nodes (Fig. 2). Culture of the biopsy of one of the skin lesions identified the growth of a dimorphic fungus consistent with *Histoplasma* sp. With pancytopenia, marked elevation of ferritin, along with low fibrinogen, abnormal LDH and sustained fever, a bone marrow biopsy was performed that confirmed haemophagocytic syndrome, as well as mild spongiosis and the presence of chronic lymphoplasmacytic inflammatory infiltrate with some histiocytes with intracytoplasmic and interstitial fungal structures consistent with *Histoplasma* sp. with special Gomori and periodic acid-Schiff diastase (PAS-D) stains. Co-infection with other opportunistic microorganisms was ruled out (Fig. 3).

The patient had a good clinical response to liposomal amphotericin B, and the haemophagocytic syndrome was reversed by treating its triggering cause.

Fourteen days after the start of the antiretroviral therapy, the patient's submandibular lymphadenopathies was found to have increased in size and the fever returned. After ruling out other opportunistic infections (mycobacteria) with a lymph node biopsy, which confirmed *Histoplasma* sp., the patient was diagnosed as having immune reconstitution syndrome, which improved with a short course of corticosteroids and itraconazole was added to his antifungal treatment.

Histoplasmosis is transmitted through the inhalation of spores released mainly by *Histoplasma capsulatum* from the droppings of bats and some birds. Primary infection is usually asymptomatic or causes acute respiratory symptoms, which usually resolve within a few weeks.

It is an endemic disease in some regions of America and has also been reported in certain countries in Asia and Africa (where the *duboisii* variety causes African histoplasmosis). As the majority of the population is immunocompetent, the rate of spread is low. In this specific case, the infection was probably acquired in an endemic country, remaining latent initially. However, in relation to the decline in cell-mediated immunity in the context of HIV infection, *Histoplasma* sp. can be activated and spread, with the most severe forms in patients with major immunosuppression (<150 cells/mm³).