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Diagnosis at first sight

Acute disseminated histoplasmosis with immune reconstitution syndrome after initiation of antiretroviral therapy in a patient with HIV

Histoplasmosis diseminada aguda con síndrome de reconstitución inmunitaria tras el inicio de tratamiento antirretroviral en un paciente con VIH

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Case report

This was a 25-year-old man with a history of human immunodeficiency virus (HIV) category C-3 infection with an initial viral load of 2,590,000 copies/mL and CD4 nadir 10, diagnosed in the previous three months after admission for *Pneumocystis jirovecii* pneumonia. On treatment with darunavir/cobicistat/emtricitabine/tenofovir alafenamide. He was born in Colombia and had been in Spain for two years, with no other travelling.

He came to the emergency department with five-day history of fever of 38°C, cough with whitish expectoration and asthenia.

Physical examination revealed widespread moist crackles in both lung fields. On assessment the patient was afebrile with normal blood pressure.

COVID-19 antigen and PCR (polymerase chain reaction) were negative.

Posterior-anterior and lateral chest X-rays showed a bilateral diffuse interstitial micronodular pattern (Fig. 1).

Complete blood count showed leucopenia (3.7×10^9/l) with lymphopenia (0.14×10^9/l). Biochemistry showed a C-reactive protein of 22.43 mg/dl and lactate dehydrogenase of 468 U/l. In view of the findings, the patient was admitted.

Clinical course and diagnosis

Blood cultures, stool culture, *Leishmania* serology and sputum culture were negative.

Chest CT angiography revealed reactive mediastinal lymphadenopathy and a bilateral diffuse micronodular interstitial pattern (Fig. 2).

Based on these findings, fibre-optic bronchoscopy was performed, showing multiple papular formations in the trachea, predominantly in the lower portion (Fig. 3a); bronchoalveolar lavage was performed and bronchial aspirate and biopsy of the lesions taken. Bronchoalveolar lavage, Gram stain, quantitative bacterial and *Legionella* culture, cryptococcal antigen, Ziehl-Neelsen and respiratory virus panel were negative.

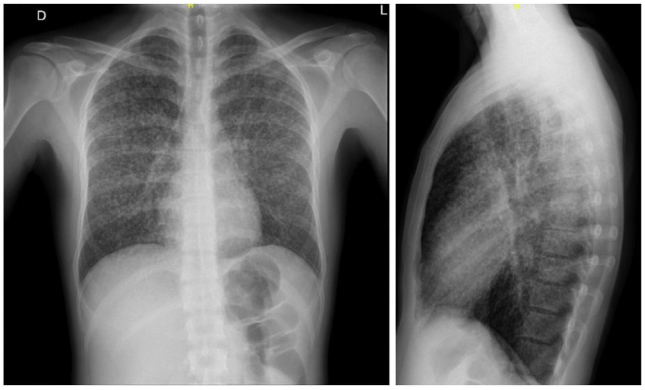

Fig. 1. Posterior-anterior and lateral chest X-ray showing a universally distributed micronodular interstitial pattern.

Tracheal biopsy showed necrosis of the lamina propria, with the presence of yeasts compatible with *Histoplasma capsulatum* (Fig. 3b). Mycological culture media showed the growth of a thermally dimorphic fungus identified as *H. capsulatum*. Cultures on solid and liquid media for mycobacteria were negative.

Treatment consisted of intravenous liposomal amphotericin B (mg/kg/24 h) for 14 days followed by oral itraconazole 200 mg/12 h, and the patient responded well.

Comments

H. capsulatum is a thermally dimorphic fungus whose mycelia look like microconidia (2–4 μm) and macroconidia (8–15 μm).

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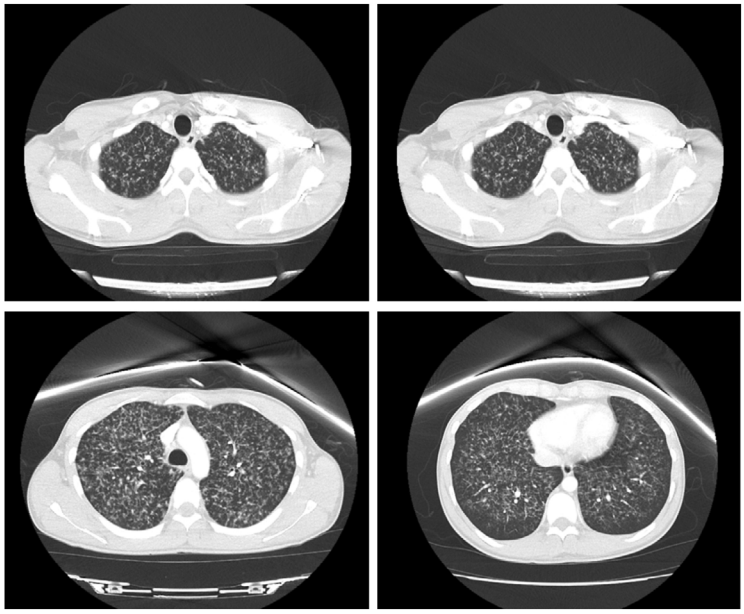

Fig. 2. Chest computed tomography angiography with presence of *bilateral diffuse* micronodular interstitial pattern.

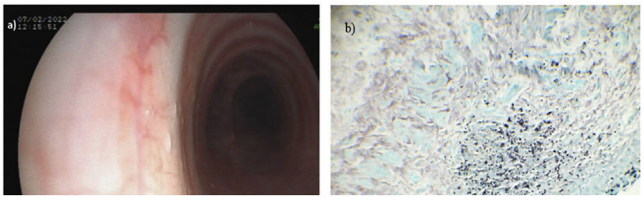

Fig. 3. a) Bronchoscopy image with papular lesions in the trachea. b) Histological image of the biopsy of the papules with presence *of yeasts compatible with Histoplasma capsulatum* by Grocott stain.

It has two variants: *capsulatum* (endemic to the Americas) and *duboissi* (endemic to Africa).

Transmission occurs in river basins enriched by bat or bird droppings through aerosol dissemination. Risky activities include caving, digging, cleaning of chicken droppings, work in henhouses, demolition of old buildings and pruning of dry trees.[1]

Most cases are asymptomatic, but distant dissemination (bone marrow, spleen, liver or adrenal glands) may occur in individuals with cell-mediated immunodeficiency.

Symptoms begin one to four weeks post-exposure, the patient usually developing an influenza-like syndrome.

In patients with severe immunosuppression (CD4 < 200/μl), advanced age, high numbers of inhaled conidia, immunosuppressants (methotrexate and anti-TNF), haematological malignancy or in transplant recipients, it can progress to a disseminated form in the form of respiratory failure, hepatosplenomegaly, disseminated intravascular coagulation, shock, multi-organ failure and even haemophagocytic syndrome.[2]

The diagnostic method of reference in the disseminated form, with a sensitivity of 75%, is culture of the tissue sample on Sabouraud dextrose agar at 25°, which facilitates mycelial growth. Histological staining enables the detection of compatible 2–4 μm, narrow-based oval yeasts with a sensitivity of 50%.

Antigen detection by enzyme immunoassay has a sensitivity of 95% in urine and 86% in serum in patients with disseminated form. Serology can detect antibodies with a sensitivity of 70% and these may remain positive for several years after infection.

The treatment of choice is liposomal amphotericin B (3–5 mg/kg/day) for one to two weeks, followed by oral itraconazole (400 mg/day) for at least 12 months in the disseminated form.[3]

We have presented a case of acute disseminated histoplasmosis with immune reconstitution syndrome after starting antiretroviral therapy in a patient with HIV, where fibre-optic bronchoscopy and pathology examination played a crucial role in the diagnosis and early initiation of treatment. In conclusion, pulmonary histoplasmosis should be ruled out in immunocompromised patients from endemic areas and with a miliary pattern on X-ray.

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Conflicts of interest

All the authors declare that they have no conflicts of interest directly or indirectly related to the contents of the manuscript.

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