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Scientific letter

Pulmonary Cryptococcosis Mimicking Lung Cancer

Criptococosis pulmonar que simula un cáncer de pulmón

Dear Editor:

The following case highlights the necessity to consider cryptococcosis in the differential diagnosis of a wide range of clinical scenarios, including isolated pulmonary nodules in HIV-negative immunocompromised patients. This scenario needs to be considered by clinicians, since it is an emerging profile in which this option is not usually considered.

A 62-year-old male former smoker was referred to the Respiratory Department Clinic for evaluation of a pulmonary nodule. The man was from Curitiba, Brazil, works as a sales representative, and has lived in Spain for many years.

In February 2019 he was diagnosed with rectal adenocarcinoma (cT3N1M0) and in April of the same year, he was started on neoadjuvant chemotherapy with six cycles of the FOLFOX-panitumumab scheme (monoclonal antibody that blocks the epidermal growth factor receptor). In September 2019 he underwent surgery for anterior rectal resection with end-to-end anastomosis. In November, he finished chemotherapy and was followed by regular oncology check-ups. During follow-up, a control thoracoabdominal computed tomography (CT) scan was performed at the beginning of January 2020, showing ground glass pseudonodular opacities in the lower right lobe (LRL). In this context, the patient was administered empirical antibiotic therapy with amoxicillin-clavulanate for one week. A control chest CT scheduled one month later showed a significant increase in the size of the pleuropulmonary opacities, poorly defined in the LRL, ruling out a neoplastic process. A whole-body positron emission tomography (PET)/CT study was requested and performed in February 2020, showing the presence of poorly defined hypermetabolic pulmonary opacities of an indeterminate nature (Fig. 1). Respiratory function tests were within normal limits, and on March 17th, a fiberoptic bronchoscopy was performed in which scant bronchial secretions were observed with the absence of endobronchial or extrinsic lesions up to accessible limits. Bronchial aspirate (BAS) and bronchoalveolar lavage (BAL) were carried out with negative conventional mycological cultures and cytologies ruling out malignancy. On April 3rd, 2020 a CT-guided needle puncture was performed, and samples were sent for pathological study, confirming absence of malignancy and observing an important parenchymal necrosis with the presence of fungal spores.

Polymerase chain reaction (PCR) analysis for Pneumocystis jirovecii was negative. The study was completed with a general laboratory test including serology for human immunodeficiency virus (HIV), which was negative. Determination of IgE and IgG was carried out for several fungi, which were also negative, but a 1/80 titer for Cryptococcus serum antigen was revealed by immunochromatography. Cryptococcus serum antigen test was positive, but the mycological culture of samples obtained by fiberbronchospy failed to identify the presence of *Cryptococcus* spp. A diagnosis of pulmonary cryptococcosis was established, and a 6-month course of treatment with fluconazole 400 mg bis in die orally was started. In August 2020, a control chest CT was performed and showed a reduction in the size of the lesions.

Pulmonary malignancy can be highly suspected based on clinical manifestations and radiological findings. However, other pathological processes such as fungal diseases can mimic pulmonary cancer.[1] Cryptococcal disease (cryptococcosis) is caused by *Cryptococcus* spp. a ubiquitous basidiomycetous yeast, with some species being endemic to several countries such as Brazil, Australia, India or United States of America.[1–4] The clinical manifestations can be diverse and involve many organs. Cryptococcal meningoencephalitis is the most frequent and severe form in both HIV and non-HIV patients. The second most frequent form is pulmonary disease, but it is usually underdiagnosed. Pulmonary cryptococcosis is acquired by inhalation of spores and is usually presented as pulmonary infiltrates and/or cryptococcomas with no other symptoms.[2–4] In general, nodular lesions (more than 60% of multiple cases) and peripheral masses are the most common findings. The sensitivity of serum cryptococcal antigen test for cryptococcal meningitis and disseminated disease is 93–100%, and the specificity is 93–98%.[4] In the absence of randomized clinical trials, according to the recommendations of experts and data obtained from retrospective studies, the treatment of mild forms of the disease is the oral administration of fluconazole for 6-12 months.[1] Some authors described complete resolution within 2-18 months in treated patients, even so it is relatively common the persistence of pulmonary lesions despite antifungal treatment.[5]

In patients with isolated pulmonary nodules, as the cryptococcal burden is usually very low, it is difficult to obtain a diagnosis based on traditional techniques such as cultures. In our patient, despite performing BAS and BAL cultures, *Cryptococcus* spp was not isolated. Neither was the culture of the CT-guided lung biopsy diagnostic, and interestingly, the diagnosis was achieved in the context of serum antigen positivity and positive response to specific treatment with fluconazole. Thus, we report a case of a middle aged non-HIV immunocompromised male submitted to the lung cancer diagnosis clinics who presented serum cryptococcal antigen positivity and was finally diagnosed with pulmonary-localized cryptococcosis with good treatment response. This case highlights the necessity to consider cryptococcosis in the differential diagnosis of a wide range of clinical scenarios, including pulmonary nodules in HIV-negative immunocompromised patients, since it is an emerging profile in which this option is not usually considered.

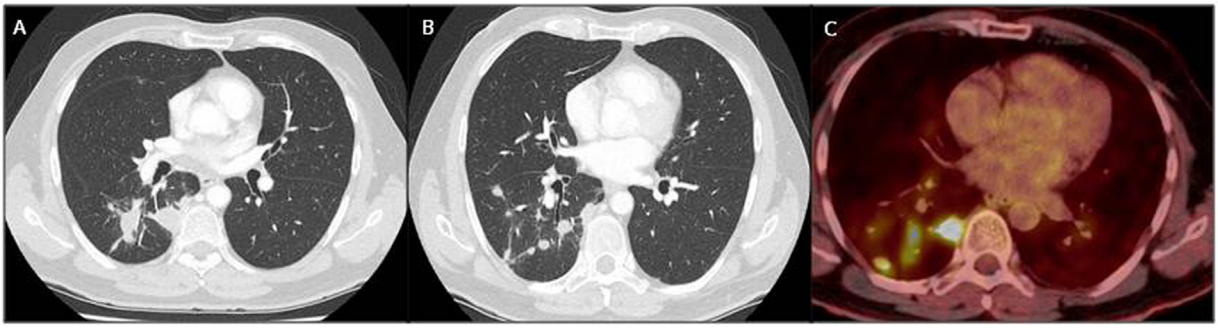

Fig. 1. (A, B) Chest CT scan showing lower right lobe opacities; (C) Positron emission tomography showing hypermetabolic opacities in the lower right lobe.

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Author contribution

All authors substantially contributed to the conception and design of the study, acquisition, formal analysis and interpretation of data, draft, revision and final writing of the manuscript, and they all approved its final version to be submitted.

Patient consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflicts of interest

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