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Pulmonary Aspergillus Nodule – Still Challenging?*



Aspergillosis pulmonar nodular, ¿todavía supone un desafío?

To the Editor,

On rare occasions, fungal infections can resemble lung cancer.¹ While surgery may be indicated in both cases, a differential diagnosis before surgical intervention is essential, due to the differences in the prognosis and therapeutic approach for these entities, and since other diseases cannot be ruled out by imaging procedures alone. We report the case of a patient with a solitary pulmonary nodule, suggestive of malignancy, which was determined to be aspergillosis and was treated with antifungal agents.

An otherwise healthy 63-year-old woman presented with a 3-month history of recurrent hemoptysis. Computed tomography (CT) revealed a spiculated nodule (27 mm) in the left lower lung lobe (Fig. 1A) and small cylindrical bronchiectasis in the right middle lobe. Bronchoscopy was normal, cytology and bronchial lavage fluid cultures were negative, and no changes were seen on bronchial artery angiography. Transthoracic needle biopsy (TTNB) showed fungal structures that were identified as *Aspergillus fumigatus*.

tus (AF) (Fig. 1E). AF and HIV-1 and HIV-2 serologies were negative and serum lymphocyte populations and immunoglobulin levels were normal. Treatment was started with voriconazole (200 mg, twice a day) but discontinued about 2 months later due to signs of hepatic toxicity. CT performed at that time (Fig. 1B) showed that the nodule had decreased in size (17 cm). One month later, after resolution of the hepatic toxicity, antifungal treatment was reinitiated with itraconazole (200 mg, twice a day). After 2 months, the nodule had increased in size (27 mm) and had formed cavities (Fig. 1C). No additional information was obtained from repeated bronchoscopy with bronchoalveolar lavage and TTBNB. Voriconazole was gradually reintroduced, and after 5 months only fibrotic changes were observed on CT (Fig. 1D). However, the patient's liver enzymes had increased again, so voriconazole treatment was discontinued. One year later, the patient remains asymptomatic and images are unchanged.

Chronic pulmonary aspergillosis (CPA) often affects patients with underlying chronic diseases or mild immunosuppression.² *Aspergillus* nodules are an unusual form of CPA, and sometimes do not show the radiological characteristics typical of invasive aspergillosis (halo and crescent signs). Diagnosis is established if the lung parenchyma shows invasion by the septate hyphae

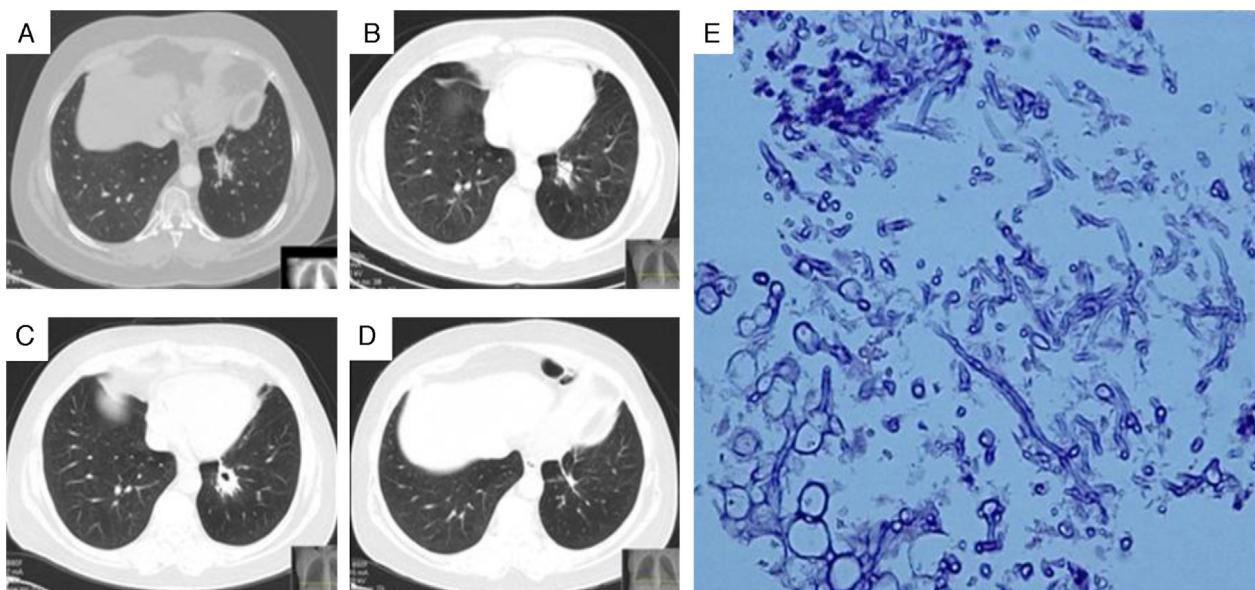


Fig. 1. (A) Chest computed tomography (CT), showing a nodule in the left lower lobe; (B) chest CT 2 months after starting treatment with voriconazole, showing the nodule reduced in size; (C) chest CT during itraconazole treatment, showing nodule growth with cavities; (D) chest CT performed after 7 months of voriconazole treatment, showing residual fibrotic changes; (E) nodule biopsy, showing infiltration of mononuclear cells and fungal structures identified as *Aspergillus fumigatus*.

* Please cite this article as: Dabó H, Marinho A, Gomes I. Aspergillosis pulmonar nodular, ¿todavía supone un desafío?. *Arch Bronconeumol.* 2015;51:603–604.

typical of *Aspergillus* and growth of these hyphae on culture. However, histological confirmation is not always possible, so diagnosis must be based on a combination of clinical, radiological, microbiological, and immunological findings.^{2,3} Azoles are the primary treatment option in CPA.⁴ Our patient showed disease progression during itraconazole treatment, which may have been a consequence of the temporary interruption of treatment or resistance to that compound. Wild-type resistance to azoles has been reported in *Aspergillus* strains in azole-naïve patients.⁵ Disease progression may also have been caused by sub-therapeutic serum levels of itraconazole during treatment, despite the administration of a higher than recommended dose. Surgical treatment is controversial, since it is associated with significant post-operative complications and disease recurrence, even at distant sites, so should be reserved for selected patients.^{2,3} In our case, surgery did not appear to be the best therapeutic approach, since the patient had bronchiectasis in the contralateral lung, which may have been associated with fungal colonization.⁶ Nevertheless, this option could have been considered if medical intervention had failed. Although the patient showed no evidence of immunosuppression, still undefined immune deficiencies cannot be ruled out.⁷ Consequently, while medical treatment appears to have clear advantages in cases in which it is well tolerated, the long-term outcome is unknown.

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Psychogenic Cough: A Rare Cause of Chronic Cough[☆]



Tos psicógena: una rara causa de la tos crónica

To the Editor:

Psychogenic cough is a rare cause of chronic cough in adults. It is typically persistent, disrupts daily activities and causes long-term morbidity. In contrast with cough of organic etiology, there is no clinical or laboratory evidence of disease.^{1,2}

Efforts to make an early diagnosis will reduce morbidity, prevent fixation of symptoms and avoid unnecessary procedures and therapies.²

We report the case of a 45-year-old woman, Caucasian, non-smoker, no habitual medication and no known previous allergies.

The patient consulted her family doctor due to a 9-week history of coughing fits.

The cough started and persisted after an upper respiratory tract infection treated with antibiotics (amoxicillin/clavulanic acid) and antihistamine (hydroxyzine). It was described as violent, nonproductive, occurring every few minutes, disrupting speech, work and daily activities, but not sleep because it disappeared at night.

Physical examination, including ear, nose and throat evaluation was normal, and no noticeable motor tic was observed.

No organic etiology was detected on medical examinations, including chest and sinus X-rays, skin-prick test for allergies, spirometry with bronchial challenge, thyroid ultrasound and chest computed tomography.

Pharmacological therapy with antihistaminic/decongestant (pseudoephedrine+triprolidine), inhaled corticosteroid (budesonide) and bronchodilator (salbutamol) was ineffective. A trial of

acid suppression (omeprazole), prokinetic (metoclopramide) and dietary modification also failed.

During investigation, regular consultations were scheduled. In the course of these consultations, she reported depressive symptoms. She related them to work-related distress, which began 2 months before the coughing fits, when she was moved to a new position. We perceived that cough was always present except when she spoke about her work-related distress. This observation, in association with negative findings on diagnostic tests, lack of response to therapy and the clinical characteristics of the cough, raised the suspicion of a psychogenic etiology.

A plan of weekly cognitive psychotherapy, in addition to antidepressant therapy with sertraline, was initiated. After five weeks, the cough disappeared and depressive symptoms decreased. No relapses were reported in the following twelve months.

In adult patients with chronic cough, doctors should always work toward a clear diagnosis, considering common and rare illnesses.³

Little has been published on diagnostic approaches.^{1,4} However, when extensive evaluation and therapy fail to detect an organic cause, psychogenic cough should be considered.^{1,3,5} Upper respiratory infections, depressive disorders and work distress have been described as precipitating factors.^{3,5} In this case, a psychogenic origin was first suggested by cough absence during sleep and while speaking about work distress.^{1,4}

Non-pharmacological therapies have been reported to be more effective than pharmacological treatments.³ However, there is a lack of randomized, controlled studies comparing different strategies.²

This case highlights the role of an empathic and integrated approach by the family doctor. It made early diagnosis possible, and non-pharmacological and pharmacological treatments could be started immediately, thus avoiding specialist referral and iatrogenic complications.

In conclusion, psychogenic cough is a rare entity, diagnosed after extensive exclusion of organic causes, positive clinical findings and response to specific therapy.

[☆] Please cite this article as: Oliveira R, Martins V, Moreira C. Tos psicógena: una rara causa de la tos crónica. *Arch Bronconeumol*. 2015;51:604–605.