Fatal Case of Chronic Pulmonary Aspergillosis and Tuberculosis: A Case Report from an University Hospital in Colombia

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Abstract

Background

The term aspergillosis from a clinical point of view includes allergic bronchopulmonary aspergillosis, invasive forms of the airway, cutaneous and extrapulmonary aspergillosis and finally chronic non-invasive or semi-invasive pulmonary forms. All of them produced by different species of Aspergillus. In addition, the presentation of aspergillosis together with tuberculosis are rare in scientific literature. We report a case of Chronic pulmonary aspergillosis and tuberculosis in a 72-year-old man.

Case presentation

The patient is a 72-year-old man who was admitted with a 2-year history of constitutional syndrome, dry cough and moderate exertion dyspnea. Chest X-ray showed a rounded mass in the upper lobe of the left lung surrounded by radiolucent areas that suggest cavitations. Computed tomography with chest contrast revealed "tree in bud" pattern in the upper right and middle lobe and lesions of a cystic appearance with the presence of multiple masses with a density of soft tissues. Bronchioalveolar lavage analyses demonstrate Aspergillus fumigatus.

Conclusions

Chronic cavity aspergillosis is an uncommon form characterized by cavitation, fibrosis and pleural thickening seen in immunocompetent or mildly immunocompromised patients with chronic respiratory diseases, especially TB.

Background

The term aspergillosis from a clinical point of view includes diseases of different pathogenesis, such as allergic bronchopulmonary aspergillosis, noninvasive or semi-invasive chronic pulmonary forms, invasive forms of the airway, cutaneous and extrapulmonary and/or disseminated forms. All produced by different species of Aspergillus. (1)

Chronic pulmonary aspergillosis (CPA) is an uncommon form characterized by cavitation, fibrosis, and pleural thickening. It is seen in immunocompetent or slightly immunocompromised patients with chronic respiratory diseases (2). Pulmonary tuberculosis (TB) is the most important risk factor in the progression of CPA. Globally, there are an estimated 1.2 million patients with CPA with a history of TB sequelae. In Colombia, the presence of post-TB CPA is estimated to be around 2000 people, with an annual incidence after TB of 458 cases (1/100000) (3).

Patients may present with a variety of respiratory and constitutional symptoms, although they are often asymptomatic. The diagnostic criterion includes one or more cavities with or without a fungal ball or nodules present in the chest image for more than 3 months (4), direct evidence of Aspergillus spp infection and exclusion of alternative diagnoses (5). Microbiological isolation may be obtained after a
bronchoalveolar lavage or biopsy. The ideal diagnosis of all mycosis should be established on the anatomopathological evidence combined with the isolation in culture of the causative agent (6).

The IgG test of Aspergillus is essential to confirm the infection by *Aspergillus*, which in the presence of a fungal ball will be positive in more than 90% of the cases. In addition, a positive *Aspergillus* IgG test has a positive predictive value of 100% in differentiating infected patients from colonized patients (7).

**Case Presentation**

A 72-year-old male enters with 2-year-old clinical picture of asthenia, adynamia, occasionally wet dry cough associated with functional class deterioration and moderate exertion dyspnea. He consults in another health center one year before the admission to our institution for the same symptoms where they perform fibro bronchoscopy and bronchoalveolar washing without insulation. He has an unclear history of untreated miliary tuberculosis. Since then he has presented multiple respiratory cases that resolved themselves. For 4 months with unexplained weight loss, increased symptoms with changes in the coloration of sputum and dyspnea of small efforts.

Family members indicate two weeks ago worsening of symptoms, functional class decrease, with dyspnea at rest and oxygen requirement by nasal cannula. He reports intermittent antibiotic administration, latest schema two months ago, does not remember which one.

At admission, the patient was emaciated, cachectic BMI 17, tachycardic 112 lpm, tachypneic 26 rpm, afebrile, with reduction of generalized vesicular murmur and rales in right lung base, the rest of the physical exploration was not remarkable.

Blood count of admission with mild leukocytosis 13000 cell/mm³ and neutrophilia 11000 cell/mm³, as well as elevated PCR (26 mg/dl). Chest X-ray showed decreased size of left lung, cleared left diaphragmatic angle cost and parenchyma presence of bilateral alveolar opacities, In addition, there is a rounded mass in the upper lobe of the left lung surrounded by radiolucent areas that suggest cavitations.

Computed tomography with chest contrast revealed "tree in bud" pattern in the upper right and middle lobe, peripheral consolidation patches and extensive frosted glass opacities in the lower right and left lobe. In the upper left lobe, there are lesions of a cystic appearance with a thick wall, the largest of 58 mm, with the presence of multiple masses with a density of soft tissues, the largest of 32 mm. Given the findings it is indicated to take thoracic tomography in prone.

The patient was taken to bronchial lavage with macroscopic evidence of purulent and greenish secretions of predominance in the bronchus for upper left lobe without endobronchial lesions, results are sent to pathology.

Bronchioalveolar lavage analyses demonstrate presence of +++ polymorphonuclears. Colorations of Ziehl neelsen, KOH, Giemsa and Gram were negative. Gene Xpert MTB-RIF was negative for *Mycobacterium tuberculosis*. The coloration of Gomory and Pas was positive for fungal structures, with
evidence of hyphae with acute angles. Galactomannan in the bronchioalveolar lavage was negative, however, the culture was positive for *Aspergillus fumigatus*

**Discussion**

According to the guide Chronic pulmonary aspergillosis: rationale and clinical guidelines for diagnosis and management (1), different spectra of chronic aspergillosis can be found from Aspergilloma, Chronic cavitated aspergillosis, Chronic fibrosing aspergillosis, and Chronic necrotizing aspergillosis or subacute aspergillosis. In our patient was identified the single aspergilloma defined as a single cavity containing a fungal ball with positive serological or microbiological tests.

For histopathological diagnosis, stains such as methenamine of Gomory silver, periodic Schiff acid or the application of fluorescent dyes such as calcofluor (8) are used. Morphologically, hyaline tabulated hyphae, 2 to 5 µm in diameter, branching dichotomously at an acute angle (45 degree) will be demonstrated, being the presence of conidiophores, vesicles, phialides or conidia very rarely evidenced in the tissues (9). Other diagnostic-serological methods are: ELISA, C reactive protein (CRP), Aspergillus antigen and galactomannan, the latter being the least specific and in many cases its result can be negative without being able to rule out the diagnosis (10), as in our case.

In diagnostic images such as CT, a solid, round, or oval fungal ball with soft tissue density (mycetoma) can be seen inside a pre-existing lung cavity usually related to tuberculosis or sarcoidosis (11). It has the special characteristic of being mobile and is generally separated from the wall of the cavity by a density of gas, which results in the tomographic “air crescent” or Monod sign (12). This sign is nonspecific and can be found in other entities such as Angio invasive aspergillosis, bacterial pneumonia, and vasculitis (13).

Azoles, such as Voriconazole (VRCZ), itraconazole (ITCZ) or posaconazole (PSCZ), are the cornerstone of APC treatment. The goal of treatment is to improve symptoms, prevent or limit hemoptysis, and prevent the formation of fibrosis. The response rate varies from 30–82.1% when the duration of treatment is between 4 and 12 months, respectively. The prognosis improves as treatment with azoles is given for longer periods, but increases the risk of resistance, which has been reported up to 50% by molecular methods (14). In addition, the risk of adverse reactions such as hepatotoxicity and neuropathy should be considered. Specifically, itraconazole may cause peripheral oedema, hypertension, and heart failure, and voriconazole may be associated with photosensitivity. In cases of intolerance, the use of amphotericin B or echinococcine as second-line management has been proposed (14).

Relapse is common in post-antifungal withdrawal APC and the mortality rate is high. Up to 27% of patients die in a 30-month follow-up, rising to 50% after 5 years (15).

**Conclusion**
Chronic cavity aspergillosis is a disease that occurs in immunocompetent patients with the presence of pulmonary comorbidities, especially TB. Early diagnosis by clinical history, tomographic study with evidence of crescent sign, laboratory findings (galactomannan, IgG from Aspergillus) and microbiological examination by isolation of Aspergillus spp. will allow timely management and will avoid complications and increased mortality risk. Its treatment is based on the use of itraconazole or voriconazole in patients with functional involvement. In the present case, the patient had a torrid evolution despite the established treatment, had hypoxemic respiratory insufficiency and died within the second week of hospitalization.

**Abbreviations**

APC: Chronic pulmonary aspergillosis

TB: Tuberculosis

CT: Computed tomography

CRP: C reactive protein

BMI: Body mass index

VRCZ: Voriconazole

ITCZ: Itraconazole

PSCZ : Posaconazole

**Declarations**

**Ethics declarations**

The study was approved by the ethics and institutional research committee of Hospital Universitario San Ignacio.

**Consent for publication**

Written informed consent for publication of their clinical details was obtained from the relative of the patient.

**Availability of data and materials**

All data relating to this study are presented within the manuscript. Other materials are available from the corresponding author upon reasonable request.

**Competing interests**
All authors of this manuscript declare no competing interests.

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**Authors’ contributions**

CBP and OLP co-wrote the first and final drafts of this case report. CACP, JTG and LAC, all made significant contributions to the first major revision of the manuscript, final manuscript revisions and approval of the final version. All authors read and approved the final manuscript.

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