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Cor pulmonale complicating chronic pulmonary aspergillosis with fatal consequences: Experience from Uganda

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ABSTRACT

Cor pulmonale is a rare complication of pulmonary aspergillosis (CPA). A 45-year-old Ugandan male with a history of recurrent community-acquired pneumonias was admitted with symptoms of progressive difficulty in breathing, chronic productive cough, non-exertional left sided chest pain and progressive weight loss occurring over a 12-month period. Chest CT scan and echocardiography confirmed the diagnosis of CPA with an aspergilloma complicating bronchiectasis, complicated with *cor pulmonale*. However, this was previously clinically misdiagnosed as PTB.

1. Introduction

Chronic pulmonary aspergillosis (CPA) is a slowly progressive and destructive parenchymal lung disease caused by *Aspergillus* species, typically *Aspergillus fumigatus* [1]. It occurs in ostensibly immunocompetent or subtly immunocompromised patients with current or prior lung diseases [2]. CPA is estimated to affect approximately three million people worldwide [3]. Patients with CPA can be classified into; chronic fibrosing pulmonary aspergillosis (CFPA), chronic necrotizing pulmonary aspergillosis (CNPA) and chronic cavitary pulmonary aspergillosis (CCPA) based on histopathology, clinical findings and radiology findings [1]. Patients with CPA commonly present with pulmonary symptoms such as a persistent and/or productive cough, breathlessness, chest discomfort and haemoptysis, and constitutional symptoms; usually lasting up to 24 weeks or more. This makes it clinically indistinguishable and more often misdiagnosed as pulmonary tuberculosis (PTB) [4]. CPA can mimic smear-negative PTB. Herein, we present a case of a human immunodeficiency virus (HIV) sero-negative Ugandan male with a past medical history of recurrent community acquired pneumonias that progressed into bronchiectasis leading to CPA with an aspergilloma, but was clinically misdiagnosed as PTB with several complications.

2. Case

In December 2018 (day 0), we received a 45-year-old Ugandan male who was referred to Mulago National Referral Hospital with symptoms of progressive difficulty in breathing, chronic productive cough, non-exertional left sided chest pain and progressive weight loss occurring over a 12-month period. His cough was productive of mucopurulent sputum without associated haemoptysis. Eight months prior to this admission, he also noted lower limb swelling that was painless but associated with abdominal swelling, easy fatigability, orthopnoea and paroxysmal nocturnal dyspnoea. He was commenced on anti-tuberculous therapy on clinical basis/suspicion despite negative sputum microbiology for PTB and was on third month of continuation phase at the time of admission. He had never smoked, and his routine testing for HIV was negative. He was a non-alcoholic and employed as a pastor/preacher. He had a significant past medical history of previous hospitalisations for recurrent community acquired pneumonia. He had right inguinal herniorrhaphy eight months before this admission.

Physical examination (day 0) revealed that the patient was a middle-aged man, moderately wasted, with bilateral pitting non-tender pedal oedema, and moderate-pallor without any palpable peripheral lymphadenopathy. He had no digital clubbing neither did he have peripheral or central cyanosis. He had no obvious anatomical chest abnormality, but was in obvious respiratory distress and he had a tachypnoea of 28 breaths per minute. Bronchial breath sounds were auscultated in the left supramammary region with bilateral diffuse coarse crepitations. He had a tachycardia of 110bpm, however, radial pulses were of normal volume and synchronous. There was a loud P2 without a split, raised jugular venous pressure and the point of

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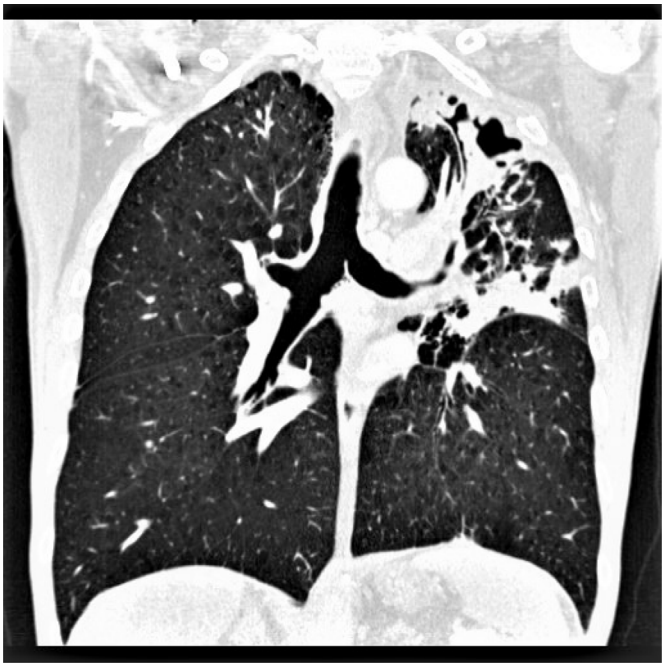

Fig. 1. Chest CT scan: The scan shows left apical cavitation with visible fungal balls and pericavitary fibrosis.

maximum impulse was at the 5th intercostal space left mid-clavicular line with an apical heave. His abdomen was mildly distended, with a positive shifting dullness and tender hepatomegaly of about 4 cm below the coastal margin. The rest of the examination was essentially normal.

Chest computed tomographic (CT) scan (day +1) showed bilateral bronchiectasis, right lower lobe bullae, left upper lobe cavity with a mass and pericavitary fibrosis (Fig. 1). A complete blood count (day +1) done was essentially normal, except for normocytic normochromic anaemia of 10.1g/dl. Urea and creatinine (day +1) were 15.9mg/dl and 1.6mg/dl respectively. He had a serum aspartate transferase and alanine transferase levels of 41.9 IU/L and 19.2 IU/L respectively with a hypoalbulinaemia of 28.6mg/dl. Repeat HIV serology and sputum Gene Xpert MTB/RIF (day +3) were negative. Abdominal ultrasound (day +3) showed moderate ascites, hepatosplenomegaly and normal kidneys. Cardiac echocardiography (day + 3) showed moderate pulmonary hypertension and dilated right cardiac chambers. Electrocardiography (day + 3) demonstrated sinus tachycardia and features of right atrial enlargement. Chest x-ray was not done since a CT scan was available. With these investigations, based on radiology, we made a diagnosis of CPA with an aspergilloma complicating bronchiectasis post-recurrent community acquired pneumonia, complicated with *cor pulmonale* (day +3).

The patient was first (day 0) initiated on ceftriaxone 2g once daily in combination with azithromycin 500mg once daily for a presumptive diagnosis of pneumonia as PTB was being ruled out and prior to the confirmation of the diagnosis of CPA. The patient meanwhile continued his *anti*-TB medication that he came with. After the CPA diagnosis (day +3), he was initiated on oral itraconazole 200mg twice daily for the treatment of CPA, heart failure regime (intravenous frusemide at a dose of 40mg twice daily and oral bisoprolol at a dose of 5mg once daily) and sildenafil 100mg once daily for pulmonary hypertension. Supplemental oxygen therapy was given via nasal prongs to address his hypoxaemia (day +3 to day + 14). He also received 2 doses (day +4 and day + 5) of intravenous albumin to correct his hypoalbuminaemia. However, he progressively deteriorated and passed on 2 weeks (day +14) after admission possibly due to cardiorespiratory failure. Autopsy was not performed.

3. Discussion

According to a recent publication that aimed to make a unified case definition of CPA in resource-constrained settings [5], CPA is defined by "illness of ≥ 3 months and all of: 1) weight loss; persistent cough and/or haemoptysis; 2) chest images showing progressive cavitary infiltrates and/or a fungal ball and/or pericavitary fibrosis or infiltrates or pleural thickening; and 3) a positive *Aspergillus* IgG assay or other evidence of *Aspergillus* infection". However, for this case we did not use the third criterion (i.e. a positive *Aspergillus* IgG assay). Serological diagnosis of CPA is unavailable in our hospital. However, the CT scan was typical for CPA. This report therefore illustrates a classic case of radiologically diagnosed CPA previously misdiagnosed as PTB resulting into complications and eventually death. Detection of *Aspergillus* antibodies is still an important tool in the diagnosis and management of the patients with pulmonary aspergillosis. However, the detection of Aspergillus-specific antibodies does not imply that the patient has an active fungal disease. A previous study done in Uganda showed that "*Aspergillus*-specific IgG antibodies were elevated in 4% of HIV-infected Ugandan adults at the start of TB treatment and in 9% at the end of TB treatment" [6].

The burden of CPA in Africa is not well described. Recent evidence shows that CPA can account for progressive destruction of the lungs and the persistence of pulmonary symptoms after successful completion of TB treatment [4,6–8] and can also mimic smear-negative PTB, as it was the case in this patient. In patients with CPA, creation of new cavities or expansion of existing ones is typical, manifesting with prominent respiratory and/or systemic symptoms. A review done in Uganda showed that "CPA was estimated to affect up to 22% of TB patients with cavities and 4% in those without cavities in Uganda" [9]. Similarly, a recent prospective study done in Uganda showed that 5% of the participants had pulmonary cavities at the end of TB treatment [6]. These cavities can get colonized with fungi to form a fungal ball, which essentially is a biofilm.

This patient had recurrent community acquired pneumonias that could have predisposed him to bronchiectasis. The recurrent pneumonias together with bronchiectasis could have caused the cavities leading to non-invasive forms of *Aspergillus* lung disease. The patient developed *cor pulmonale* as one of the complications. However, there are case reports that have described *cor pulmonale* before in pulmonary aspergillosis among immunocompetent Africans [10].

Conflict of interest

There are none.

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