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Case Report

Incidental cardiac aspergillomas in an immunocompromised woman

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ABSTRACT

We report a case of 3 autopsy proven incidental cardiac aspergillomas, a rare and yet deadly manifestation caused by *Aspergillus*. A 48-year-old Caucasian woman affected by a large B-cell lymphoma was referred to our institute for a whole-body fluorine-18 fluorodeoxyglucose positron emission tomography/contrast-enhanced computed tomography restaging examination, which demonstrated 3 intracardiac masses. The patient was hospitalized, and both a transthoracic echocardiogram and a cardiac magnetic resonance imaging examination were performed. None of the imaging modalities provided a definitive diagnosis. A positive serum galactomannan assay allowed for the initiation of antifungal therapy, but, nevertheless, the patient died a few days later. This case highlights the need to consider cardiac aspergilloma in the differential diagnosis of cardiac masses, especially in immunocompromised patients. Though noninvasive imaging modalities and cardiac magnetic resonance imaging, in particular, help determine the nature of a cardiac lesion, cardiac aspergilloma shows no distinctive radiological features. A high degree of clinical suspicion is therefore key to achieving a timely diagnosis. Histopathological examination with microbiological confirmation remains the diagnostic gold standard.

Introduction

Aspergillus spp. are ubiquitous opportunistic molds capable of causing a broad spectrum of clinical syndromes, usually in immunocompromised hosts. Prolonged neutropenia, allogenic hematopoietic stem-cell transplantation, solid organ transplantation, inherited or acquired immunodeficiency, and corticosteroid use are some of the well-known risk factors [1].

Although *Aspergillus*-related diseases can affect several body organs, cardiac involvement is rare. Possible manifestations of cardiac aspergillosis include intracavitary masses

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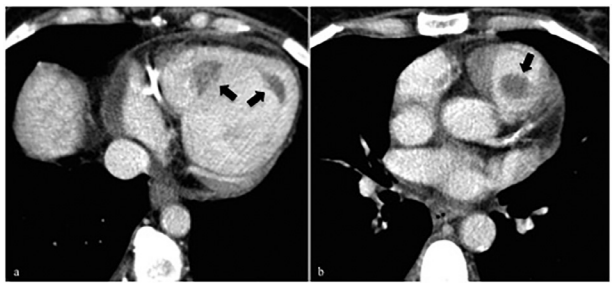

Fig. 1 – Three cardiac aspergillomas incidentally found in a 48-year-old immunocompromised woman. Axial contrast enhanced CT images show 2 intracardiac thrombus-like masses at the ventricular apexes (arrows in a) and a round-shaped mass in the subvalvular right ventricular outflow tract (arrow in b).

(aspergilloma/s), intramyocardial abscesses, myocardial infarction, pericarditis, and/or valvular endocarditis [2]. The diagnosis remains difficult and cardiac aspergillosis usually leads to death.

In this report, we describe a case of 3 autopsy proven cardiac aspergillomas incidentally found in an immunocompromised patient.

Case report

A 48-year-old Caucasian woman affected by a relapsed double-expressor lymphoma (Ann Arbor stage IV) under treatment with rituximab and lenalidomide was referred to our institute for a whole-body fluorine-18 fluorodeoxyglucose positron emission tomography/contrast-enhanced computed tomography (18F-FDG PET/ceCT) restaging examination.

The patient's medical history included appendectomy, type 2 diabetes mellitus on treatment with oral hypoglycemic agents, acute myocardial infarction treated by percutaneous transluminal coronary angioplasty and stenting, and residual left ventricular dysfunction. Previously, the double-expressor lymphoma had been treated with autologous peripheral stem cell transplantation and several chemotherapy regimens.

Together with a significant tumor burden reduction, the restaging 18F-FDG PET/ceCT study revealed 3 intracardiac masses, 2 of which were located at the ventricular apexes and showed a thrombus-like morphology (Fig. 1a). The third mass was found in the subvalvular right ventricular outflow tract and showed a rounded morphology (Fig. 1b). A small amount of pericardial and right-sided pleural effusions also coexisted. Smooth hepatomegaly associated with peripheral reticular regions of poor parenchymal enhancement suggested the presence of congestive hepatopathy. No area of abnormal 18F-FDG uptake was detected.

On the basis of these findings, the patient was taken to our Emergency Department and hospitalized. No relevant signs or symptoms were observed, except for mild asthenia and low-grade fever. Investigations revealed severe pancytopenia (total leucocyte count, 1.44×10^9/L; hemoglobin, 7.4 g/dL; platelet count, 1×10^9/L), significantly increased N-terminal pro-brain natriuretic peptide levels (2025 ng/L), and elevated C-reactive protein values (10.2 mg/dL). Transthoracic echocardiography confirmed the presence of 3 intraventricular masses and assessed the mobility of the mass located in the subvalvular right ventricular outflow tract.

A cardiac magnetic resonance (CMR) imaging examination was requested in order to better characterize the cardiac lesions. The CMR protocol included: cine imaging with steady-state free-precession sequences in conventional cardiac planes (short-axis, vertical long axis, and 4-chamber view); black-blood T1-weighted sequences acquired using a breath-hold fast spin-echo method; black-blood T2-weighted sequences in the short and long axes; perfusion imaging during intravenous bolus administration of gadolinium chelate; early gadolinium enhancement performed within 2 minutes after contrast agent administration in the imaging plane that best demonstrated the larger cross-section of the subvalvular mass; and late gadolinium enhancement imaging consisting of an inversion-recovery gradient echo sequence acquired in the short and long axes, 10 minutes after contrast agent injection.

The examination confirmed the morphology and the location of the masses (Fig. 2). Low signal intensity on T1- and T2-weighted images and absence of both early and late enhancement were common to all the lesions (Figs. 3, 4). Moreover, the CMR imaging confirmed the mobility of the mass located in the subvalvular right ventricular outflow tract and revealed a

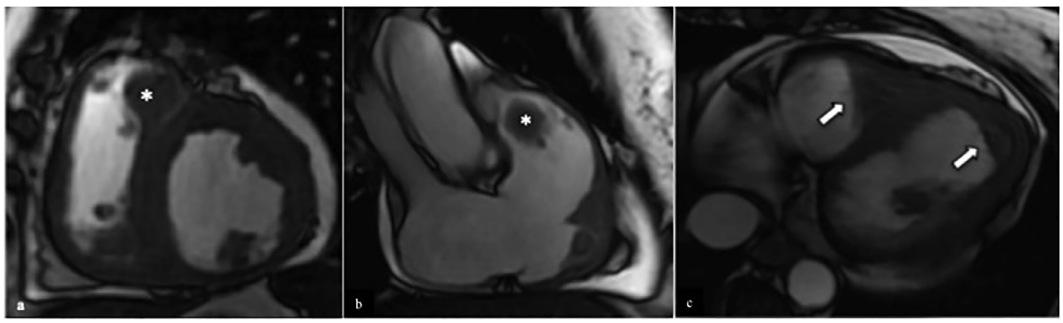

Fig. 2 – Steady-state free-precession cine CMR images (a: short-axis view; b: right vertical long axis; c: 4-chamber view) confirm the presence of 2 thrombus-like masses at the ventricular apexes (arrows) and a round-shaped mass in the subvalvular right ventricular outflow tract (*).

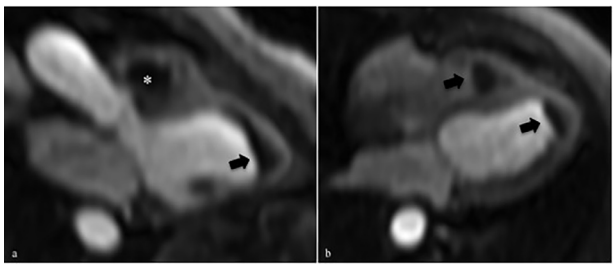

Fig. 3 – First-pass imaging after intravenous administration of gadolinium chelate (a: 3-chamber view; b: 4-chamber view): both the apical masses (arrows) and the mass located in the subvalvular right ventricular outflow tract (*) do not show contrast enhancement.

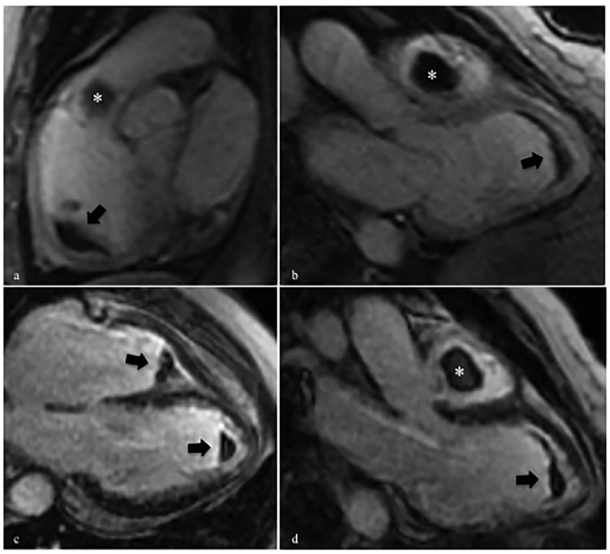

Fig. 4 – Early gadolinium enhancement images (a: right ventricular outflow tract; b: 3-chamber view) and late gadolinium enhancement images (c: 4-chamber view; d: 3-chamber view) demonstrate the absence of contrast enhancement (arrows: thrombus-like apical masses; *: round-shaped mass located in the subvalvular right ventricular outflow tract).

severe biventricular dysfunction, greater on the left side, in the presence of multiple areas of dyskinesia and diffuse delayed enhancement with subendocardial distribution.

Blood cultures from both the central venous catheter and peripheral vein were positive for *Pseudomonas aeruginosa*. Therefore, the central venous catheter was removed, and an antibiotic regimen based on the antimicrobial susceptibility profile was initiated. Neither other bacteria nor fungi were isolated.

In the absence of any signs of extracardiac aspergillosis, the clinical suspicion of cardiac aspergillosis was mainly supported by the medical history. A positive serum galactomannan (GM) assay allowed to start antifungal therapy (eg, intravenous voriconazole) even without histopathological

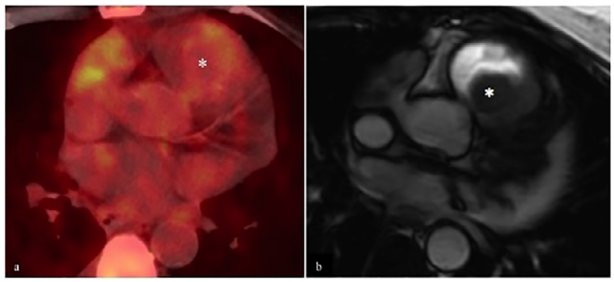

Fig. 5 – 18F-FDG PET/CT imaging (a) compared to steady-state free-precession cine CMR imaging (b). The mass located in the subvalvular right ventricular outflow tract (*) does not show an abnormal 18F-FDG uptake, while it is clearly depicted at CMR imaging.

confirmation, but, nevertheless, the patient died a few days later.

An autopsy confirmed the presence of 3 ventricular masses adherent to the endocardium. Microscopic examination revealed dense stratification of fungal hyphae with dichotomous branching, consistent with organisms from the *Aspergillus* genus, as previously shown [3].

Discussion

Cardiac aspergilloma is a rare potential manifestation caused by *Aspergillus*, with only a few cases reported in the literature [2,4-8]. Most of these descriptions concern immunocompromised patients with nonspecific symptoms, such as fever, shortness of breath, abdominal pain, and weight loss.

Similarly, our patient was immunocompromised and showed nonspecific symptoms.

Investigations highlighted elevated levels of N-terminal pro-brain natriuretic peptide, an established biomarker for diagnosing and monitoring heart failure [9], therefore suggesting the presence of a cardiac dysfunction.

The 18F-FDG PET/ceCT examination allowed to identify the quantity, location, and gross morphology of the cardiac masses. Although 18F-FDG PET does not have an established role in the routine evaluation of cardiac tumors, the few available studies suggest that it can provide useful information about the malignant potential of doubtful masses [10]. In this case, the mass located in the subvalvular right ventricular outflow tract did not show an abnormal 18F-FDG uptake (Fig. 5), whereas the apical masses could not be clearly evaluated because of the overlap of normal 18F-FDG uptake of the adjacent myocardium. Moreover, the evaluation of attachments, possible infiltration, and contrast enhancement were limited by the lack of a proper cardiac computed tomography protocol.

Transthoracic echocardiography was subsequently performed in the Emergency Department. Transthoracic echocardiography remains the first-line diagnostic test for cardiac mass evaluation. Although the widespread availability of echocardiography is a major advantage, there are also several limitations, including operator dependence, a restricted field

of view (particularly in obese patients and those with chronic lung disease), and limited imaging capability of the right heart and extracardiac structures [11]. In our case, echocardiography confirmed both the number and the location of the masses; however, a definitive diagnosis or rule out malignancy was not possible.

According to relevant consensus statements [12,13], CMR imaging was considered the best imaging modality to complement 18F-FDG PET/ceCT and echocardiography in the evaluation of the cardiac masses. CMR imaging does not expose patients to ionizing radiation and offers increased temporal resolution and additional tissue characterization compared to computed tomography [14,15].

In this case, all masses had low signal intensity on both T1- and T2-weighted images without contrast material uptake. The masses showed well-defined margins without signs of invasion of adjacent tissue planes. Therefore, the combination of avascular masses with multiple wall motion abnormalities was strongly suggestive of a diagnosis of biventricular thrombi.

Though noninvasive imaging modalities and CMR imaging, in particular, are essential to assess the likelihood of malignancy of cardiac masses [14-17], cardiac aspergilloma shows no distinctive radiological features. Moreover, considering that the clinical presentation of cardiac aspergillosis is almost always nonspecific, a high degree of clinical suspicion is key to achieving a timely diagnosis. Blood cultures are almost always negative and even if serum GM assay is a useful test to establish an early diagnosis, histopathological examination with microbiological confirmation remains the diagnostic gold standard [1,18].

Early administration of proper antifungal therapy is mandatory and rapid surgical intervention is generally required to improve the chance of survival.

In this case, blood cultures were negative for *Aspergillus* spp., and a positive GM test allowed for the initiation of antifungal therapy. Surgical excision of the masses could not be performed on account of patient's general condition.

Conclusions

Although aspergillosis of the heart is a rare entity, it should be considered in the spectrum of differential diagnoses of cardiac masses, especially in immunocompromised patients. CMR imaging is useful to evaluate the cardiac involvement and helps determine the nature of the cardiac lesions. Although molecular methods can detect the infection sooner than was previously possible, the diagnosis of cardiac aspergillosis is often delayed or made at post-mortem. Despite pharmacologic and surgical treatments, cardiac aspergillosis remains associated with a high mortality rate.

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