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An unusual presentation of pulmonary aspergilloma and review of available literature

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Abstract. – INTRODUCTION: Aspergilloma is a non-invasive form of pulmonary aspergillosis usually presenting as a clump of mold in pre-existing cavitary lung disease. *Aspergillus* related lung diseases have been classified into four types, whose manifestation is often related to previous lung diseases and host immunologic status.

CASE REPORT: Cases of cavitary pulmonary aspergillosis without any evidence of pre-existing cavities, are rarely reported. We present here a case of pulmonary aspergillosis in which cavity formation appeared apparently after the establishment of infection.

CONCLUSIONS: The occurrence of atypical presentations and the importance of recognizing these unusual cases of pulmonary aspergilloma is discussed.

Key Words:
Pulmonary aspergilloma, Cavitation, Nodular air crescent signs.

Introduction

Aspergillus is a ubiquitous saprophytic mold that can cause severe syndromes especially in immunocompromised individuals. Pulmonary aspergilloma (PA) is a manifestation of non-invasive aspergillosis with clinical symptoms that include a chronic cough, low-grade fever and bloody sputum. However, a fair number of patients are asymptomatic[1,2]. Typical chest computed tomography (CT) findings include cavitary lesions with fungus ball-like shadows, air crescent signs, meniscus signs and double arches. Most of these findings can also occur in other infectious lung diseases, such as tuberculosis and echinococcosis[3]. These findings are frequently found in the upper lobes of the lungs[4]. Aspergilloma is usually found in patients with previously formed cavities in the lungs due to underlying condition such as tuberculosis, echinococcosis and lung cancer. Aspergilloma has been described also in cavities caused by other fungal disease such as paracoccidiomycosis[5] and histoplasmosis[6]. We present here a case of pulmonary aspergillosis after chemotherapy and radiotherapy treatment for lung squamous cell carcinoma in which cavity formation apparently occurred after the establishment of infection.

Case Presentation

A 69-year-old male with a history of smoking (25 years), affected by type 2 diabetes mellitus and vasculopathy, was admitted for a squamous cell carcinoma of the right lung. The lung cancer, diagnosed by total body CT, extended from the right upper lobe to the ventral lower lobe (clinical stage III B; Figure 1A). After the lesion was treated with chemotherapy and radiotherapy, a CT scan did not show any sign of cavitary lesions (Figures 1B and 1C). A new CT performed after 10 months showed a posterior pulmonary cavity closely resembling aspergilloma, characterized by "nodular air crescent signs" extending from the apex to the middle and lower lobes of the right lung (Figure 1D). The cavity was clear, lined by a thick wall, and contained amorphous material (Figure 1E). *Aspergillus* infection was suspected based on these radiological findings. Three specimens were processed for fungal culture while the patient was put on fluconazole treatment. The diagnosis was confirmed by isolation of *Aspergillus flavus* and according to the current guidelines for the treatment of aspergillosis, initial therapy with fluconazole was replaced by voriconazole and itraconazole. A new CT scan performed after two months showed a significant reduction of the mass of fungal mycelia in the right lower lung field after antifungal therapy (Figure 1F).

Available Literature

A bibliographic search was conducted on PubMed using the key words: "pulmonary aspergilloma" and "pulmonary aspergillosis". Only case reports or case series articles in which the clinical presentation of the case was complete with photos and text were included.

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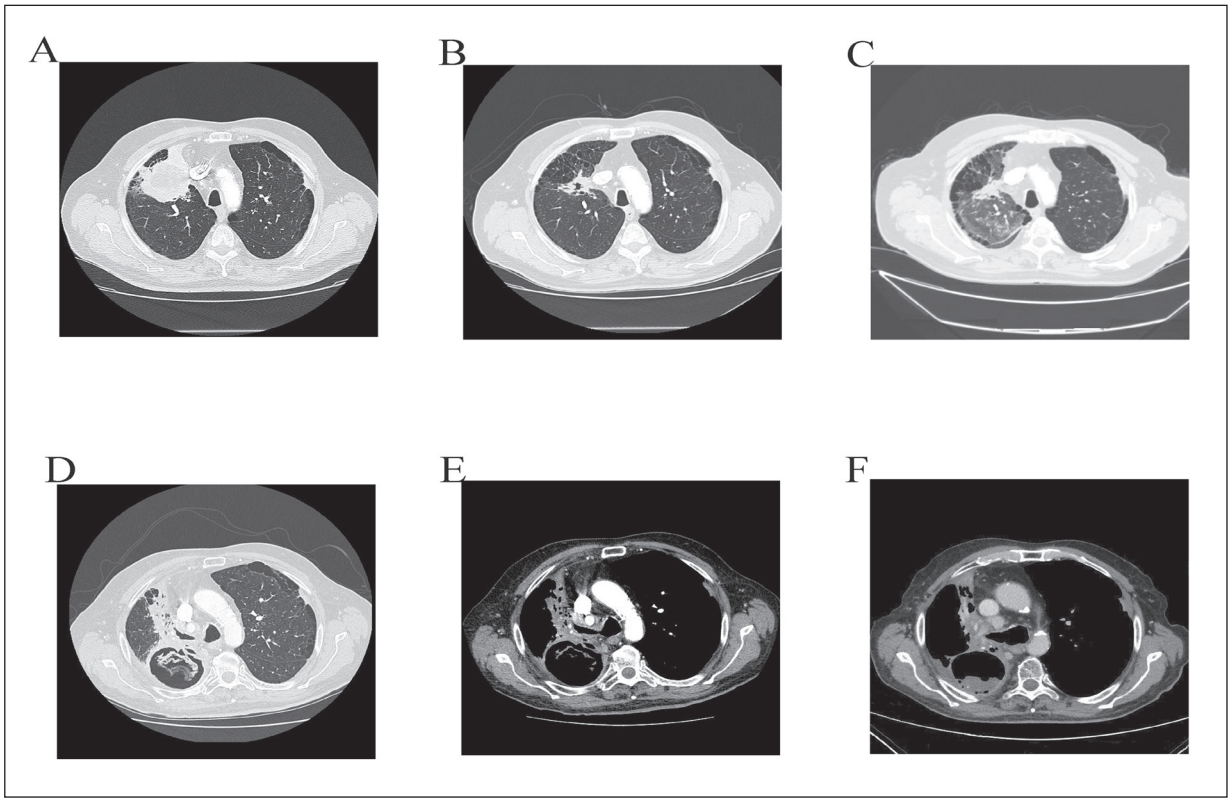

Figure 1. Chest CT scan during invasive pulmonary aspergillosis. ***A***, Anatomy of right lung on CT before chemotherapy treatment. ***B***, Anatomy of right lung on CT after chemotherapy treatment. ***C***, Anatomy of right lung on CT after radiotherapy treatment. It is evident the presence of fibrous tissue as a conseguence of post radiation therapy. There is no evidence of any cavity formation; ***D***, CT scan shows multiple bilateral cystic lesions with air-fluid level. ***E***, CT scan shows an intracavitary aspergilloma. ***F***, CT scan showing reduction of the mass of fungal mycelia in the right lower lung field after antifungal therapy.

Reviews, meta-analysis or clinical trials have not been included. In accordance with the criteria set out, 122 case reports were selected.

Pulmonary aspergillosis was considered "classic" if the clinical spectrum of pulmonary infection met the criteria established by Watts and Chandler[7]: fungal growth in a preexisting lung cavity, tracheobronchitis, chronic destructive infection of the lung parenchyma and progressive fungal invasion of the lung parenchyma. Data collected were analyzed by Chi-square test (χ^2). A p-value <0.05 was considered statistically significant.

Results

According to our criteria, we found 107 cases (87.7%) of classical PA and 15 cases (12.3%) of non-classical PA. The patients' age at presentation ranged from 5 to 81 years with a mean age of 57 years. No significant differences of age were detected between patients with classical or non-classical types (Table I). Men were more than woman, and the risk of classical PA was higher in males' group (F:M=4:1). There were not relevant gender differences for the risk of non-classical PA.

Previously treated TB and cancer that resulted in the formation of an air-filled cavity were the most common association of classical PA (36.4% and 24.2%, respectively), although in 27.1% of cases the presence of associated comorbidity was not specified. In classical PA cases, hemoptysis was the commonest symptom (55.1%), followed by chest pain (47%), cough (44%), dyspnea (42%) and weight loss (33%). In the majority of both classical and non-classical PA cases, it was not possible to exactly determine how long, after the underlying respiratory pathology, pulmonary aspergillosis occurred. Right upper lobe was the favorite site of classical PA (89 patients, 83%) while lesions in non-classical PA were found in peripheral lung zones. In classical PA, other preferred sites were left upper lobe (11 patients, 10.2%), left lung (3 cases), right lower lobe (2 cases) and right middle lobe (2 cases).

Table I. Differences between classical and non-classical PA.

	Classical PA (n=107)		Non-classical PA (n=15)		
	No.	%	No.	%	
Man	89	83.1	8	53.3	$p<0.05$
Women	18	16.8	7	46.6	$p<0.05$
Tb	39	36.4	-		$p<0.05$
Cancer	26	24.2	-		$p<0.05$
Bronchiectasis	11	1	-		$p<0.05$
Hemoptysis	59	55.1	3	20	$p<0.05$

About two-thirds (66.7%) of all cases were painful, equally in classical and non-classical types. In both classical and non-classical PA cases, *A. fumigatus* was the most common species recovered from lesions (90%). Other reported pathogenic species include: *A. niger, A. flavus* and *A. versicolor*. Chronic destructive infections of the lung parenchyma and rapidly progressive fungal invasions of the lung parenchyma, two of the criteria established by Watts and Chandler[7] to define classic PA, were not described in the majority of cases.

Discussion

Aspergillus spp. can produce a wide range of pulmonary infections. Four distinctive patterns of *Aspergillus* related lung diseases are recognized, as follows: saprophytic colonization, pulmonary aspergilloma, aspergillosis-induced hypersensitivity and invasive pulmonary aspergillosis[2]. Patients with bronchogenic carcinoma are more prone to secondary pulmonary aspergillosis, due to cancerous involvement of the pulmonary tissue as well as long-term steroid, anticancer and antibacterial therapy[8,9]. Most cases of aspergilloma are detected in the upper lobes, in residual tuberculosis cavities[10]. Unusual presentation of the present case was that no signs of cavitation were observed before the establishment of *Aspergillus* infection. In addition, the cavitation was extensive both involving the upper to the mid-lower lobes of the right lung. Kang et al[11] described unusual cases of pulmonary aspergillosis in immunocompetent hosts without a preexisting underlying lung lesion. In these reported cases, CT evidenced a single nodule or mass with or without an air crescent or a localized consolidation. The mechanisms underlying cavity formation during fungus infections are unclear and lung disorders with cavitary lesions can vary depending on the patient's immune conditions. In patients with a mild to moderately weakened immune system, such as diabetes, liver cirrhosis and corticosteroid therapy, cavitation in fungal infection is observed more frequently than in the immunocompetent patients and can mimic malignant cavity[12]. Finally, classical and non-classical forms are significantly different with regard to radiological presentation, since non-classical PA primarily manifests as a single nodule or mass with or without an air crescent.

Differential diagnosis should include lung tuberculosis, lung suppuration, pulmonary mycosis (aspergillosis), Wegener's granulomatosis and primary lung cancer[13]. In this study, sputum culture has been important to confirm diagnosis and guide treatment. The patient was severely immune compromised, and it was not possible to perform lung biopsy. Microbiological identification was essential for a targeted therapy, allowing a significant improvement of clinical condition.

Conclusions

Aspergilloma principally occurs in the upper lobes of the lungs of patients with previously formed cavities because of underlying diseases such as tuberculosis. We present here a case of pulmonary aspergilloma without a preexisting underlying lung lesion. The present report suggests that cavity formation can also occur during or after the establishment of aspergillosis infection. Moreover, we highlight here the importance of clinical, radiological and microbiological findings for an early diagnosis of aspergilloma.

Conflicts of Interest

The authors declare no conflict of interest.

Informed Consent

The patient gave the permission to use his clinical image and data.

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