

## Aspergilloma: Clinical Manifestations after Tuberculosis Infection

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### Abstract

Aspergilloma is a mass-like fungus ball consisting of *Aspergillus fumigatus*. Aspergilloma occurs in patients with pulmonary structural abnormalities in which the presence of a previous cavity is the predisposing factor that most often results in *Aspergillus* colonization, especially in tuberculosis endemic countries. Female patients who were 28 years old and 33 years old complained of hemoptysis, chest pain, weight loss, and a history of TB treatment. Chest X-ray and CT scan revealed a solid lesion with an “aircrescent sign”, indicating an Aspergilloma lesion. The patients were then given symptomatic, anti-fungal drugs, and supported by an embolization procedure to reduce hemoptysis. The patient's condition began to improve after treatment. Imaging findings in X-rays and CT scans that point to Aspergilloma will help doctors in further management to provide a better prognosis for the patient.

**Keywords:** *Aspergilloma, tuberculosis, imaging*

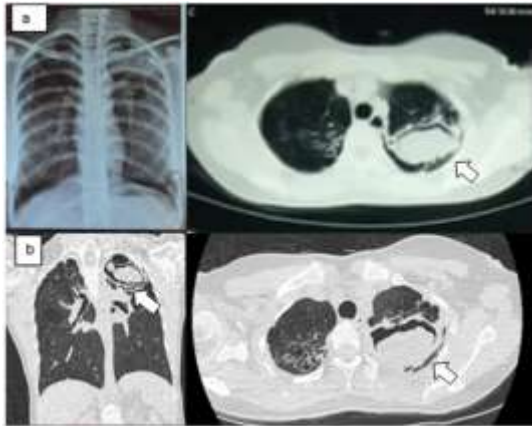
### INTRODUCTION

Aspergilloma is a mass-like fungus ball consisting of *Aspergillus fumigatus*. Aspergilloma occurs in patients with an abnormal lung structure in the presence of a previous cavity.<sup>(1)</sup> Pulmonary aspergilloma can develop at any age, but it is most common in the elderly, which is possible due to the aging process of patients with post-tuberculous pulmonary lesions. Pulmonary Aspergilloma can occur in both men and women, but most authors report its predominance in male patients.<sup>(2-4)</sup> Aspergilloma development can occur in immunocompetent or immunocompromised patients. Sequelae of the parenchyma and cavity due to tuberculosis is the predisposing factor that most often results in *Aspergillus* colonization, especially in tuberculosis endemic countries.<sup>(2,4)</sup>

Clinical suspicion is based on a history of Tuberculosis or other lung diseases that predispose to pulmonary Aspergilloma. Sometimes, pulmonary aspergilloma is asymptomatic for several years. The most common symptom found in reported cases is hemoptysis.<sup>(2,3)</sup> Hemoptysis occurs due to the erosion of adjacent secondary vessels as a result of systemic hypervascularization,

entailing arterial bronchial hypertrophy and neovascularization via the parietal artery. Hemoptysis should be taken into consideration in patient management decisions through surgery. Chest pain is caused by peripheral pulmonary Aspergilloma that is in contact with the pleura. Often in patients with destroyed lung aspergilloma, the presence of bronchorrhea and dyspnea can also be observed, with the addition of fever in patients with generally unfavorable conditions.<sup>(5)</sup>

Diagnosis of pulmonary aspergilloma can be obtained through chest X-ray images or CT scans. If the imaging shows Aspergilloma, evidence of an immunological response to *Aspergillus spp.* or direct evidence of *Aspergillus* via bronchoscopy or sputum specimens can help confirm the diagnosis.<sup>(6)</sup>



**Figure 1 A.** First case. Chest X-rays showed a cavity with an opacity in it, forming an “air-crescent sign” in the upper plane of the left lung. **B.** CT scan image shows a cavity with an opacity in it, forming an “air-crescent sign” with the location of the opacity following the direction of gravity leading to Aspergilloma lesion in the superior lobe of the left lung (arrow).

#### Case 1

A 28-year-old woman presented with a bloody cough for  $\pm$  3 years. The cough was accompanied by intermittent chest pain and weight loss. The patient had undergone a complete category 1 pulmonary tuberculosis treatment program.



**Figure 2 A.** Case 2. The chest X-ray shows infiltrates in the upper plane of the right lung, which suggests pulmonary tuberculosis. **B.** CT scan image shows cavity with opacity in it that forming an “air crescent sign” (arrow) with the position of opacity following the direction of gravity, leading to Aspergilloma lesion in the superior lobe of the right lung.

The chest X-ray result shows a cavity with opacity in it, which formed an air crescent sign. On the high-resolution computed tomography (hereafter named HRCT) examination, there is a thick-walled

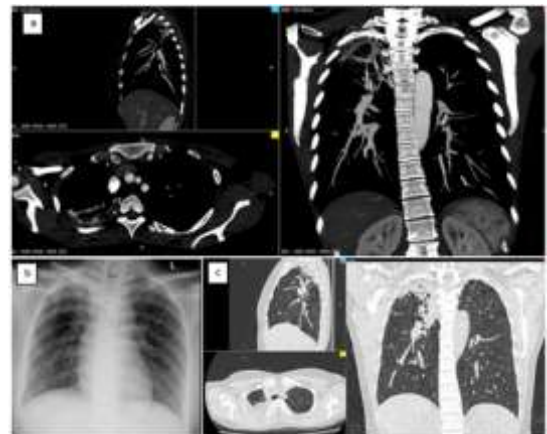
cavity with clear boundaries and a solid lesion inside with an air crescent sign, accompanied by multiple cavities and fibrosis around it, which corresponds to Aspergilloma on the apex of the right lung accompanied by pulmonary TB.

In laboratory tests, complete blood count was within normal limits. Microbiological examination using sputum samples from bronchoalveolar lavage (BAL) did not reveal the typical morphology of fungi or the growth of pathogenic bacterial colonies.

The patient received symptomatic treatment in the form of tranexamic acid and codeine. In addition, the patient also received treatment for fungi, which was fluconazole. The patient's condition began to improve after treatment.

#### Case 2

A 33-year-old woman came with complaints of recurrent blood coughs of 8 years, which has grown worse in the last 9 months. She usually coughs up  $\pm$  250 cc of blood, accompanied by chest pain. The patient had a history of pulmonary tuberculosis  $\pm$  8 years ago and had undergone a complete category 1 treatment program.



**Figure 3 Case 2.**

**Figure A.** CT scan angiography shows the feeder artery of the right bronchial artery, right supra- intercostal artery, and right pulmonary segment of the posterior subsegmental branch.

**Figure B.** Post-embolization chest X-ray shows an infiltrate at the apex of the right lung.

**Figure C. CT scan evaluation indicates multiple cavities and consolidation images with a fungus ball, inside which forms an air crescent sign with a reduced size.**

The results of the chest X-ray suggest that there are infiltrates in the upper field of the right lung, which showed an impression of pulmonary TB compared to the previous chest X-ray on July 28, 2020, in which the infiltrates were reduced. The examination was continued by performing a CT scan angiography, showing pulmonary tuberculosis with Aspergilloma of the apical segment of the superior lobe of the right lung with the feeder artery from the right bronchial artery, the right supra intercostal artery, and the right pulmonary segment of the apical posterior subsegmental branch. The patient performed a CT scan evaluation, and the results were multiple consolidation and cavity images with a fungus ball in it, which formed an air crescent sign with a relatively reduced size.

In laboratory tests, the obtained complete blood results were within normal limits. Examination of the TCM sputum for detecting *Mycobacterium tuberculosis* showed negative results, microbiological examination through sputum samples from bronchoalveolar lavage (BAL) was not indicative of the morphology of fungus, and *Pseudomonas oleovorans* was found in sputum culture. The patients received symptomatic treatment in the form of tranexamic acid and codeine, fluconazole for mycosis, and antibiotics for bacterial infections. The patients also received radiological intervention with embolization to stop the bleeding.

## DISCUSSION

Globally, it is estimated that about 1.2 million people suffer from chronic pulmonary aspergillosis (CPA) as a sequela to TB, especially in TB-endemic areas, such as Africa, the West Pacific, and Southeast Asia. <sup>(6)</sup> The diagnosis of Aspergilloma is difficult to establish in developing countries with a high prevalence of TB due to hemoptysis often equated with TB without

consideration of other diagnoses, such as Aspergilloma. Hemoptysis patients with negative microbiological results often receive TB treatment or drug-resistant TB treatment. Therefore, the diagnosis of Aspergilloma morbidity is unknown due to the limited availability of serologic, radiological, and human resources. <sup>(6)</sup>

Primary aspergilloma is very uncommon and likely to occur in patients with immunocompromised states, such as patients with neutropenia, long-term use of glucocorticoids, or AIDS with bronchial disorders invaded by *Aspergillus spp.* <sup>(1)</sup> Secondary Aspergilloma occurs in immunocompetent patients with previous pulmonary pathologies, such as TB, sarcoidosis, lung abscesses, bronchogenic cysts, or lung tumors that are being exposed to *Aspergillus* spores from the environment. <sup>(1)</sup> However, the most common preexisting pulmonary pathology is TB with the time interval between TB diagnosis and aspergilloma ranging from <1 year to 30 years. <sup>(1)</sup> In these two cases, the patients had a history of pulmonary TB, which renders the patient susceptible to Aspergilloma. Both patients had recurrent hemoptysis despite having completed first-line TB treatment and negative TCM test results for *Mycobacterium tuberculosis*. There is a 3–8-year interval of clinical diagnostic challenges between the initial diagnosis of a patient with pulmonary TB and the final diagnosis of Aspergilloma.

Most Aspergilloma cases are asymptomatic, and 10% show spontaneous resolution. <sup>(7)</sup> Non-specific symptoms include hemoptysis, cough, chest pain, and fever. Massive hemoptysis, coughing, and chest pain occurred in both patients, an uncommon complication thought to occur as a result of mechanical or endotoxic irritation of blood vessels or direct invasion by fungus balls. <sup>(7)</sup> Hemoptysis results from the erosion of adjacent secondary blood vessels due to systemic hypervascularization, leading to bronchial artery hypertrophy and neovascularization through the parietal arteries. <sup>(5)</sup> Both patients complained of hemoptysis, but the second

patient experienced more severe recurrent complaints (hemoptysis grade II); this allowed vascular involvement.

Based on the 2016 Practice Guidelines for the Diagnosis and Management of Aspergillosis, CT scan is recommended whenever there is clinical suspicion for Aspergillosis regardless of the results of chest radiographs. A contrast-enhanced chest CT scan is recommended if the nodule or mass is close to a large blood vessel.<sup>(8)</sup> A follow-up chest CT scan is recommended to assess treatment response after at least 2 weeks of treatment, and early assessment is indicated if the patient is clinically worse. When a nodule is close to a large vessel, a more frequent observation is necessary.<sup>(8)</sup>

Imaging features of Aspergilloma look like a simple, expanded cavity lesion with thick walls accompanied by a fungus ball that develops within the cavity. Typical features are opacities with an "air crescent sign".<sup>(5)</sup> This image may also be seen in necrotic lung cancer, hydatid cysts, or even foreign bodies in the lung. If the diagnosis is doubtful, a chest CT scan in the lateral decubitus position can be helpful by showing mobilization of the fungus ball in the direction of gravity (Monod sign). A chest CT scan also makes it possible to differentiate simple from complex Aspergilloma through the identification of cavity wall condition, the presence or absence of pachypleuritis, and the condition of the surrounding lung parenchyma.<sup>(5)</sup> For inoperable pulmonary aspergilloma, a chest CT scan can be used for percutaneous treatment planning through the injection of an anti-fungal product, or to consider percutaneous lung biopsy when the diagnosis has not been established. Pulmonary aspergilloma is more frequently found in the upper lobe of the lung and the upper part of the lower lobe segment where tuberculosis is more likely to develop.<sup>(5)</sup> In the first case, plain radiographs and CT scans show a well-defined cavity with solid lesions inside with an air crescent image, accompanied by multiple cavities with adjacent fibrosis. In the second case, the plain radiograph showed an

infiltrate in the upper plane of the right lung accompanied by multiple cavities within it. The CT scan of the second patient showed an opacity within the cavity, forming an "air crescent" image and a gravity-following fungus ball position suggesting Aspergilloma features. The patient complained of worsening hemoptysis, then the clinician ordered a CT chest angiography examination to identify the involvement of blood vessels. CT angiography of the chest showed pulmonary tuberculosis with aspergilloma of the apical segment of the right lung with pooling contrast on the cavity wall, which is fed from the right bronchial artery, suprema intercostal artery, and apical segment of the posterior subsegmental branch of the right pulmonary artery. The patient then underwent embolization to reduce the experienced hemoptysis symptoms. After embolization and treatment, she underwent medical control through chest HRCT as a post-treatment evaluation. In post treatment HRCT, there was a consolidation of the right lung apex with a fungus ball image with reduced lesion size.

If the means are available, serologic examination, blood-based polymerase chain reaction (PCR), histopathological examination/cytological examination, and culture are recommended.<sup>(8)</sup> Serologic testing for precipitin antibody [immunoglobulin G (IgG) to Aspergillus] allows for a definitive diagnosis and will be found in > 90% of cases.<sup>(6)</sup> There is a debate on the clinical utility of PCR in diagnosing Aspergillosis.<sup>(8)</sup> Recommendations for PCR testing are based on publications that validate PCR when used in conjunction with other tests, such as the antigen detection test for diagnosing Aspergillosis and/or reduce the use of prophylactic antifungals.<sup>(8)</sup> PCR tests are promising but cannot be recommended for routine use in clinical practice.<sup>(8)</sup> When PCR testing is used, diagnostic testing should be considered.<sup>(8)</sup> Bronchoscopy with bronchoalveolar lavage (BAL) is recommended in patients with suspected Aspergillosis. Before BAL is performed, clinicians must be aware of the

patients' comorbidities, such as severe hypoxemia, bleeding, and platelet transfusion refractory thrombocytopenia. BAL results are not good for detecting peripheral nodular lesions, thus, a percutaneous or endobronchial lung biopsy should be considered.<sup>(8)</sup> The absence of *Aspergillus fumigatus* in the sputum does not mean that there is no *Aspergillus* infection, but the presence of *Aspergillus fumigatus* in bronchoscopy specimens is much better as a marker of infection. Sputum microscopy or bronchoscopy specimens often show the presence of fungi, but the published culture-positive rate is around 56–81%.<sup>(9)</sup> Both patients underwent bronchoscopy with bronchoalveolar lavage (BAL) to obtain microbiological samples, and sputum examinations did not reveal the characteristic morphology of the fungus. Then, the examination was followed by a culture examination. The absence of fungal morphology on sputum examination does not indicate the absence of fungal infection, because literature mentions that the published culture-positive rate is about 56–81%.<sup>(9)</sup>

Asymptomatic patients with single Aspergilloma and no progression of cavity size for 6–24 months should be continued for evaluation. Symptomatic patients, especially severe hemoptysis, with single Aspergilloma, should undergo resection, assuming no contraindications. Peri- / post-operative antifungal therapy is not routinely required, but if surgery is of moderate risk (related to cavity location and morphology), antifungal therapy is recommended with voriconazole (or other azole classes) or echinocandin to prevent *Aspergillus empyema*. Both patients received symptomatic therapy (codeine and tranexamic acid) and antifungal (fluconazole) according to the 2016 Practice Guidelines for the Diagnosis and Management of Aspergillosis. Both patients showed improvements post-therapy.

Hemoptysis is one of the most common symptoms in patients with respiratory disease and has a mortality rate of more than 50% in massive hemoptysis. Treatment of patients with massive hemoptysis through

conservative management or surgery may lead to increased morbidity and mortality.<sup>(10)</sup> Bronchial artery embolization (BAE) is a safe and effective emergency management procedure for both massive hemoptysis and recurrent chronic hemoptysis. The reported success rate of bronchial arteriography and direct embolization is 75–98%.<sup>(10)</sup> The common etiologies of hemoptysis are tuberculosis (55.2%), bronchiectasis (28.8%), and malignancy (5.8%).<sup>(10)</sup> To reduce symptoms of hemoptysis, the second patient received embolization therapy using 355–500-micron PVA, and post embolization with PVA showed 60%–70% decrease in supply. The patient's condition improved after the embolization procedure and she did not complain of hemoptysis during the treatment process.

## CONCLUSION

Aspergilloma is a mass-like fungus ball consisting of *Aspergillus fumigatus*, which occurs in patients with pulmonary structural abnormalities in the presence of a previous cavity. Tuberculosis is a predisposing factor that most often results in *Aspergillus* colonization. Patients may complain of coughing up blood, chest pain, and weight loss. The finding of a cavity with an internal solid lesion forms an air crescent sign and a Monod sign indicating Aspergilloma lesion. PCR and microbiology can provide a diagnosis, and the therapies given are asymptomatic and anti-fungal drugs. Embolization and operative measures can be considered to reduce symptoms of hemoptysis.

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