Case report

Co-existing active pulmonary tuberculosis with aspergilloma in a diabetic patient: A rare case report✩

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A R T I C L E   I N F O

Article history:
Received 11 October 2021
Revised 27 December 2021
Accepted 30 December 2021

Keywords: Aspergilloma Pulmonary tuberculosis Monod sign

A B S T R A C T

Pulmonary aspergilloma is commonly associated with tuberculosis. Pulmonary aspergilloma is found in residual tuberculosis cavities and potential for other pathogens' infections due to its sufficient oxygen and necrotizing tissue. A 48-year-old woman came with shortness of breath and cough for 7 months. She was diagnosed with pulmonary tuberculosis 9 months ago and was still under anti-tuberculosis drug therapy. She also suffered from type II diabetes mellitus. Chest examination showed vesicular sound decreased in third to fourth left intercostal spaces. A chest x-ray revealed a thick-walled cavity with the air-crescent sign in the left upper lobe lung leads to aspergilloma and active pulmonary tuberculosis. This finding was confirmed by the contrast-enhanced CT scan of the chest and continued to lobectomy. Histological examination confirmed the presence of a granuloma formation, necrosis, hyphae structure with the conclusion of Aspergillus sp. infection.

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Key messages

Aspergilloma is commonly caused by Aspergillus sp. which often grows on pre-existing single or multiple cavities of pulmonary tuberculosis. It was a rare case even in the tropical country. Imaging radiography plays a vital role in identifying pulmonary aspergilloma with the typical appearance. Anti-tuberculosis and thoracotomy lobectomy are the recommended treatment.

✩ Acknowledgments: The authors would like to thank to -blinded- for their allowance to do this research. The authors also want to say many thanks to all radiology residents for their support of collecting data. This work was funded by Department of Radiology, Faculty of Medicine Universitas Sebelas Maret/Dr. Moewardi General Hospital.

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https://doi.org/10.1016/j.radcr.2021.12.064

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Introduction

Pulmonary aspergilloma is commonly associated with lung tuberculosis (TB). Aspergilloma is a fungal infection most often caused by the genus Aspergillus sp. which grows on a pre-existing single or multiple cavities as an intracavitary fungus ball [1]. Aspergilloma is a less pathogenic fungal infection in a healthy host. The organism enters the respiratory mucosa from inhalation with subsequent invasion causing necrosis and ulceration. Generally, pulmonary aspergilloma is seen in residual tuberculosis cavities which are suitable for various organisms’ development including the fungus due to its sufficient oxygen and necrotic tissue [2]. Aspergilloma is diagnosed by the characteristic radiographic findings and histopathology. Co-existing active pulmonary tuberculosis with aspergilloma has rarely been reported.

Fig. 1 – Chest x-ray showed air surrounding the fungal ball in a pulmonary cavity as pointed by arrow.
Globally in 2016, there were 10.4 million incidents of TB (CI 8.8 million-12 million) equivalent to 120 cases per 100,000 population. The 5 countries with the highest case incidence are India, Indonesia, China, Philippine, and Pakistan. The number of new TB cases in Indonesia is 420,994 cases in 2017 [3,4]. Most of these patients have been able to be treated until they are declared negative on sputum examination. The availability of anti-tuberculosis drugs up to the village has been accompanied by mentoring programs from the Public health center and village cadres to avoid potential drug withdrawal and handling side effects. Therefore, cases of pulmonary TB with co-existing antituberculosis drug therapy with aspergilloma are rare and interesting to be discussed further amid the high success rate of OAT therapy.

Case history

A 48-year-old woman came with shortness of breath and cough for 7 months. The patient has a history of type 2 diabetic mellitus and has been undergoing treatment for 3 years since diagnosis. The patient received fast-acting insulin 8-0-8 units subcutaneously. Admission baseline investigations

Fig. 2 – Contrast-enhanced chest CT scan in axial, sagittal, and coronal view. Arrow: the Aspergilloma lesion called as Monod’s sign.
showed HbA1c 8.5%. She was then diagnosed with pulmonary tuberculosis and still consumed anti-tuberculosis drug therapy. The TB case in this patient was new and was not relapse or drop-out case. During the period when the patient was taking OAT, the patient complained of coughing and shortness of breath that got worse.

Chest examination showed vesicular sound decreased in third to fourth left intercostal spaces. HIV serology testing was negative. The results of the BTA sputum examination/Gene expert gave the results of Mycobacterium Tuberculosis (MTB) detected low and Rifampicin resistance not detected. Chest x-ray revealed a thick-walled cavity with Monod sign in the left upper lung lobe leads to aspergilloma and infiltrates accompanied by multiple cavities in the left upper lobe lung leads to active pulmonary tuberculosis (Fig. 1).

This finding was confirmed by a contrast-enhanced CT scan of the chest. It showed a fungal ball surrounded by air in a pulmonary cavity with Monod sign, size 5.1 × 6.1 × 3 cm. Tree in bud sign and Y sign in the left upper lung lobe had also been shown. No centrilobular nodules were seen (Fig. 2).

She underwent a left thoracotomy upper and lower lobectomy. Histology examination confirmed the presence of a granuloma formation, necrosis, hyphae structure with the conclusion of Aspergillus sp. infection (Fig. 3). The necrotic area is histologically amorphous and characterized by a grossly white and cheesy appearance as caseous necrosis. This pattern at the center of granulomas surrounding foci of Mycobacterium tuberculosis infection may be due to the release of large amounts of Mycolic Acids from the M. tuberculosis cell wall. Currently, patients are still in regular control, con-
tinued anti-tuberculosis and anti-fungal therapy with a good result.

Ziehl-Neelsen’s smear examination 3 months after thoracotomy was performed 2 times (morning and morning examination) with negative results, and then the patient was routinely controlled. The patient was declared cured after 3 months of continued treatment with Category 1 OAT (rifampicin/isoniazid) at a dose of 450/300 mg for 3 months and fluconazole/itraconazole antifungal therapy for 3 months after thoracotomy.

Discussion

Pulmonary aspergilloma is caused by the colonization and proliferation of Aspergillus sp. Aspergilloma may coexist with any underlying condition, which usually occurs in a pre-existing cavity in the lungs [5]. Aspergillus sp. has a diameter of 2-3 m with a habitat in the soil and is mostly found in dust and decaying organic matter. The spore formation of Aspergillus called conidia is found in the air. Humans inhale hundreds of conidia every day. The immunocompetent host can destroy conidia in the presence of the pulmonary immune system. Aspergillosis to Aspergilloma formation occurs when the host response is too strong or too weak to aspergillus antigens.

In immunocompromised hosts, Aspergillus fungi cause great morbidity and mortality. Conidia measuring 3-5 m easily reach the distal airway on inhalation. Most of the conidia that enter the upper respiratory tract can be eliminated by the ciliary movement of the complex pseudo-columnar epithelium. To avoid the host elimination system, Aspergillus produces the protein gliotoxin, fumagillin, and helvolic acid. The protein produced can inhibit the movement of cilia and facilitate the internalization of conidia in endothelial cells and epithelial cells. Conidia can interact with respiratory tract leukocytes, invade tissue hyphae and interact with endothelial cells [6]. Conidia that enter the host body tissue can be recognized by the distinctive Pathogen Associated Molecular Patterns (PAMPs) structure that is not shared by other organisms. Macrophages will recognize the structure of conidia PAMPs through specific Pattern Recognition Receptors (PRRs). Inhaled Aspergillus conidia contain a small amount of -glucan and trigger an inflammatory response. The process of germinating conidia will change the composition of the cell wall, and -glucan will be exposed when conidia swelling (swelling) and hyphae grow [7]. The above process occurs repeatedly and within a certain period of time. The combination of these processes over a period of time forms a complex that we call aspergilloma.

Imaging radiography, especially a chest x-ray and CT scan, has an important role in diagnosing pulmonary aspergilloma [8,9]. Characteristic CT finding is the typical appearance of air surrounding the fungal ball in a pre-existing pulmonary cavity, this is known as Monod’s sign, typically shown as a round or oval intracavitary mass on the upper lobe. This mass is mobile in a prone position [10,11]. No enhancement has been found on fungus balls after contrast administration [12]. In this case, pulmonary aspergilloma was shown as a single fungal ball in a cavity, no progression was found over months of observation with very few symptoms. The 10-year survival rates for simple aspergilloma was varied between 69% and 90%. Meanwhile, the predicted mortality was reported at a rate of 6% per annum. The treatment consisted of thoracotomy lobectomy and anti-fungal therapy [13]. Indications for surgery in aspergilloma were a definitive treatment for patients with adequate pulmonary function [9,14]. Usually, pul-

Fig. 4 – X-ray evaluation 2 months post thoracotomy.
monary aspergilloma is diagnosed based on its histologic features after an excision biopsy.

The patient did not need antifungal therapy since it was a single aspergillus nodule, except in the immunocompromised patient [15]. In this case, the patient also had poorly controlled diabetes as a risk factor for active tuberculosis and fungal infection. Therefore, anti-tuberculosis therapy with thoracotomy lobectomy surgery was the recommended treatment. The patient was declared cured after undergoing advanced phase 1 OAT with Rifampicin 450 mg and isoniazid 300 mg for 3 months post-thoracotomy, as well as anti-fungal therapy Fluconazole/Itraconazole for 3 months post thoracotomy (Figs. 4 and 5)

**Declaration of Competing Interest**

The authors have declared that no competing interests exist.

**Patient consent**

An informed consent was obtained from the patient.

**Supplementary materials**

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.radcr.2021.12.064.

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