Case Report

C-Arm Fluoroscopy-Guided Bronchoscopic Biopsy for Diagnosing Aspergilloma With Massive Hemoptysis After Pulmonary Tuberculosis: A Case Report

Rifka Wikamto[1], I Dewa Putu Ardana[2], Suhendro[2]

[1]Moyo Hilir Primary Health Care, Sumbawa, West Nusa Tenggara, Indonesia
[2]H.L. Manambai Abdulkadir Hospital, Sumbawa, West Nusa Tenggara, Indonesia

Abstract

Background: Aspergilloma usually develops in the pulmonary cavity that already exists, including tuberculosis. The most frequent symptom is hemoptysis. Diagnosis of proven fungal infection requires a tissue sample obtained from a disease location to be subjected to histological examination or culture. A specimen taken using bronchoscopy alone is quite challenging because of its location. In this case, a C-arm fluoroscopy-guided bronchoscopic biopsy may be a solution to get specimens for a proven diagnosis.

Case: A 53-year-old male presented to the emergency department following a massive hemoptysis with a previous history of tuberculosis. Chest radiography revealed opacity and hilar restriction in the left upper lobe. A chest CT scan without contrast revealed suspected aspergilloma. The patient underwent a C-arm fluoroscopy-guided bronchoscopy for a biopsy sample. The biopsy sample referred to *Aspergillus niger*.

Discussion: *Aspergillus sp.* leads to parenchymal damage and causes several symptoms, mostly hemoptysis. Aspergilloma usually develops in the pulmonary cavity that already exists, including those from tuberculosis. The diagnostic effectiveness of bronchoscopy guided by C-arm fluoroscopy for peripheral lung lesions has consistently improved.

Conclusion: Aspergilloma usually develops in the pulmonary cavity that already exists, including tuberculosis. The patient came to the emergency department with massive hemoptysis and met all the criteria for diagnosis of proven fungal infection. The diagnosis was made by analyzing biopsy samples, which was taken by C-arm fluoroscopy-guided bronchoscopy.

Keywords: Aspergilloma, C-arm fluoroscopy-guided bronchoscopy, post-treatment tuberculosis, massive hemoptysis

Corresponding Author:
Rifka Wikamto | Moyo Hilir Primary Health Care, Sumbawa, West Nusa Tenggara, Indonesia | rifkawikamto@gmail.com

Submitted: May 10th, 2023
Accepted: February 10th, 2024
Published: April 30th, 2024

J Respirol Indones. 2024
Vol. 44 No. 2: 119–24
https://doi.org/10.36497/jri.v44i2.529

INTRODUCTION

Aspergilloma usually develops in the pulmonary cavity that already exists, including those from tuberculosis (TB).[1] Aspergilloma develops when *Aspergillus sp.* colonizes and grows inside pre-existing single or multiple lung cavities and forms a ball-like structure called a fungus ball. The fungus ball is composed of hyphae of *Aspergillus*, fibrin, mucus, inflammatory cells, blood, and epithelial cell components. More than 90% of aspergilloma is caused by *Aspergillus fumigatus* which is widely found in people with TB. Other species that can cause aspergilloma include *Aspergillus niger, Aspergillus terreus, Aspergillus flavus,* and *Aspergillus nidulans*.[2,3]

Aspergilloma can be asymptomatic for several years. The most frequent symptom is hemoptysis, which may be simple recurrent hemoptoic sputum or life-threatening hemoptysis.[4] Massive hemoptysis may lead to hemodynamic instability and cause death from suffocation or shock. Massive hemoptysis is becoming one of the main reasons patients with aspergilloma come to the emergency department and require hospitalization.[5] Other symptoms are chest pain, bronchorrhea, dyspnea, poor general condition, and fever.[4,6]

The most complete guideline for the diagnosis and treatment of chronic pulmonary aspergillosis, including aspergilloma, was released by the European Society for Clinical Microbiology and Infectious Diseases in partnership with the European Respiratory Society.[7]

Consistent radiographic findings, together with serological and microbiological evidence of Aspergillus species in a person with symptoms lasting more than three months, are required for a diagnosis.[7] Furthermore, the diagnostic criteria can be divided into 3 levels, namely proven, probable, and possible (Figure 1).

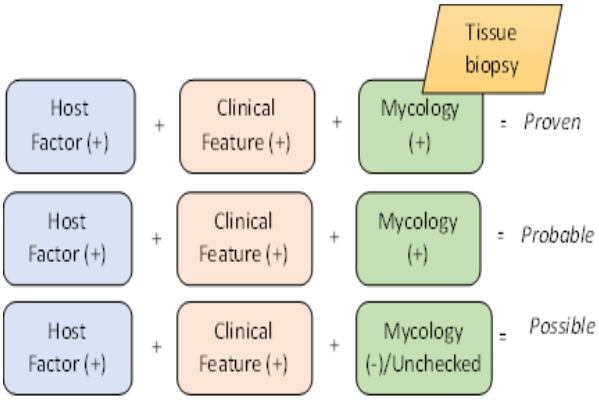

Figure 1. Diagnostic criteria for lung mycosis.[10]

A proven fungal infection needs a tissue sample taken from a disease location to be histologically analyzed or cultured to identify a fungus. A probable fungal infection requires a host factor, clinical features, and mycological proof. Possible fungal infections are defined as cases having the necessary host characteristics and clinical data supporting a fungus infection but without any mycological support.[8] Histological analysis of a specimen taken from a site of aspergilloma by using bronchoscopy alone is a bit difficult because of its location. Diagnosis is important for the treatment that will be received.[9,10]

Treatment for aspergilloma can be surgical or non-surgical. The most effective method of treating symptomatic aspergilloma, especially for massive hemoptysis, entails the surgical removal of infected lung lobes. Non-surgical treatment is an option for patients who have a variety of surgical contraindications, such as inadequate respiratory reserve, numerous or bilateral aspergillomas, or personal preference. For those patients, systemic administration of an antifungal drug, intracavitary instillation of an antifungal drug, or endobronchial instillation of an antifungal drug may be recommended.[11–13]

CASE

A 53-year-old male presented to the emergency department on March 9, 2023, following a hemoptysis of about 400 ml of fresh blood. For more than 10 years, the patient had recurring episodes of blood-tinged sputum, along with fever and occasionally chest pain. He had previous two histories of TB and completed standard treatment in 2007 and 2015.

The patient was conscious, oriented, and hemodynamically stable when examined. Pallor was present. Low vesicular breathing was discovered during a respiratory system assessment in the left hemithorax region. Examinations of the nervous system, heart, and abdomen were all normal. Initial blood tests revealed severe anemia with a hemoglobin (Hb) level of 6,0 g/dL. Xpert MTB-RIF Assay G4 did not detect *Mycobacterium tuberculosis*. Chest radiography is shown in Figure 2.

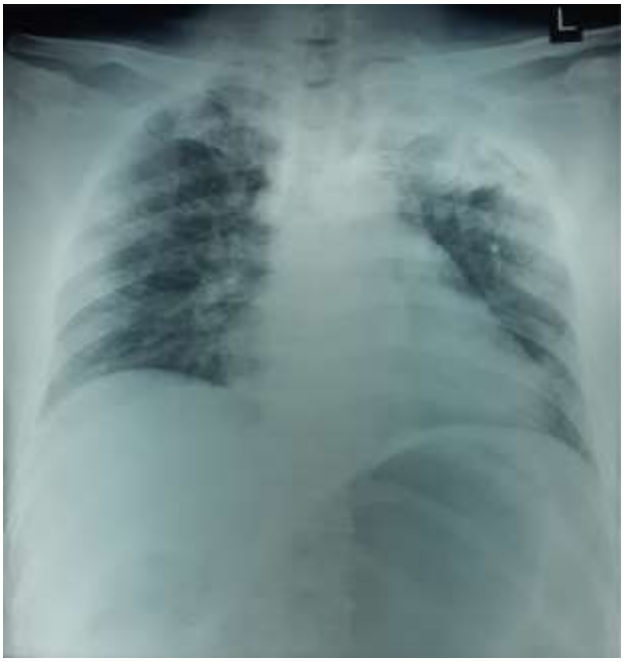

Figure 2. Chest radiography revealed opacity and hilar restriction in the left upper lobe

A chest CT scan (Figure 3) without contrast infusion revealed lobulated, regular edge-space-occupying lesions (SOL) in the posterior segment of the upper lobe. An irregular hyperdense appearance is shown around the SOL. Inside the SOL showed solid hyperdense irregular lobulated lesions with a strict line and air around them, suspected aspergilloma.

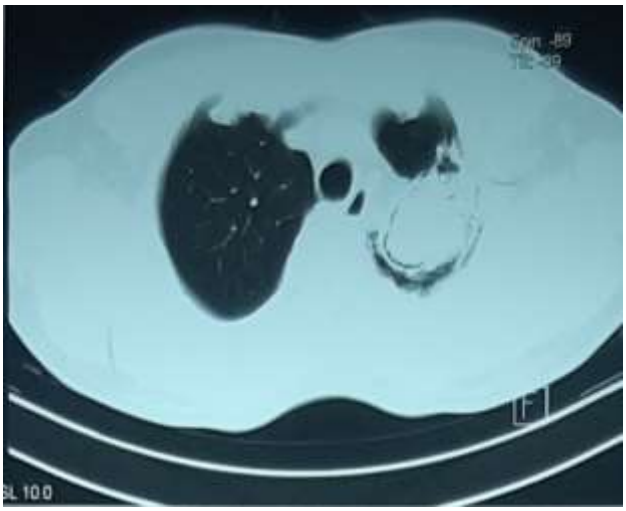

Figure 3. Suspicious aspergilloma shown in chest CT scan

The patient underwent a bronchoscopy after getting 4 units of packed red blood cells due to severe anemia. Under general anesthesia, the tube was put through LMA into the bronchus and bronchioles. We found stenosis at the left segmental bronchus of B1+2/Apicoposterior (Figure 4).

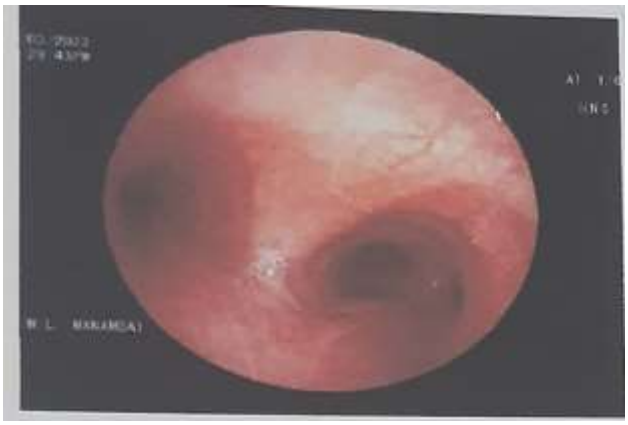

Figure 4. Stenosis at left B1+2 (Apicoposterior)

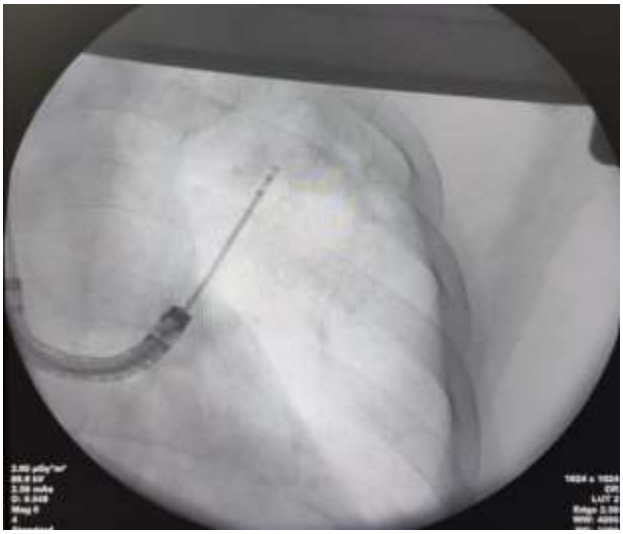

Figure 5. The biopsy sample was taken by C-arm fluoroscopy-guided bronchoscopy at the left B2 segment.

No active bleeding was found. A sample to be examined was taken by bronchial washing, brushing, and forceps biopsy (Figure 5). The sample is checked for histology, cytology, and KOH smear. The results can be seen in Figure 6.

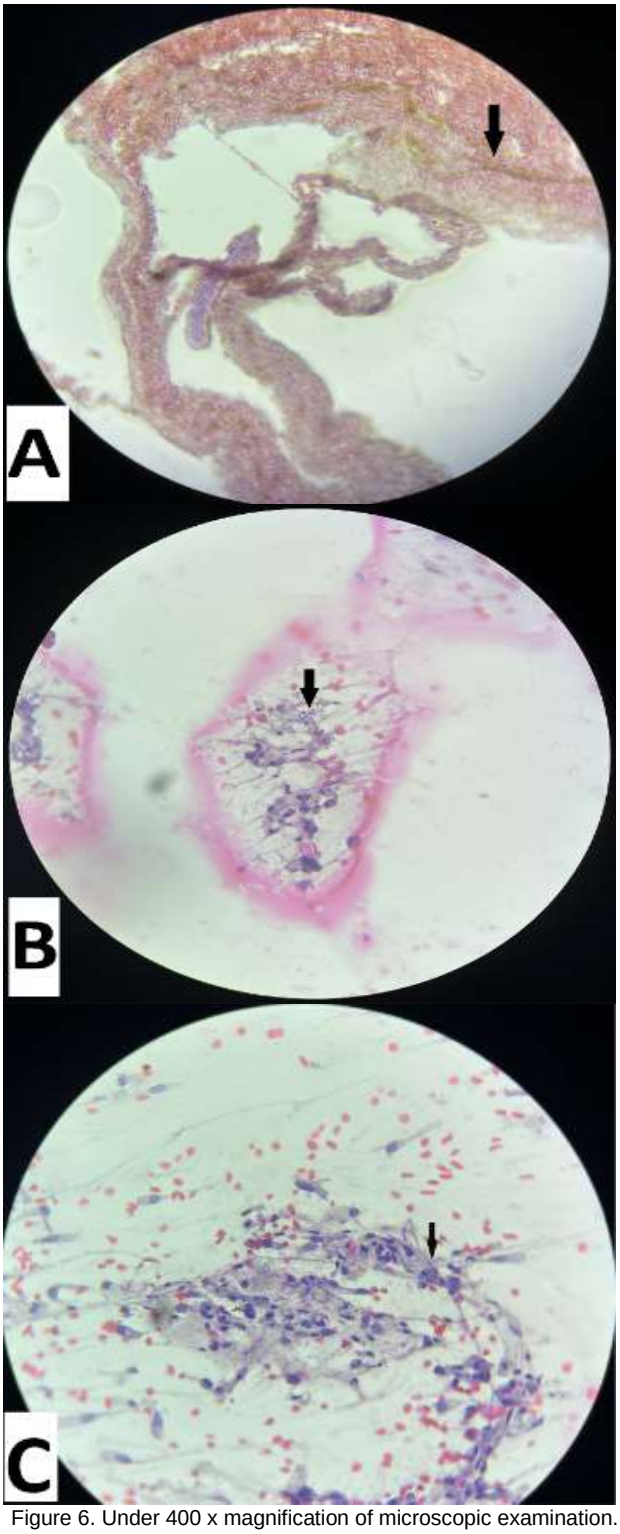

Figure 6. Under 400 x magnification of microscopic examination. (6A). Hyphae with brownish dark pigment shown in the histologic sample (pointed by arrow) referred to *Aspergillus niger's* hyphae. (6B) and (6C) Spore and hyphae surrounding respiratory epithelium in cytology sample of bronchoscopy (pointed by arrow).

The patient is treated with itraconazole 100 mg twice daily. The patient went home on March 11, 2023, with no more symptoms like hemoptysis, fever, or chest pain.

DISCUSSION

After breathing in its spores from the environment, Aspergillus species can colonize and thrive in the pulmonary cavity. By creating an intricate assemblage of Aspergillus hyphae, tissue fragments, inflammatory cells, and mucin known as a fungus ball (aspergilloma), it causes parenchymal injury. The cause of *Aspergilloma* in our case was *Aspergillus niger*. The most common *Aspergillus sp*. that causes Aspergilloma in post-TB disease, according to a comprehensive review and meta-analysis of cross-sectional studies in Asia and Africa, is *Aspergillus fumigatus.*[14,15] *Aspergillus niger* is an uncommon cause of aspergilloma, especially invasive pulmonary aspergillosis, even though some authors report it.[16,17]

Massive hemoptysis was the reason our patient came to the emergency department. He coughed around 400 ml of fresh blood. Aspergilloma can remain asymptomatic, but once the patient has hemoptysis, it can be life-threatening.[18] Rarely, a rapidly growing cavity might encroach on the intercostal arteries and pleural surface, leading to a huge, usually fatal hemoptysis that is very challenging to control. The bleeding can be caused by some factors, such as erosion (local invasion) of vessels nearby, mechanical irritation of exposed vessels within the cavity, endotoxin and trypsin-like proteolytic enzyme release from the organism, direct penetration of the wall lining's capillaries, or acute bacterial infection as comorbid.[7,19]

Younger age, blood-tinged sputum, and cavitary lesions with thick walls are some risk factors for severe hemoptysis in aspergilloma patients.[20] The patient has had a blood-tinged sputum for more than 10 years, a risk factor that can develop into severe hemoptysis.

As seen in Figure 1, diagnostic criteria depend on three parameters, i.e., host factors, clinical features, and mycology examination. Host factors, including risk factors (long-term therapy of antibiotics, ongoing chemotherapy, long-term therapy of corticosteroid), and underlying chronic disease (diabetes mellitus, cancer, pulmonary chronic disease). Clinical features include clinical symptoms, radiology examination, and general laboratory results. Mycology examination includes culture or identification of fungus, serology, or molecular basic examination.[9]

A diagnosis of proven fungal infection requires the detection of fungus by histological analysis or culture of a specimen of tissue taken from a site of disease. In this case, our patient met all the criteria for diagnosis of a proven fungal infection. A cytology sample of the patient was taken by washing and brushing techniques while the biopsy sample of the patient was taken using C-arm fluoroscopy-guided bronchoscopy (Figure 4). Without guidance from C-arm fluoroscopy, it will be difficult to biopsy because a bronchoscope alone is unable to reach peripheral lung parenchyma. A study revealed that the diagnostic effectiveness of bronchoscopy guided by C-arm fluoroscopy for peripheral lung lesions consistently improved and that biopsy was more effective than the other sampling methods.[9]

According to several studies, surgical aspergilloma treatment has positive results and should be the first line of treatment. In terms of long-term survival and a low likelihood of recurrence, the long-term outcomes of aspergilloma surgery are favorable.[21–23] However, some significant risks occurring after surgery should be considered. Those include post-lobectomy empyema, excessive postoperative bleeding, prolonged air leaks, and residual pleural space.[24]

Non-surgical treatment is an option for patients who have a variety of surgical contraindications. Systemic administration of antifungal medication, intracavitary instillation of antifungal medication, or endobronchial instillation of antifungal medication can be preferred for those patients. Itraconazole, the most widely used antifungal agent, is the medication best adapted to treating a persistent illness like aspergilloma. Nevertheless, due to possible poor

drug penetration, it acts slowly, especially for aspergilloma, and may not be helpful for patients with significant hemoptysis.[11,13]

A study revealed only 49% of patients with aspergilloma showed a radiological response to itraconazole 200 mg daily for 3 months.[25] Another study discovered that a weight-based variable dose schedule of itraconazole is both an efficient and secure treatment option for aspergilloma and that treatment should be continued for longer than six months, particularly in individuals with simple aspergilloma. Moreover, patients with simple pulmonary aspergillosis who do not react to the medication should have access to surgical options.[12] The patient in our case was given itraconazole 100 mg twice daily as treatment.

LIMITATIONS

Further investigation needs to be done to determine the effectiveness of itraconazole as a treatment for massive hemoptysis in aspergilloma because this case does not explain the long-term outcomes of patient after hospitalization.

.

CONCLUSION

Aspergilloma usually develops in the existing pulmonary cavity due to TB. C-arm fluoroscopy-guided bronchoscopy may be a good solution to get a biopsy sample of pulmonary aspergillosis in the peripheral site so the diagnosis can be established.

REFERENCES

1. Rozaliyani A, Jusuf A, ZS P, et al. Infeksi jamur paru di Indonesia: Situasi saat ini dan tantangan di masa depan. Jurnal Respirologi Indonesia 2019;39(3):210–214.
2. Lee SH, Lee BJ, Jung DY, et al. Clinical manifestations and treatment outcomes of pulmonary aspergilloma. Korean J Intern Med 2004;19(1):38.
3. Hayes GE, Novak-Frazer L. Chronic pulmonary aspergillosis-Where are we? and where are we going? J Fungi (Basel) 2016;2(2):18.
4. Harmouchi H, Sani R, Issoufou I, Lakranbi M, Ouadnouni Y, Smahi M. Pulmonary aspergilloma: From classification to management. Asian Cardiovasc Thorac Ann 2020;28(1):33–38.
5. Karlafti E, Tsavdaris D, Kotzakioulafi E, et al. Which is the best way to treat massive hemoptysis? A systematic review and meta-analysis of observational studies. J Pers Med 2023;13(12):1649.
6. Ding WY, Chan T, Yadavilli RK, McWilliams R. Aspergilloma and massive haemoptysis. BMJ Case Rep 2014;2014.
7. Chakraborty RK, Gilotra TS, Tobin EH, Baradhi KM. Aspergilloma. Treasure Island (FL): StatPearls Publishing, 2024;
8. Pauw B De, Walsh TJ, Donnelly JP, et al. Revised definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group. Clin Infect Dis 2008;46(12):1813–1821.
9. Emre JÇ, Baysak A, Öz AT, Çok G, Göksel T. Endobronşiyal lezyon saptanmayan olgularda C kollu skopi eşliğinde yapılan bronkoskopinin tanı değeri. Journal of Clinical and Analytical Medicine 2016;7(4):449–453.
10. Perhimpunan Dokter Paru Indonesia. Panduan umum praktik klinis penyakit paru dan pernapasan. Jakarta: Perhimpunan Dokter Paru Indonesia, 2021;
11. Lang M, Lang AL, Chauhan N, Gill A. Non-surgical treatment options for pulmonary aspergilloma. Respir Med 2020;164:105903.
12. Gupta PR, Jain S, Kewlani JP. A comparative study of itraconazole in various dose schedules in the treatment of pulmonary aspergilloma in treated patients of pulmonary tuberculosis. Lung India 2015;32(4):342–346.
13. Maturu V, Agarwal R. Itraconazole in chronic pulmonary aspergillosis: In whom, for how long, and at what dose? Lung India 2015;32(4):309–312.

14. Hosseini M, Shakerimoghaddam A, Ghazalibina M, Khaledi A. Aspergillus coinfection among patients with pulmonary tuberculosis in Asia and Africa countries; A systematic review and meta-analysis of cross-sectional studies. Microb Pathog 2020;141:104018.
15. Bongomin F. Post-tuberculosis chronic pulmonary aspergillosis: An emerging public health concern. PLoS Pathog 2020;16(8):e1008742.
16. Atchade E, Jean-Baptiste S, Houzé S, et al. Fatal invasive aspergillosis caused by Aspergillus niger after bilateral lung transplantation. Med Mycol Case Rep 2017;17:4–7.
17. Person AK, Chudgar SM, Norton BL, Tong BC, Stout JE. Aspergillus niger: An unusual cause of invasive pulmonary aspergillosis. J Med Microbiol 2010;59(Pt 7):834–838.
18. Kokkonouzis I, Athanasopoulos I, Doulgerakis N, et al. Fatal hemoptysis due to chronic cavitary pulmonary aspergillosis complicated by nontuberculous mycobacterial tuberculosis. Case Rep Infect Dis 2011;2011:1–4.
19. Soedarsono, Widoretno ETW. Aspergilloma pada tuberkulosis paru. Jurnal Respirasi 2017;3(2):58–65.
20. Kim TH, Koo HJ, Lim CM, et al. Risk factors of severe hemoptysis in patients with fungus ball. J Thorac Dis 2019;11(10):4249–4257.
21. Kasprzyk M, Pieczyński K, Mania K, Gabryel P, Piwkowski C, Dyszkiewicz W. Surgical treatment for pulmonary aspergilloma - early and long-term results. Kardiochir Torakochirurgia Pol 2017;14(2):99–103.
22. Khan MA, Dar AM, Kawoosa NU, et al. Clinical profile and surgical outcome for pulmonary aspergilloma: nine year retrospective observational study in a tertiary care hospital. Int J Surg 2011;9(3):267–271.
23. Akbari JG, Varma PK, Neema PK, Menon MU, Neelakandhan KS. Clinical profile and surgical outcome for pulmonary aspergilloma: A single center experience. Ann Thorac Surg 2005;80(3):1067–1072.
24. Chen QK, Jiang GN, Ding JA. Surgical treatment for pulmonary aspergilloma: A 35-year experience in the Chinese population. Interact Cardiovasc Thorac Surg 2012;15(1):77–80.
25. P G, Aruna V, R M, S K, Devesh K, S J. Role of itraconazole in the management of aspergillosis in treated patients of pulmonary tuberculosis. Lung India 2005;22(3):81–85.