



Outcome of Surgery for Chronic Pulmonary Aspergillosis, Collaborated Experience of Four Centers within the Kingdom of Saudi Arabia (KSA)

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Abstract

Background: Aspergilloma is the most common form of pulmonary involvement by *Aspergillus* sp, which usually develops in a pre-existing cavity within the lung. The aspergilloma (commonly known as fungus ball) is composed of fungal hyphae, inflammatory cells, fibrin, mucus, and tissue debris. The most common species of *Aspergillus* recovered from such lesions is *A. fumigatus*. For the study, over 10 years of data were collected for examination, on the outcomes of surgery for pulmonary aspergilloma, from the respected four Saudi German Hospitals referenced within KSA.

Methods: Retrospective study of forty (40) patients, dating from January 2008 until September 2018, who underwent lung resections at any one of the four institutes. Each patient's preoperative, diagnostic, operative, and postoperative and follow-up data were collected for analysis. The indication for surgery was recurrent hemoptysis, asymptomatic simple aspergilloma and complex aspergilloma.

Results: Findings of 40 patients who underwent surgery for aspergilloma, thirty-three (33) had clinical diagnosis. While, remaining seven (7) were confirmed post-resection. The median age was 41.3 years old, +/- 12.8 (aged 13 to 74 years). Risk assessment identified that greater probability for the left lung to be infected and increase if gender was male (2:1). The main presentation was hemoptysis, seen in 70% of cases, while symptoms of cough and expectoration occurred in 45% of them. The most prevalent predisposing factor was Tuberculosis (TB), present in 57.5% of cases. All the patients underwent pulmonary resection, with 82.5% of cases having lobectomy. The main postoperative complication was prolonged air leak 15% (6/40). The in-hospital mortality rate was 7.5% (3/40) patients.

Conclusion: Surgery in patients with chronic pulmonary aspergillosis (fungus ball) offered beneficial outcomes with an acceptable morbidity. The mortality observed within these cases, was predominantly due to high risk patients, with complex aspergillosis. Recommendations for a multidisciplinary approach, in future cases, are paramount for better selection criteria.

Keywords: Fungus ball; Aspergilloma; Lobectomy; *Aspergillus*

Introduction

Aspergillosis is most often caused by the fungus *Aspergillus fumigatus*; it occurs mainly in immunodeficient individuals and as a form of colonization of previously existing cavities in the lungs. Aspergilloma (fungus ball) one of the clinical forms of aspergillosis, develops primarily in post-tuberculous cavities. It may constitute a significant therapeutic problem due to recurrent hemoptysis and symptoms of chronic infection. Antifungal agent penetration into the cavity of the fungus ball is scant; therefore, in many cases, the only treatment option is to resect the pulmonary parenchyma colonized by the fungus. Notwithstanding, surgical treatment is associated with many technical difficulties and a relatively high risk of postoperative complications, particularly in patients who are emaciated or treated with immunosuppression [1]. Air Crescent Sign (ACS) is the cardinal radiological feature of the fungus ball of aspergillosis that is formed of condensed hyphae. The ball can be large or small, solitary or multiple. It may move when the patient's position changes or remain fixed, projecting into the cavity's lumen like a polyp [2].

Although it is often indolent with few or no symptoms in the beginning, the process frequently presents with massive hemoptysis, which can sometimes be fatal. Its differential diagnosis includes

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pulmonary hydatid cyst, other fungi, blood clot or Rasmussen aneurysm in a tuberculous cavity, lung abscess with inspissated pus, staphylococcal pneumonia, nocardial infection, carcinoma of the lung, and lung gangrene or hematoma [3,4].

Since antifungal has a poor penetration to thick cavity wall open thoracotomy and anatomical resection has become widely accepted as the main treatment for pulmonary aspergilloma in patients who are suitable candidates for an operation. VATS resections started to get a role in the surgical treatment of pulmonary fungal ball [5].

These procedures control symptoms, and especially prevent hemoptysis and prolong life. The most common procedure performed was lobectomy. This prevents the pleural dissemination that usually occurs with limited resections such as wedge or segmental resections and cavectomies [3,4,6]. In our study we analyzed the outcome of surgical intervention in patients with aspergilloma.

Methods

A retrospective study of 40 patients with pulmonary aspergilloma treated at Saudi German Hospital Series in Kingdom of Saudi Arabia, covering a decade of cases from January 2008 and September 2018. Extensive review of all the available data and records within our systems were undertaken. Clinical suspicion and radiologic examination with +ve meniscus sign, surgical and pathological findings were our keys to have a diagnosis. Chest X-ray, CT chest, Fiber-optic bronchoscopy and pulmonary function tests were routinely done. IV Amphotericin B was given for at least one week to sterilize the field except in true emergencies. Follow-up of the liver and kidney functions and potassium level was mandatory with anti-fungal therapy. If the patient was on chemotherapy, 4 weeks interval of no chemo was routine and strictly followed except in cases of massive hemoptysis. Conventional lung resection was done for all patients using single lung ventilation. Strict pain control was routine using both pethidine and non-steroidal anti-inflammatory drugs as needed.

Postoperative complications were reported and managed accordingly. Follow-up in both thoracic surgery and pulmonology clinic was done monthly for most of the survivors. Clinical examination, Chest X-ray and complete blood picture were routinely done in our follow-up.

Results

Findings for the retrospective study of 40 cases of pulmonary aspergilloma surgically treated during the 10 years referenced are as follows:

The mean age in this study was 41.3 +/- 12.3, range (13 to 74 years). There were 27 males, resulting with a ratio of 2:1 to the female sex. The most common predisposing factor was tuberculosis TB present in 40% of cases. The main presentation was recurrent hemoptysis in 70% of patients. No patient with severe or massive hemoptysis was encountered during this study. The radiological findings showed 33/40 patients 82.5% showed positive meniscus sign while the rest 17.5% showed a pulmonary nodule. There were 17 patients simple aspergilloma 42.5%, while 23 patients showed a complex form (57.5%). The left side was affected in 67.5% with predominant left upper lobe affection. The relevant laboratory tests revealed seropositive results in 12.5% and positive culture from protected bronchial lavage 9/40 patients (22.5%). Preoperative patient data (Table 1).

In this series majority of patients underwent lobectomy, except 7

Table 1: Preoperative patient data.

Age	Mean 41.3 (range:13-74)
Sex	Male no. 27 / Female no. 13 (2:1)
Predisposing factor	
TB	23/40 (57.5 %)
Renal Transplantation	6/40 (15 %)
Lymphoma	4/40(10 %)
Leukemia	4/40 (10 %)
HIV	2/40 (5%)
Lung transplantation	1/40 (2.5 %)
Presentation	
Hemoptysis	28/40 (70%)
Shortness of breath	20/40 (50 %)
Cough and expectoration	15/40 (37.5%)
Radiological findings	
Simple Aspergilloma	23/40 (57.5 %)
Complex Aspergilloma	17/40 (42.5%)
Site of lesion	
Right side	13/40 (32.5%)
Upper lobe	8/40 (20%)
Middle lobe	1/40 (2.5%)
Lower lobe	4/40 (10%)
Left side	27/40 (67.5%)
Upper lobe	21/40 (52.5 %)
Lower lobe	6/40 (15%)
Laboratory findings	
Positive Serological tests	5/40 (12.5 %)
Positive Bronchial lavage	9/40 (22.5 %)

patients had wedge resection, the mean operative time was 140 min (75-220), and two patients went to the ICU with packs to control apical adhesions bleeding and were re-explored 48 h later.

All patients were transferred to the ICU (the mean ICU stay was 48 h, with next morning transfer to ward. Hospital stay ranged from 7 to 35 days with a mean of 9 days. All patients after removal of the drains and free of complications were transferred to the medical ward to start their antifungal regimen according to the hospital policy and were followed up. Data analysis showed a follow up range of 1 to 5 years post procedure.

During the study we noted the most common complication was prolonged air leak in 6 patients (15%) that ranged from 5 to 18 days with a mean of 10 days. Wound infection was present in 4 patients 10% of which one patient needed vacuum assisted device. Re-exploration was needed in 2 patients (5%) who were packed and re-explored to remove packing. Cardiac arrhythmia was encountered in 3 patients (7.5%). In this series we encountered 3 mortality (7.5%) cases. Two patients suffered respiratory failure following severe chest infection and one patients developed DVT and massive pulmonary embolism.

Discussion

Aspergillus fumigatus spores are widespread in the environment, and its hyphae are relatively often found in sputum samples [7].

Colonization may lead to pulmonary aspergillosis; the course is determined by patient immune system and/or existence of pulmonary parenchymal cavity. In immunodeficient patients, after chemotherapy, or undergoing chronic immunosuppression therapy (mostly with steroids), the fungal infection may lead to the development of invasive aspergillosis with a severe clinical course [8]. In such cases, the pathology is often multifocal, and the options of surgical treatment are very limited. On the other hand, aspergilloma is a limited form of infection developing in previously existing cavities in the pulmonary parenchyma mainly caused by previous TB.

Within the study Tuberculosis (TB) was found in 23/40 (57.5%) of our patients, while 42.5% of patients had previous chemotherapy for cured malignancy or chronic immunosuppression after organ transplantation. Similarly, in most other publications, pulmonary tuberculosis is presented as the disease most likely to promote the development of aspergilloma (32% to 45% of cases) [9,10]. TB has the incidence of 14-17/100000 in KSA where 48% are non-Saudis [11]. The presence of active cadaveric organ transplantation foundation in the kingdom has increased the number organ transplanted yearly [12].

The main presenting symptom in this series was hemoptysis, previous reports has recognized hemoptysis as high as 70%. The radiological diagnosis of aspergilloma is positive when positive meniscus sign and mobile ball with patient position is confirmed. Chest CT scan are useful for diagnosis of simple and complex aspergillosis as well as underlying lung parenchyma. In simple form the aspergilloma develops in a thin-walled cavity that has adjacent normal lung parenchyma. Herein the disease process is much more localized. The pleura is not involved in the disease process [13,14]. In the complex form, the disease process is much more aggressive and diffuse. There is much more destruction of the lung parenchyma than a simple cavity. In most instances, the adjacent pleura is also involved in the pathology. The lung and pleural pathology are usually due to pre-existing disease processes (most commonly tuberculosis) [15]. These patients are not uncommonly sicker and may even have reduced pulmonary function tests. Cavities are usually thick walled due to repeated infections. There may also be more widespread lung pathology in other lobes of the lung and even bilateral disease. Within the study, 7 patients had a solitary pulmonary nodule and upon pathological report aspergilloma was confirmed.

Furthermore, within the study of patient surgery was indicated in asymptomatic simple aspergilloma in 7 cases were to achieve a diagnosis, where postoperative pathology results showed aspergilloma. The fundamental question remains whether to operate on asymptomatic patients or not. It is our policy to perform surgery in asymptomatic simple aspergilloma as a prophylaxis against 20% chance of severe hemoptysis that can be encountered during the course of the disease.

Patients with recurrent hemoptysis either with or without previous bronchial embolization were enrolled in our indication. Failed medical treatment and complex forms were indicated for resection as long as the residual pathological lung showed good pulmonary function and patients have good functional performance.

Complex form showed technical challenges with dense pleural adhesions, absence of interlobar fissure, fibrosis and inflammation at hilar vessels. These challenges reflect on postoperative complications as most series have previously mentioned. It is expected in this

situation that patients suffer from prolonged air leaks, failure of lung expansion and postoperative bleeding [1].

We encountered 12/40 (30%) postoperative complications. Half of which were due to prolonged air leaks and failure of lung expansion. Uncontrolled apical oozing was encountered in two patients who were transferred to the ICU packed and were re-explored and packs were removed 48 h later. Almost all previous experiences have faced the same complications and were proportion to the extensive pathology and residual lung condition, complications ranged from 25% to 70% [1,9,10]. Our mortality of 7.5% was to the lower side of most series. Although mortality was variable in different authors experiences, ranging from 1% and up to 43%, this was due do the difference between each series in the percentage of high-risk patients, complex aspergillosis and pneumonectomies per study [16,17].

Our reasonable mortality could be explained in view that 57.5% were simple aspergilloma with localized disease and less challenging. Our 3/40 mortality patients were in the complex group. Two developed respiratory infection and respiratory failure and were renal transplanted patients, the third was a cancer patient who developed DVT in spite of anti-coagulation and was lost when he developed massive pulmonary embolism.

It is our hospital policy to manage these patients in Multidisciplinary Team (MDT) approach, the decision for management is usually taken with chest physicians, intervention radiologist and surgical team. Anti-fungal therapy at the perioperative period, as well as adjustment of preoperative co-morbidities as diabetes and nutrition status was paramount. The indication for anti-fungal therapy was directed to those with multiple cavities or those anticipated with the risk of pleural spillage during resection. Those with simple or contained aspergilloma are in no need for antifungal therapy. In some patients with residual or other lung affection are given postoperative antifungal therapy to prevent recurrence. Other series adopted similar policy with ours [1,18].

Postoperative follow up extends for 5 years in our series, there was no recurrence in our group and close monitoring was our policy including clinical and radiological parameters.

Although we present a small group of patients within this study, we emphasized the valuable lessons learned and complications discovered within the complex group. Consequently, we recommend MDT approach for the management of these patients with close follow up. Despite the high risk of postoperative complications, the long-term results of aspergilloma surgery are good in terms of the low rate of recurrence and long-term survival.

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