

Original Article

TREATMENT OF PULMONARY ASPERGILLOMA- IS SURGERY A SAFE OPTION?
A REVIEW OF 289 CASES AT TWO CENTERS IN PAKISTAN

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Objective: To determine outcome of surgery in adult Pakistani population with aspergilloma.

Methods: A total of 289 adults of both sexes with unilateral aspergilloma cavity were enrolled in this prospective study spanning 16 years carried out in Services Institute of Medical Sciences and Surgimed Hospital Lahore. Out of 289, only 102 patients were electively fit for surgery. Exclusion criteria involved any patient with extensive bilateral disease, advanced age (65+) and lack of consent. Data was collected on hard copy forms with entry and analysis done in SPSS version 23. Follow up period was of 36 months.

Results: Our study consisted of 289 patients with 102 selected for surgical intervention. The median age of the patients was 33.4. The most common presenting complaint was recurrent hemoptysis, seen in 75 patients (73.5%). The most common underlying lung pathologies predisposing to Aspergilloma were Tuberculosis (76.4%) and Bronchiectasis (14.7%). The most common co-morbidities were Hepatitis C 23.5% and Diabetes 20.5%. Out of 102 cases postoperative complications were documented in 24 (23.5%) patients of which 9(37%) patients had more than one complications. 10 (9.8%) patients had prolonged air leak, 8 (7.8%) had surgical site wound infection, 8 (7.8%) had mild hemoptysis for couple of weeks, 5(4.9%) had bronchopleural fistula, 5(4.9%) had intra thoracic haemorrhage (>1500 ml blood loss), 4 (3.9%) had post resection loculated empyema and 4(3.9%) had pneumonia. Post-operative mortality was 1.96% with zero per-operative mortality. One patient died due to pulmonary embolism on 5th postoperative day and the other patient died of myocardial infarction. Follow up was for 36 months postoperatively.

Conclusions: Although surgical intervention for aspergilloma is technically difficult, scrupulous selection of patients, meticulous surgical techniques and good postoperative care can reduce mortality and morbidity and favourable outcome can be achieved.

Keywords: pulmonary aspergilloma, mycetoma, fungal infection & haemoptysis.

Introduction

The term Pulmonary Aspergilloma also known as mycetoma (fungal ball) refers to colonization of pre-existing lung cavities with the aspergillus fungus, most commonly the fumigatus species.¹ The lesion itself consists of a tangled mass of fungal hyphae, fibrin, epithelial cells, mucus, debris, and blood cell.^{2,3} Aspergilloma secondary to cavitary disease is now considered a frequently encountered disease. After the formation of a fungal ball, antifungals are generally considered ineffective.⁴ Tubercular lesions are the most common cause of such cavities; however, they may occur within cavities of diverse aetiologies including sarcoidosis, bronchiectasis, cysts and bullae, neoplasms, ankylosing spondylitis, granulomatosis polyangiitis (Wegener's granulomatosis), and pulmonary infarction.^{5,6} Tuberculosis and bronchiectasis are common diseases in developing countries such as Pakistan.

According to a study conducted in 2011, in absolute numbers Pakistan ranked 5th out of 22 high burden countries.⁷ There is a paucity of literature and limited data on aspergilloma and its clinical presentations in Pakistan, possibly due to under reporting.⁸ Aspergillus fumigatus is an airborne filamentous fungus favouring a habitat of moist soil having a diameter of 2-3 micrometre.^{9,10} In an immunocompetent person, it is normally eliminated by the immune and mucociliary clearance mechanisms. Hinson and colleagues have classified pulmonary aspergillosis into allergic, invasive and saprophytic infections.^{1,11} The diagnosis is usually made radiographically without lung biopsy. Haemoptysis is commonly reported as the main symptom, that can be mild to moderate but at times it can be massive and life threatening. Massive haemoptysis represents one of the most challenging conditions encountered by thoracic surgeons and pulmonologists. In a few cases patients may be asymptomatic. Bleeding is usually

caused by local invasion and endotoxic or Mechanical irritation of exposed bronchial blood vessels. Symptoms like cough and dyspnoea are more likely related to underlying diseases, making a clear diagnosis difficult.^{11,12} Sputum cultures for *Aspergillus* spp. are negative in >50% cases. Serum IgG antibodies to *Aspergillus* are positive in most cases, but may be negative in patients under corticosteroid therapy or in rare cases of pulmonary aspergilloma caused by species other than *A. fumigatus*.^{13,14} Chest radiographies show intracavitary mass (fungus ball) with an air crescent (Monod sign) in about two-thirds of the cases.¹⁵ Controversy still exists concerning the optimum management of aspergilloma. It is important to decide which patient should be offered treatment. 10% of asymptomatic cases resolve spontaneously but if patient is symptomatic and has significant morbidity in terms of hemoptysis then treatment should be offered to the patient. Clinical cases and retrospective series have reported that various oral triazoles provide suitable treatment for broncho-pulmonary aspergillosis in immunocompetent patients.¹⁶ In inoperable cases treatment with antifungal agents can be tried. There have been inconsistent results with intracavitary, and endobronchial instillations of antifungal agents. Among antifungals, itraconazole and voriconazole have been effective. Definitive treatment for an aspergilloma is surgical resection of the diseased area. However, surgical resection of the affected lung is associated with considerable morbidity and mortality and outcome depends upon various preoperative, interoperative and postoperative factors. Depending upon the extent of disease, lobectomy, segmentectomy, pneumonectomy, or cavernostomy can be done.^{17,18} Studies show that in carefully selected patients long term results of surgical treatment of aspergilloma is quite satisfactory.¹⁹

Methods

Between January 2002 and December 2017 289 patients were enrolled in this prospective study conducted at Services Institute of Medical Sciences and Surgimed Hospital, Lahore. Adults of both sexes and unilateral aspergilloma cavity were enrolled in the study whereas patients having extensive bilateral disease, advanced age and lack of consent were excluded. The diagnosis of aspergilloma was CT scan based. Preoperatively, Fiberoptic bronchoscopy was performed in all patients. Bronchoalveolar lavage and sputum was

sent for acid fast bacilli smear, AFB, fungal and bacterial culture & sensitivity. Preoperative anaesthesia assessment was performed in all the patients. Two hundreds eighty nine aspergilloma patients were enrolled in the study but only 102 finally underwent surgery either due to loss of follow up or were declared unfit for surgery by anaesthesia department. One lung ventilation was maintained in all the patients using double lumen endobronchial tube. Posterolateral muscle sparing thoracotomy was used to enter the chest cavity through the 5th or 6th intercostal space depending on the type of resection (segmentectomy, lobectomy, pneumonectomy or any other possibility anticipated). Video-assisted thoracoscopic (VATS) wedge excision was performed in patients with either small peripheral lesions or poor respiratory functional reserve. All the patients had been infected by chronic recurrent infection and destructive tuberculosis with subsequent pleural reaction and patchy pleuritis. In most of cases we have to do decortication, which is a procedure by which fibrotic tissue between the visceral and parietal pleura is removed to free the lung for anatomical lung resection and enable remaining lung to expand adequately. Resected specimens were sent for histopathology, acid fast bacilli, fungal and bacterial cultures. Bleeding was considered excessive when the sum of peroperative and postoperative drainage in first 24 hours exceeded 1500ml. Air leaks was considered important if it lasted beyond 7 days. Operative deaths and deaths from all causes were included in the survival statistics. Operative death was defined as any death occurring during the first 30-day period or during the initial hospital stay. Follow up period was 36 months.

Results

Out of 102 patients 62 (61%) were male and 40 (39%) were female with median age of 33.4 years. (Fig 1).

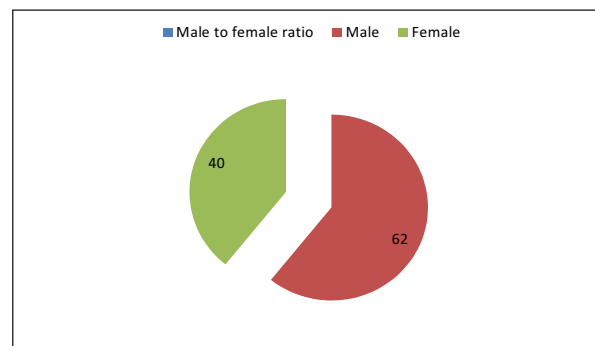


Fig-1: Male to female ratio.

Majority patients were symptomatic. Presenting complaints included recurrent hemoptysis seen in 75

(73.5%), productive cough in 15(14.7%) patients whereas 12 (11.7%) were asymptomatic (**Table-1**). In 78(76.4%) cases, aspergilloma developed in tuberculosis cavity, 15(14.7%) in bronchiectasis, 5 (4.9%) in bullous emphysema and 4(3.9%) developed in cavities of treated cases of lung abscess. (**Fig-2**)

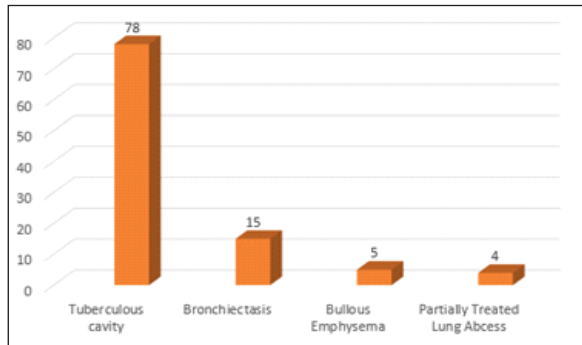


Fig-2: Factors causing formation of aspergilloma.

Sputum and BAL cultures done preoperatively were positive for aspergillus fumigatus in 3(2.9%) and 14(13.7%) cases respectively. Culture of resected lung tissue revealed growth of aspergillus fumigatus in 85.2% cases, mucormycosis in 4.9% cases and AFB culture was positive in 8.8% cases (**Table-2**). Depending upon the cases, appropriate surgical procedures were opted and all cases were followed for 36 months postoperatively. Wedge resection was done in 6 (5.9%) whereas 67(65.7%) patients underwent lobectomy among which right upper lobectomy was performed in 33 (49%), left upper lobectomy 18(27%), left lower lobectomy 9(13.4%) cases and right lower lobectomy in 7(10.5%) cases. Bi-lobectomy (right upper and middle lobe) was performed in 9 (8.8%) patients. 15 patients (14.7%) underwent pneumonectomy among which 9 (60%) was right sided and 6(40%) were left sided. Bronchial stump was covered with pleural flap in all patient with lung resection (Fig 3). We used fibrin glue as sealant at pulmonary parenchymal suture line and broncho-vascular stumps in 29 patients. Thoracoplasty was done in 5 (4.9%) patients. Three patients underwent right apical thoracoplasty whereas 2 patients had left apical thoracoplasty (**Table 3**).

The postoperative course was uneventful in 78 (76.4%) patients. Postoperative complications were documented in 24 (23.5%) patients of which 9(37%) patients had more than one complications. 10 (9.8%) patients had prolonged air leak, 8 (7.8%) had surgical site wound infection, 8(7.8%) had mild hemoptysis for couple of weeks, 5(4.9%) had

bronchopleural fistula, 4(3.9%) had intra thoracic hemorrhage (>1500 ml blood loss), 4 (3.9%) had post resection loculated empyema and 4(3.9%) had pneumonia. Two (1.96%) patients died in our study. One patient died due to pulmonary embolism on 5th postoperative day and other patient died of myocardial infarction (**Table 4**).

Table-1: Clinical Presentation.

		n=102	Percentage
Symptoms	Hemoptiysis	75	73.5%
	• Mild moderate	15	58.8%
	• Severe	09	8.8%
	• Massive	06	5.8%
	Productive Cough	15	14.7%
	Asymptomatic	12	11.7%
	Anti HCV	24	23.5%
	Diabetes	21	20.5%
	Asthmatic	6	5.8%

Table-2: Pathological Features of 102 Surgical Patient.s

		n=102	%Age
Preoperative sputum	Positive for aspergillus fumigates	3	2.9
	Positive for AFB smear	0	0
	Positive for culture	0	0
Preoperative BAL	Positive for aspergillus fumigates	14	13.7
	Positive for AFB smear	0	0
	Positive for culture	0	0
Postoperative llung tissue with cavity cultures	Positive for aspergillus fumigates	87	85.2
	Positive for smear	0	0
	Positive for culture	9	8.8
	Positive for mucomycosis	5	4.9

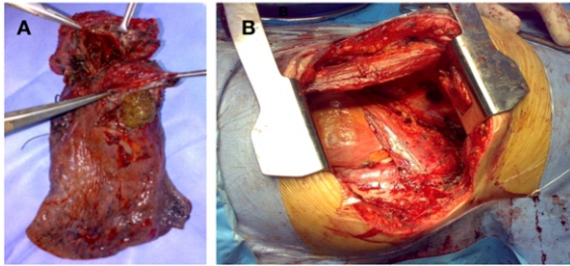
Table-3: Surgical procedures performed in 102 patients.

Procedure	n=102	%Age
Wedge resection (right upper lobe)	06	5.9
Lobectomy	67	65.7
• Right upper lobectomy	33	32
• Right lower lobectomy	07	6.8
• Left upper lobectomy	18	17.6
• Left lower lobectomy	09	8.8
Bilobectomy (right upper and middle lobes)	09	8.8
Pneumonectomy	15	14.7
• Right pneumonectomy	09	8.8
• Left pneumonectomy	06	5.8
Thoracoplasty	05	4.9
Subsequent thoracoplasty	05	4.9

Table-4: Postoperative outcome of surgical procedures.

Varibales	Wedge resection (n=4)	Lobectomy (n=66)	Lobectomy (n=66)	Pneumoectomy (n=14)	Thoracoplasty (n=9)
Hemorrhage (>1500ml)	-	3	1	-	-
Pneumonia	-	3	1	-	-
Prolonged air leak (>7 days)	-	9	1	-	-
Bronchopleural fistula	-	4	-	1	-
Empyema	-	3	-	1	-
Wound infection	1	4	-	1	2
ICU stay (days)	1	3±1	3±1	2±1	4±1
Mortality	-	1	-	1	-

Fig 3: A) resected lung showing fungal material in the cavity , **B)** bronchial stump covered with pleural flap after pneumoectomy



Discussion

Aspergillus fumigatus, a saprophytic fungus is ubiquitously present in our environment. Mostly it colonizes a pre-existing cavity. According to World Health Organization (WHO) Global TB report 2017, Pakistan ranks 5th in 22 high burden countries with 510,000 new cases and 15,000 MDR TB cases each year.²⁰ According to British cooperative study patients having thick walled lung cavities for more than 7 years who were treated for tuberculosis bear higher risk for *Aspergilloma*.²¹ In our study 78% of aspergillomas developed in residual tuberculous cavities. Preoperatively Sputum and BAL cultures for *Aspergillus fumigatus* were positive only in 3 (2.9%) and 14 (13.7%) cases respectively whereas postoperatively resected lung grew *Aspergillus Fumigatus* in 85% cases. This emphasizes the point that preoperative immunological or culture testing is not required to make diagnosis in fact sputum cultures have a low yield in detection of mould.²² A majority of patients who are offered surgical treatment have hemoptysis for which they present to pulmonologist.²³ According to most studies, the percentage of symptomatic patients is around 80%,^{23,25} which is confirmed in our study where 75% patients were symptomatic. There is no consensus on the management of pulmonary aspergilloma. Due to poor results of treatment with local and systemic antifungal agents, surgery remains the most promising option.⁶ Due to risk of bleeding, surgery is mainly recommended in cases who are in

good health and does not have complex disease. In our study we enrolled 289 cases but only 102 underwent surgery due to fitness issues and due to fear of surgery many patients refused to take this option and were lost to follow up. Depending upon the extent of disease, lobectomy, segmentectomy, pneumonectomy, and cavernostomy were done in our study. Standard thoracotomy and lobectomy were the preferred surgical procedures in a series of 212 patients, done by Qian-Kun et al.²⁶ The most commonly encountered complications listed in the literature are bleeding, prolonged air leaks and residual pneumothoraces.²⁷ Pleural space problems were the most common postoperative complications in our study, seen in 20 patients (19.61%). We used fibrin glue in 29 patients, which was shown to be an effective sealant for pulmonary parenchymal suture line and broncho-vascular stumps. We agree with Babatasi et al and Massard et al that thoracoplasty may be indicated subsequent to space problem after lung resection for *Aspergilloma*.^{28,29} In our study, 5 patients had subsequent thoracoplasty for bronchopleural fistula or empyema as a second procedure. Three patients had thoracoplasty after lobectomy whereas 2 patients had pneumonectomy. The outcome after thoracoplasty was good with no post-operative mortality. In our study 5(4.9%) patients had bronchopleural fistula whereas in a previous series by Barik et al, BPF was reported between 2.5 and 15.8.³⁰ 10 (9.8%) patients had prolonged air leak, 8 (7.8%) had surgical site wound infection, 8(7.8%) had mild hemoptysis for a few weeks, 4(3.9%) had intra thoracic haemorrhage (>1500 ml blood loss) which was managed with blood transfusions and volume replacement. 4(3.9%) had post resection loculated empyema & 4(3.9%) had pneumonia. No adjuvant anti fungal treatment was offered to the patients as there no is significant data to back up post-operative use.³¹ The long term outcome in our cases remained encouraging.

Conclusions

Although surgery of aspergilloma is considered to be a technically difficult surgery with scrupulous selection of patients, good surgical skills and postoperative care, morbidity and mortality can be reduced significantly and long term surgical outcome can be very favourable. Based on literature and on our experience, we suggest that surgery should be offered to these patients especially those who are having recurrent haemoptysis.

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