Short papers

Surgical treatment for pulmonary aspergilloma: a 28 year experience

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Abstract

***Background* – Pulmonary aspergilloma has been treated surgically for many years but the mortality rates of larger surgical series, varying from 7% to 23%, is not considered acceptable by today's standards. The authors report their experience in the surgical treatment of pulmonary aspergilloma and present a review of the literature.**

***Methods* – Sixty seven patients who underwent thoracotomy for pulmonary aspergilloma from 1968 to 1995 were studied retrospectively by reviewing their medical records.**

***Results* – The most common clinical presentation of pulmonary aspergilloma was haemoptysis which occurred in 61 patients (91.0%). Tuberculosis was the most common pre-existing disease, occurring in 54 patients (80.6%). The plain chest radiograph showed the typical "air-crescent" sign in 36 patients (53.7%). Systemic antifungal therapy neither palliated the clinical symptoms nor eradicated the aspergilloma, and transarterial embolisation was also unsuccessful. Surgery offered the only chance of cure for both unilateral and bilateral disease. Procedures varied from segmentectomy to pneumonectomy with most (61.4%) undergoing lobectomy. There was one death following surgery from pneumonia and 15 postoperative complications occurred in 12 patients – empyema (7), massive bleeding (3), bronchopleural fistula (2), wound infection (2), and Horner's syndrome (1). Postoperatively, most of the patients were symptom-free.**

***Conclusions* – With appropriate preoperative evaluation and judicious surgical technique, surgery is the preferred treatment for pulmonary aspergilloma, both for eradicating the tumour and for curing the underlying disease.**

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Keywords: pulmonary aspergilloma, surgical treatment, tuberculosis.

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Since 1947 when Gerstl performed the first surgical resection of aspergilloma,[1] pulmonary aspergilloma has been extensively reported and of particular interest to the surgeon. The overall mortality following surgery of the collected series of Kilman *et al*[2] was about 7%. In larger single series reported by Jewkes *et al*[3] and Daly *et al*[4] the mortality following surgery was as high as 14% (seven of 49) and 23% (12 of 53), respectively. Even in the more recent study reported by Massard *et al* in 1992[5] it was around 9%. The major cause of surgical mortality remains obscure and the most common type of morbidity is not well known. We present a review of the surgical mortality and morbidity reported in the literature and present our experience with the surgical treatment of pulmonary aspergilloma at the National Taiwan University Hospital over a period of 28 years.

Methods

Between 1968 and 1995, 72 patients were identified pathologically at the National Taiwan University Hospital as having pulmonary aspergillomas. Treatment with transarterial embolisation was tried unsuccessfully in nine patients and all eventually resorted to surgery. Antifungal chemotherapy with amphotericin B (1.0–1.5 mg/kg/day), alone or combined with flucytocine (100–150 mg/kg/day), was given to 19 patients, five of whom are excluded from the study because they did not undergo surgery. Thus, a total of 67 cases (46 men) of mean age 40.2 years (range 20–73) were enrolled into the study. The aspergillomas were classified according to the system of Belcher and Plummer.[6] Simple aspergillomas had thin-walled cysts with little or no surrounding parenchymal lung disease and complex ones had thick-walled cavities with substantial surrounding parenchymal lung disease or associated infiltrates.

The indications for surgery included symptomatic "air-crescent" lesions, indeterminate lung mass, destruction of the lung or a lung lesion with clinical haemoptysis. The extent of lung resection was determined by the amount of involvement by the aspergilloma and the degree of lung function. In difficult cases it was sometimes necessary to cut two ribs (fourth and fifth or fifth and sixth) to get a better surgical exposure. Preoperative lung function was determined by comparing the forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and the FEV_1/FVC (FEV_1%) with the predicted values. These percentage predicted values were 78.5 (32.2–116.4) for FVC, 65.0 (31.7–113.6) for FEV_1,

and 81.5 (38.8–104.7) for FEV_1%. In patients who underwent a pneumonectomy the percentage predicted values for FVC and FEV_1% were both over 50%.

The medical records were reviewed for presenting symptoms, preceding lung disease, chest radiographic findings, location of mycetomas, type of operation, amount of bleeding during and after the operation, surgical mortality and morbidity, and outcome. Nine were lost to follow up; the rest had follow up periods ranging from two to 107 months with a mean of 25.0 months.

Results

Haemoptysis was the most common symptom, occurring in 61 patients (91.0%). Fifteen patients had severe haemoptysis (>100 ml/day) and three had life threatening haemoptysis. The less frequently encountered presentations included cough (18), fever (4), dyspnoea (4), chest pain (3), and weight loss (1).

The most frequently reported pre-existing pulmonary disease was tuberculosis which was found in 54 patients (80.6%). The interval between the diagnosis of pulmonary tuberculosis and development of the aspergilloma varied from less than one year to 30 years with an average of 9.2 years. Other underlying pulmonary diseases included bronchiectasis (4), bronchogenic cyst (3), lung abscess (3), lung sequestration (1), and infection with the lung fluke *Paragonimus* (1). In one patient the pre-existing disease was not clear.

The chest radiographs of the patients showed the typical "air-crescent" sign in 36 cases. Other radiographic pictures included dense apical fibrocalcified lesions (14), nodular mass (8), destruction of the lung, (5) and cavitation (4). Four patients were classified as having a simple aspergilloma and the others had a complex aspergilloma. The aspergillomas were mostly located in the upper lobe (right in 31 cases and left in 28). In five patients with destroyed left lungs we had great difficulty in defining the location. Seven patients, none of whom had had pulmonary tuberculosis, had aspergillomas located in the right middle (2) or lower lobes (5). Four cases with bilateral lung involvement, one synchronous and three metachronous, all had their mycetomas in both upper lobes.

Nineteen patients had been unsuccessfully treated with antifungal agents for at least 10 days, 14 of whom were referred for surgery because their symptoms persisted. Of the other five who hesitated or refused surgery in spite of our efforts at persuasion, three died of massive haemoptysis and two were lost to follow up after being discharged from hospital. Nine patients underwent angiography but embolisation was successful in only two as it was difficult to identify most of the affected vessels. All of these patients finally resorted to surgery. The surgical procedures included segmentectomy (6), lobectomy (43), bilobectomy (5), pneumonectomy (9), lobectomy combined with segmentectomy (6), and cavernostomy with subsequent thoracoplasty (1).

In this series the average blood loss at operation was 511 (85–750) ml for segmentectomy, 722 (100–2300) ml for lobectomy, 986 (115–4000) ml for bilobectomy or lobectomy with segmentectomy, and 2065 (1200–3000) ml for pneumonectomy. The mean quantity drained during the 24 hours after the operation was 659 (155–1490) ml, 832 (170–1800) ml, 996 (380–2960) ml, and 1144 (550–2520) ml, respectively. The only death following surgery occurred in a patient with three episodes of massive haemoptysis which required a life saving endotracheal intubation. He died of overwhelming pneumonia after emergency pneumonectomy. Residual pleural space was frequent (58.2%) after operation, especially in those with pre-existing tuberculosis, because of poor lung re-expansion or dense intrapleural adhesions. In most cases the residual space could be managed by prolonged chest tube placement and was of no medical importance unless it enlarged or accumulated fluid with subsequent infection. Twelve patients, 10 with tuberculosis and two with a lung abscess, developed a total of 15 major postoperative complications. Empyemas occurred in seven cases (one following cavernostomy, four following a lobectomy, and two with a pneumonectomy), four required open drainage and three required chest tube drainage, one of whom needed instillation of amphotericin B to treat *Aspergillus* empyema. Life threatening bleeding (amount drained >200 ml/h for six consecutive hours or unstable vital signs despite normal coagulation function and transfusion) justified reoperation for haemostasis in three cases (one lobectomy with segmentectomy and two lobectomies). Major wound infection necessitated drainage in two cases (one lobectomy, one pneumonectomy). Two lobectomies resulted in bronchopleural fistulae which were managed by thoracoplasty. Horner's syndrome occurred after lobectomy from injury to the cervical sympathetic chain in one patient.

The result of surgical treatment was assessed from the relief of preoperative symptoms and the findings on serial chest radiographs. All of the patients did well following surgery except for three who still had intermittent haemoptysis which subsided after conservative management. Most of the patients had no evidence of recurrence of aspergilloma but three suffered recurrence of haemoptysis two weeks, 11 months, and 12 months, respectively, after the first operation. The plain chest radiographs demonstrated enlarged hazy lesions on the opposite upper lung fields which were initially obscured by dense fibrocalcified lesions. On reoperation these were found to be an aspergilloma. There was no further haemoptysis after the second operation.

Discussion

Tuberculosis was the preceding lung disease in approximately four-fifths of the patients in this series with pulmonary aspergilloma, which is higher than reports from other areas.[3–5 7 8] This is chiefly because the prevalence of pulmonary tuberculosis in Taiwan is still high (1.29%

in 1987), nine times higher than the level of tuberculosis (0.143%) proposed by the World Health Organisation.[9]

Clinically, haemoptysis was the most common symptom of pulmonary aspergilloma. The mortality from haemoptysis has been variously estimated to be 25–30%.[1 4 10] Although Faulkner *et al*[7] regarded patients with preceding tuberculosis to be at a greater risk of fatal haemoptysis, they suggested that the risk of haemoptysis is related to the history of preceding minor haemoptysis rather than the underlying disease.[1 3]

There is no consistently good evidence that a fungal ball is responsive to amphotericin B.[5 11 12] Systemic antifungal agents hardly penetrate a dead space such as lung cavitation and a higher minimal inhibitory concentration is required.[11] In recent years itraconazole has offered promise in the oral treatment of *Aspergillus* infections but the results of its use in the treatment of aspergilloma are varied and it has not been studied in controlled trials.[13] Even if itraconazole works, the underlying cavity remains and there is still the possibility of recurrence. The identification of bleeding vessels by angiography was difficult. Concomitant embolisation did not result in the permanent control of haemoptysis because of the presence of a massive collateral circulation,[14] and it is not possible to eradicate aspergilloma by this means. This is a matter of serious concern because such patients are at high risk of recurrent haemoptysis or death.[14] The reduction of intraoperative bleeding by embolisation is also unsuccessful,[5] as in two of our cases whose intraoperative blood loss was about 1200 and 2300 ml, respectively.

Lobectomy was the preferred procedure and was used for all the diseases in our series. Although the aspergilloma was often located in an upper lobe, an adjacent segment of a lower or middle lobe was occasionally involved. Under these circumstances, simultaneous segmentectomy – or even bilobectomy – was justified. Pneumonectomy could only be performed in cases with widespread destruction of one lung in whom the other lung provided a good reserve. The extent of resection should therefore depend upon the extent of underlying disease and the location of the aspergilloma as well as on the patient's lung reserve. If the pulmonary reserve permits, surgery can be used in cases with bilateral aspergilloma as staged resections can be carried out with good results. In patients whose lung function cannot support a lung resection, minimal procedures such as cavernostomy[3] for mycetomectomy or intracavitary instillation of antifungal agents[1 8 10 15] to prevent further loss of lung function are indicated.

In our 28 year experience we achieved a mortality rate of 1.5% and a morbidity rate of 17.9%. All of these patients had complex aspergillomas. The pre-existing lung disease, especially tuberculosis, usually caused obliteration of the pleural space, induration of the hilar structures, poor expansion of the remaining lung, and dense vascular adhesions in the thoracic cavity. Hence, tuberculosis inevitably complicated surgical management. Bleeding was the problem most frequently encountered during and after surgery. Postoperative bleeding, if not well drained, might lead to secondary infection resulting in empyema formation. Empyema and bronchopleural fistulas, as well as residual pleural space, were managed in a standard fashion such as prolonged chest tube drainage, open drainage, or thoracoplasty. Most of the patients had a good long term result in terms of absence of symptoms.

A review of 39 surgical deaths in the literature revealed that the chief cause of postoperative death was respiratory failure (table 1).[1–7 10 15–18] Preoperative pulmonary function testing is therefore mandatory to prevent respiratory failure after lung resection for aspergilloma. In addition, 171 postoperative complications in 109 patients reported in the literature are summarised in table 2.[1–8 10 15–18] Bleeding, residual pleural space, bronchopleural fistula, and empyema were the most common surgical complications encountered. The complications were not usually the result of *Aspergillus* infection per se but were related to the underlying disease of the host or infection by other organisms.[1 2 6 16 17] Systemic antifungal therapy is of little benefit in the treatment of pulmonary aspergilloma, especially when weighed against the resulting adverse effects. If the diagnosis is established at an early stage with good lung reserve, surgical resection should be undertaken as soon as possible. It is in cases where the disease has reached an advanced stage and surgery is the only means of controlling the symptoms that surgical mortality has proved to be extremely high.[16] It is therefore logical to recommend operative resection of the involved area with a thorough evaluation of preoperative

Table 1 Causes of surgical mortality in 41 patients with pulmonary aspergillomas reported in the liturature

Cause of death	*No. of patients*
Respiratory failure	16 (41.0%)
Bleeding	6 (15.4%)
Pneumonia	3 (7.7%)
Underlying disease	3 (7.7%)
Myocardial infarction	2 (5.1%)
Sepsis	2 (5.1%)
Aspergillosis	2 (5.1%)
Miscellaneous*	5 (12.8%)

* Including bronchopleural fistula, empyema, hypoxic encephalopathy, aortic graft thrombosis, disseminated intravascular coagulopathy.

Table 2 Surgical complications (n=171) in 109 patients with pulmonary aspergillomas reported in the literature

Types of complication	*No. of complications*
Bleeding	38 (22.2%)
Residual pleural space	33 (19.3%)
Bronchopleural fistula	27 (15.8%)
Empyema	23 (13.5%)
Respiratory insufficiency	14 (8.2%)
Air leakage	11 (6.4%)
Wound infection	5 (2.9%)
Sepsis	3 (1.8%)
Pneumonia	2 (1.2%)
Atelectasis	2 (1.2%)
Retained secretions	2 (1.2%)
Miscellaneous*	11 (6.4%)

* Including pleural effusion, wound dehiscence, lobar infarction, paralytic ileus and unknown in seven patients.

pulmonary function since the surgical mortality is exceedingly low, the management of surgical morbidity is feasible, and the potential for cure, even of the underlying disease, is excellent. On the other hand, in patients with limited lung reserve an alternative approach to management such as cavernostomy or intracavitary instillation of antifungal agents is recommended.

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Indications and outcome of surgery for pulmonary aspergilloma

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Abstract

Background **– The indications and the outcome of surgery for pulmonary aspergilloma remain highly controversial. The short term and long term results of lung resection or cavernostomy in 24 patients with pulmonary aspergilloma are reported.**

Methods **– The case notes of 27 consecutive patients referred for surgical assessment for pulmonary aspergilloma at the Royal Brompton Hospital over the last 14 years were reviewed. Patients were categorised into four classes according to their fitness for lung resection and the severity of their symptoms. Severe symptoms were defined as life threatening haemoptysis or other symptoms requiring more than one hospital admission. Class I (n = 1), fit individual with mild or no symptoms; class II (n = 17), fit individuals with severe symptoms; class III (n = 1), unfit individual with no symptoms; and class IV (n = 8), unfit individuals with severe symptoms. Two asymptomatic patients and one on an IVOX pump were not accepted for surgery. Lung resection was performed in all 17 patients with class II disease, comprising segmentectomy only in five patients, lobectomy and segmentectomy in seven, and a completion pneumonectomy in five patients. Cavernostomy was performed in seven patients with class IV disease.**

Results **– Surgery was often complicated by prolonged air leakage and infection of residual space. There was no operative mortality in the group treated by resection whereas two of those who underwent cavernostomy died in the early postoperative period. All survivors were followed up for a median of 17 months (range 1–72 months); 19 were alive and had no symptoms attributable to aspergilloma. Late recurrence occurred in two patients in the cavernostomy group. The only late death occurred in the resection group five months postoperatively and was attributed to end stage renal disease.**

Conclusions **– Lung resection in selected patients with complicated aspergilloma can be performed with low operative mortality. Cavernostomy is associated with high mortality and morbidity and should therefore only be performed in patients with life threatening symptoms who are unfit for lung resection.**

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Keywords: pulmonary aspergilloma, surgical treatment, outcome.

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Table 1 Clinical characteristics and rate of complications in patients undergoing surgery for aspergilloma

	Resection group (n = 17)	*Cavernostomy group (n = 7)*
Mean (range) age (years)	50 (20–79)	54 (38–71)
H/O parenchymal lung disease*	11	5
Complex aspergilloma	9	5
Severe haemoptysis	12	4
Failed conservative therapy	3	3
Mean (range) FEV_1(l)	2.4 (1.3–4.5)	0.75 (0.6–2.6)
Mean (range) FVC (l)	3.2 (1.99–5.6)	1.3 (1–1.3)
Mean (range) postoperative blood loss (ml)	1119 (150–2250)	902 (310–2200)
Infected residual space	2	3
Prolonged air leak (> 9 days)	1	4
Early mortality rate **	0% (0 to 19)	28.6% (4 to 71)
Late mortality rate **	5% (0 to 29)	0% (0 to 41)
Recurrence rate**	0% (0 to 17)	28.6% (4 to 71)

* Tuberculosis in nine patients, bronchiectasis in four, sarcoidosis in two and pulmonary fibrosis in one patient. No history of parenchymal lung disease was documented in eight patients. Two patients had bilateral aspergilloma at the time of surgical consultation.
** Rate of complication presented as a percentage of the number of the corresponding group. The 95% confidence interval, based on the binomial distribution, is shown in parentheses.

Saprophytic aspergillosis occurs as an opportunistic infection of pre-existing lung cavities by the fungus *Aspergillus fumigatus*. The detached mycelium forms an aspergilloma[1] which is a ball of amorphous material containing tangled septate hyphae and altered blood elements. An aspergilloma can be simple (if surrounded by macroscopically healthy lung tissue) or complex (if surrounded by diseased lung tissue).[2] Haemoptysis occurs in up to 83% of patients and can be life threatening in up to 30%.[3 4]

Surgery is rarely indicated in allergic aspergillosis and has recently been advocated as beneficial in some patients with invasive aspergillosis.[5] By contrast, surgical resection offers the only realistic chance of a permanent cure for aspergilloma.[3 6 7] Previous reports suggest that surgical resection for aspergilloma should be restricted to patients with severe haemoptysis who have adequate respiratory function.[6] We present the short and long term results in 24 consecutive patients with complicated pulmonary aspergilloma who underwent lung resection or cavernostomy.

Methods

The clinical characteristics of patients who underwent surgery are summarised in table 1. The diagnosis was confirmed by a computed tomographic (CT) scan in all cases. Bilateral aspergilloma was observed in one patient in each group. Surgery was offered only to those patients who were considered to have severe or life threatening complications: severe haemoptysis in 16 patients, recurrent and/or chronic chest infections requiring more than one hospital admission in three, and severe weight loss in five patients. The severity of haemoptysis was gauged according to a scale proposed by Jewkes *et al.*[6]

Lung resection was performed in 17 patients with class II disease, of which segmentectomy only was performed in five patients, lobectomy plus segmentectomy in seven, and a completion pneumonectomy in five patients. Surgery was performed under general anaesthesia with a double lumen endobronchial tube. The chest was opened via a standard lateral thoracotomy via the fifth or the sixth intercostal space. The pleural space was often obliterated with fibrous and vascular adhesions. The diseased lobe(s) were mobilised by extrapleural dissection, thus avoiding entry to the infected cavity. In four patients a second incision via the seventh intercostal space was performed to facilitate mobilisation of the lower lobe and the diaphragmatic surface of the lung. Differential ventilation aided the identification of the interlobar fissure and the isolation of the diseased segment in patients who had a segmental resection. Trimming thoracoplasty was performed as a supplementary procedure in three patients in whom the residual lung tissue could not physically compensate for the loss of the resected lobe and/or segment and consisted of resecting the posterior one third of the fourth rib, posterior two thirds of the third rib, and the whole of the first and the second ribs. The indications for completion pneumonectomy were multiple unilateral aspergilloma in one patient and aspergilloma in the remaining lobe after previous lobectomy for tuberculosis in four patients.

Cavernostomies were performed under local and/or regional anaesthesia via a 4–5 cm incision overlying the cavity, guided by the CT scans. The cavity was identified and incised and the fungal ball was removed. A short segment of the overlying rib was then excised before inserting a chest drain. In two patients, one of whom had a recurrence of aspergilloma after previous cavernostomy, the ipsilateral latissimus dorsi muscle was mobilised from its distal attachment, then tunnelled and fixed into the residual cavity.

Results

The early and late results of surgery for aspergilloma, classified according to the type of the procedure, are summarised in table 1. Excessive intraoperative blood loss occurred in four patients in the resection group secondary to an avulsed segmental pulmonary artery branch in two, and to a torn azygos vein in two. Patients required a median of 4 units (range 1–8) of blood transfusions to keep their postoperative haemoglobin levels above 10 g/dl. Infection of the residual space occurred in five patients who were later successfully treated by a rib resection and drainage. There was no laboratory evidence of fungal contamination of these empyema. Two of these patients had an atrophic muscle flap after thoracomyoplasty. The median hospital stay was 11 (7–20) and 16 (8–32) days in the resection and cavernostomy groups, respectively. The 22 survivors were followed up for a median of 17 months (range 1–72 months), following which they were discharged to the referring physician. Nineteen patients were alive and had no symptoms attributable to aspergilloma, one patient in the resection group died five months after surgery due to chronic renal failure, and two patients had a recurrence of apical aspergillosis three and seven months after cavernostomy.

Discussion

The natural history of pulmonary aspergilloma varies from spontaneous lysis to recurrent life threatening haemoptysis.[8–9] There are no consistent clinical or diagnostic criteria that predict whether an aspergilloma is self limiting or prone to complications.[6] With such a high risk of unpredictable, life threatening haemoptysis it may seem justifiable to operate on all patients with pulmonary aspergillosis. However, operative treatment of these cases carries significant morbidity and mortality.[4 6] The high risk of surgery for aspergilloma is primarily due to associated technical difficulties which are secondary to the often obliterated pleural space, indurated hilar structures, and failure of the residual lung tissue to expand after the operation. In one of the largest published series Daly *et al*[4] have reported an overall operative mortality of 24.5% and postoperative morbidity of 60%. Such a significant level of risk may nullify the potential benefits of surgery.

This report, and previous experience from our institution,[6] suggests that life threatening symptoms and/or symptoms necessitating one or more hospital admissions (classes II and IV) represent the sole indication for surgery. There is little evidence in the medical literature to suggest that lung resection for asymptomatic aspergilloma offers better long term benefits than medical treatment alone.[6 7 10] Cavernostomy alone is generally offered to symptomatic high risk individuals and is therefore associated with a prohibitive risk of morbidity and/or mortality. To minimise the operative complications in this group of patients, cavernostomy has been combined with intrathoracic transposition of extrathoracic skeletal muscle.[4] Our limited experience with thoracomyoplasty using the latissimus dorsi muscle in patients with class IV disease is disappointing as the muscle flaps atrophied within a few weeks following the operation. The potential advantages of combining a cavernostomy with intracavitary antifungal instillation or a reconstructive procedure in patients with class III and IV disease need further clinical evaluation.

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