Surgery for pulmonary aspergilloma in post-tuberculous vs. immuno-compromised patients

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Abstract

Objective: To compare the outcome of surgical resection for aspergilloma between patients with post-tuberculous complex and neutropenia.

Methods: We retrospectively reviewed our surgical experience with pulmonary resection for aspergilloma in 30 patients. Of the 20 patients with complex aspergilloma complicating healed tuberculosis (group 1), 14 were male and six were female with an average age of 54 years (SD 7). The indication for surgery was recurrent haemoptysis in all and there were 17 lobectomies, two pneumonectomies and one bilateral lobectomy. There were ten patients with acute myeloid or lymphoid leukemia (group 2), six male and four female with an average age of 26 years (SD 4). Twelve lesions required lobectomy in eight and wedge excision in four. Results: In group 1 there was one postoperative death (5%), in a patient with massive haemoptysis and completely destroyed lungs with bilateral upper lobe aspergilloma secondary to pneumonia. Morbidity accounted for 25% (five patients), two required re-exploration for bleeding, two had prolonged air leak more than 7 days and one developed empyema. The later was treated with drainage and rib resection. One patient had recurrence of haemoptysis during the follow up period (mean 42 months). In group 2 there was no mortality or morbidity and six patients proceeded to bone marrow transplantation with no complication or recurrence. Conclusions: Surgical resection for pulmonary aspergilloma in selected patients provides the best chance of cure. Pulmonary resection for post-tuberculous complex aspergilloma is associated with higher morbidity than resection for immuno-compromised patients. © 2001 Elsevier Science B.V. All rights reserved.

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1. Introduction

Aspergilloma is generally an opportunistic infection of the lung secondary to Aspergillus fumigatus. This can lead to different forms of diseases namely, allergic broncho–pulmonary form, aspergilloma (simple or complex) or invasive pulmonary aspergilloma (IPA). Aspergilloma complex usually complicate necrotic cavitary lesions mainly in tuberculosis. Once a fungal ball is formed, surgery is indicated to avoid the associated morbidity mainly haemoptysis. In the post-tuberculous complex, surgery is associated with high rate of complication secondary to the underlying disease [1,2].

More recently patients with hematological neutropenia are at high risk of developing simple pulmonary aspergilloma that can bleed or more important can progress into an invasive disease, IPA resulting in high mortality rate [3].

Surgical resection in that group of patients has a different scope of complications. In this paper we have compared the surgical outcome of pulmonary resection of aspergilloma in patients with post-tuberculous complex vs. neutopenic patients.

2. Materials and methods

Over a period of 10 years between January 1991 and January 2000, 34 patients were diagnosed to have pulmonary aspergilloma and were referred for surgical resection. The underlying predisposing disease was cavitary tuberculous complex in 20, neutropenia in 10, post-pulmonary embolism in one, post-narcotizing pneumonia following bronchial torsion in one, infected bronchogenic cyst in one, and chronic renal failure in one patient. We retrospectively reviewed the charts of 30 patients with either post-tuberculous disease (group 1) or neutropenic (group 2).

In group 1 there were 20 patients, 14 male and six female with an average age of 54 years (SD 7) ranging between 29 and 68 years. All patients were known to have post-
culous pulmonary disease, for which anti-tuberculous therapy had been given. All patients gave a history of massive haemoptysis prior to referral for surgery. Patients reported a range of 200–600 ml in an average of three attacks of haemoptysis. All patients were either known to have past history of tuberculosis or had positive sputum culture of *Mycobacterium tuberculosis* for which all had a full course of treatment. Radiological investigations included a chest roentgenogram and a computed tomogram (CT) scan of the chest and that showed the classical rounded mass with an air crescent located in a fibrotic lung cavity in all patients (Figs. 1 and 2). Two patients had bilateral lesions (Fig. 3). The distribution of the 22 lesions was upper lobe in 16, middle lobe in one and lower lobe in five cases. Pre-operative assessment of their pulmonary function revealed an average FEV1 of 72% of the predicted value (range between 40 and 80%). The FVC averaged 62% (range between 38 and 77%). Pre-operative embolization was attempted in two patients with massive haemoptysis. In those two patients the active bleeding stopped and the surgery was scheduled as elective rather than emergency 10 days after embolization.

In group 2, there were 10 patients, six male and four females with an average age of 26 years (SD 4), (range between 18 and 42 years). The primary diagnosis was acute myeloid leukemia in six, acute lymphoid leukemia in three and non-Hodgkin lymphoma in one patient. All patients received high-dose chemotherapy and that was followed by bone marrow transplantation in three patients. At time of presentation the average neutrophil count was 0.4 × 10 × 9/l (range between 0.03 to 6.5 × 10 × 9/l) Three patients were asymptomatic and the remaining patients presented with symptoms and signs of chest infection, fever and cough are being the commonest findings. All patients showed negative sputum cultures and only one out of six patients who had bronchoscopy and broncho–alveolar lavage (BAL) showed evidence of fungal infection. When the chest radiography showed any abnormality, a CT scan of the chest was performed. The classical fungal ball appearance was noted in seven patients, two patients showed consolidation with cavitory lesion giving a halo sign.
(a mass-like infiltrate with a surrounding halo of ground-glass attenuation) (Figs. 4 and 5), and one patient showed an abscess cavity. In two patients there were more than one lesion. The 12 lesions were located in the upper lobes in eight and lower lobes in four cases. At the time of surgery the neutrophil count raised to an average of $4 \times 10^9/\text{l}$ (range between 2 and $8 \times 10^9/\text{l}$). The pulmonary function test was normal in nine patients pre-operatively and one patient was on ventilator for respiratory failure secondary to pneumonia.

### 3. Results

In group 1 the operation was considered urgent (within the same week) in 13, emergency (within few hours) in four and booked in three patients. Seventeen patients had lobectomy, two had pneumonectomy and 1 had bilateral staged upper one lobectomy. All cases were performed via a posterolateral thoracotomy and extra pleural dissection was performed at the resected areas. This was performed because of the dense vascular adhesions, which was routinely found to obliterate the pleural space and the surrounding the atelectatic fibrotic lung. It also avoided opening the peripheral cavities which are adherent or occasionally eroding the chest wall.

The diseased tuberculous lung was evident with enlarged and tortuous bronchial arteries and the vascular nature of the parital pleura with diffuse oozing necessitated packing and prolonged hemostasis using Argon bean coagulation. Pleural tenting was performed in three patients after upper lobectomy in whom extra-pleural dissection was not performed. The operative time averaged 150 min (range between 90 and 240 min) and the intra-operative blood loss averaged 600 ml (range between 100 and 1800 ml) and that required an average of two units of blood to be transfused (range between 0 and 4 units). Pre-operative embolization in two patients was associated with relatively less blood loss. Post-operatively all patients were nursed in the intensive care unit and the average post-operative hospital stay was 9 days (range between 5 and 23 days). Histological evaluation revealed non-invasive form of aspergilloma in all patients. There was one post-operative death (5%), a patient with bilateral destroyed lungs and bilateral upper lobe cavities. The patient developed post-operative pneumonia in the contra-lateral lung after left upper lobectomy, that lead to respiratory failure. The patient died after 2 week of mechanical ventilation secondary to septicemia and respiratory failure. Major morbidity accounted for 25% (five patients). Two patients required re-exploration for excessive bleeding, two patients had prolonged air leak (9 and 16 days) and one patient developed post-lobectomy empyema without broncho-pleural fistula. The lung failed to fully expand and was treated initially with drainage and rib resection followed by partial thoracoplasty. Patients were followed up by 6 monthly clinical and radiological examinations. During a mean follow-up period of 42 months only one patient (5%) developed recurrence of his haemoptysis secondary to cystic bronchiactasis.

In group 2, all operations were timed for surgery after establishing an accepted neutrophil and platelet counts. Treatment with amphotericin B was started upon suspecting the diagnosis and was continued post-operatively upon
confirmation by histological findings. One patient on ventila-
tor was operated upon with low neutrophil count
(0.03 \times 10^9/l) as an urgent procedure. Via a postero-
lateral thoracotomy 11 lesions in nine patients were resected
and one lesion was excised by thoracoscopy. The procedure
was a lobectomy in eight and wedge excision using staplers
in four cases. The decision of lobectomy was based on the
site, size and associated consolidation of the lesion. Intra-opera-
tively, two patients had associated empyema that necessi-
tated partial decortication and drainage. In three upper lobe
lesions the parital pleura was infiltrated and extra-pleural
dissection was performed. The lesion infiltrated the pericar-
dium and the descending aorta sheath in two patients. The
operative time ranged between 90 and 130 min (average 105
min). Although the intra-operative blood loss averaged 180
ml (ranged 100–300 ml) an average two units of blood trans-
fusion was given to correct the underlying anemia. Post-
operative hospital stay under surgical care averaged 4 days
(range between 3 and 6 days). Histological examination of
the resected lung tissue confirmed the presence of invasive
form of aspergilloma in four out of 14 cases. There was no
postoperative mortality and morbidity was all minor. Two
patients had excessive postoperative blood loss for 48 h,
which stopped after platelets and blood transfusion. All
patients proceeded to either chemotherapy alone (n = 4) or
to bone marrow transplantation (n = 6). Follow-up included
periodic chest X-ray and clinical examinations in addition to
frequent C-T Chest when the formal were abnormal.

Long-term follow up (mean of 36 months) showed two
late deaths. One patient developed invasive aspergilloma
related to residual disease and died 3 months after surgery.
Due to the primary disease, one patient died at 6 months
after surgery.

4. Discussion

Surgery remains the best treatment modality for pulmon-
ary aspergilloma. The commonest indication is an aspergill-
oma ball in a post-tuberculous cavitary lesion. More
recently with the aggressive use of chemotherapy regimes
for hematological malignancies, more cases are noted in
neutropenic patients [3]. Although surgical resection has
similar outlines, the indications, operative findings and
outcome are completely different from the post-tuberculous
group. In the later the indication is usually recurrent or
massive haemoptysis [1–3]. Long history of productive
cough and recurrent chest infection is not uncommon. Radi-
ological findings of the classical fungal ball with air crescent
are always present in addition to the underlying post-tuber-
culous pulmonary changes [4,5]. In the neutropenic group
high index of suspicious is the key for early diagnosis [6–8].
In severely neutropenic patients periodic chest radiological
examination is warrant even in the absence of respiratory
symptoms. When that shows any abnormality a CT scan has
to follow, as it is more sensitive in detecting abnormalities
in this group of patients in particular [9]. Some patients will
remain asymptomatic and the classical fungal ball is not a
constant finding, consolidation or the halo sign is sometimes
the indication for fungal infection requiring surgical inter-
vention (Figs. 4 and 5). Aspergilloma can occasionally
occur in non-tuberculous, non-neutropenic patients when a
pulmonary cavity exists. Lung abscess, bronchiactatic
cavities and congenital bronchogenic cysts are not uncom-
mon examples. Cavitations can also occur after pulmonary
infarction by pulmonary embolism, bronchial torsion or
narcotizing pneumonia [10].

In group 1 anti-fungal therapy has a limited role and once
aspergilloma is diagnosed surgical resection is indicated [1].
In the neutropenic patients, early treatment with amphoter-
cine B therapy is advisable and should be continued during
the post operative period especially if the patient to be
further exposed to chemotherapy or bone marrow transplan-
tation that cause neutropenic [6,8]. Surgery in post-tubercu-
losus group reduces morbidity and mortality associated
with the high risk of massive haemoptysis. This is usually from
erosion into the tortuous bronchial arteries associated with

In cases presenting with massive haemoptysis, emboliza-
tion of the bronchial or other feeding arteries can completely
or partially control the bleeding. Although recurrence due to
development of collatals can occur, surgical intervention
can be done electively and with significant reduction in the
intra-operative blood loss.

Untreated Aspergillus infection in neutropenic patients is
associated with higher morbidity and mortality. The infec-
tion can lead to septicemia, progress to invasive aspergilloma
or more important can cause massive haemoptysis. The later
is usually secondary to erosion into branches of the pulmon-
ary artery especially when the lesion is centrally located [7].
Patients in the two groups are different; in group 1 they are
older age and have underlying lung disease that is clearly
reflected in their pre-operative pulmonary function. In the
other hand a neutropenic patient is young, healthy with
good pulmonary function reserve but his haemopoietic
system is abnormal. Mainly the patient is neutropenic,
anemic with low platelets count that renders him more
susceptible for septicemia and excessive bleeding. These
abnormalities should be corrected before and during surgery.

Upon exploration the dense fibrotic and vascular adhe-
sions present in post-tuberculous lungs was clearly reflected
in the prolonged operative time and higher rates of blood loss.
Pre-operative embolization of the feeding bronchial arteries
is usually effective in reducing operative blood loss and
performing the surgery as an urgent rather than an emergency
procedure [10,12]. Standard thoracotomy and lobectomy is
the favorite surgical procedure in this group. When the under-
lying lung is healthy wedge excision in selected patients can
be performed. Pneumonectomy is only indicated if the
affected lung was totally destroyed or the remaining lobe is
severely fibrotic and small. When the underlying lung is
healthy as in most of the neutropenic patients wedge excision
in selected lesions can be performed. Thoracoscopic resection is also feasible especially in single peripherally located lesions. We believe like many others that cavernostomy is associated with higher morbidity and mortality and higher rate of recurrence even in patients with poor pulmonary functions [5]. Others demonstrated that cavernostomy was found to be effective in high-risk patients [10]. Meticulous hemostasis and correction of platelets are a must if excessive post-operative blood loss and re-exploration for bleeding are to be avoided. Large well located 2 chest tubes for post-operative drainage is the routine and additional surgical procedures might be needed like pleural tenting and partial thoracoplasty to avoid prolonged air leak or residual space especially after upper lobectomy in post-tuberculous patients [13]. Bronchopleural fistula although more common after resection for inflammatory lung disease, did not occur in our series [14]. We used staplers for closure and in pneumonectomies barred the bronchial stump in all cases of pulmonary resection [15,16]. Empyema remains a risk in both groups and surgical intervention with drainage and possible thoracoplasty may be indicated. Long-term follow up showed that recurrent haemoptysis in post-tuberculous patients remain a risk. Those patients have destroyed or bronchiatcatic lungs that predispose to recurrent fungal infection in other cavities [1,3]. This risk is even higher in neutropenic patients with blood malignancies. They require either further chemotherapy or bone marrow transplantation causing further neutropenia thus the treatment with amphotericine B should continue [9,10].

Our post-operative mortality was comparable to those previously reported. The underlying primary disease remains the commonest cause of death in neutropenic patients while respiratory failure is usually the cause in the post-tuberculous patients. Invasive aspergillosa could be fatal when invading vital mediastinal structures and the great vessels [6–8].

In conclusion we noted major differences between post-tuberculous and neutropenic patients undergoing pulmonary resection for aspergillosa. The patient’s criteria were different in respect to age, presentation and pre-operative status. Post-tuberculous patients with diseased lung develops aspergillosa complex that is difficult to deal with and associated with higher rates of operative and post-operative morbidity when compared to neutropenic patients. Meticulous surgical techniques are warranting to reduce these complications. Aggressive surgical intervention in combination with antifungal therapy is an effective treatment strategy in immunocompromised with aspergillosa disease.

References


Appendix A. Conference discussion

Dr P. Thomas (Marseille, France): I have a question concerning the high rate of pleural space problem you noted in the post-TB group. What do you think about combined or at least staged thoracoplasty to manage this complication?

Dr Al-Kattan: We have always faced this problem. I tried to do a few tricks to avoid thoracoplasty because of the chest deformity. Although it’s not my routine, I take one rib out in all cases where I resect such a problem. I like to do pleural tenting, and occasionally I had to do a pneumonectomy, and the reason for the pneumonectomy was not because the aspergillosa was involving both lungs but that the remaining lung was very small and fibrotic, and the function of that lobe was assessed before operation by perfusion/ventilation scan and I knew it was not good. So I would rather do a pneumonectomy in this patient rather than having a difficult post-operative period dealing with a big space in a non-functioning, small, fibrotic lobe. But obviously, as I said, when you have a space, it’s a potential for empyema, and then you probably need to do a thoracoplasty in those patients. Pleural tenting is also another way. It’s like an extra pleural conversion, it might help, and removing a rib is maybe another trick which can help.

Dr D. Blyth (Natal, South Africa): I’m curious about your pleural tenting...
in relation to, say, an upper lobe aspergilloma. Did you have any difficulty in terms of avoiding entering the cavity, because usually the pleura of the lung itself there is very thin, and it is better to go extrapleurally, and that actually takes away your chances of doing a tent.

**Dr Al-Kattan:** On all upper lobe aspergillomas, actually I had to go extrapleural, because if you go intrapleural, it’s not just difficult, but you actually open this Aspergillus cavity. So it’s a must to do extrapleural. Tenting would occur either in the non-tuberculous group or if it was in a lower lobe where you can actually help to decrease this. But as you just mentioned correctly, all upper lobe Aspergillus in the post-tuberculous should be approached extrapleurally to avoid the bleeding and to avoid opening the Aspergillus ball, which actually sometimes even invades the pleura into the chest wall.

**Dr Blyth:** Your empyema, was that a fungal empyema?

**Dr Al-Kattan:** No, it was a tuberculous empyema.

**Dr E. Ruffini** *(Torino, Italy):* We recently had a woman, apparently asymptomatic, with no neutropenia, with no history of TB, who developed 3 or 4 years ago a pulmonary aspergilloma, and we decided to observe it because it was asymptomatic. First, do you have any suggestion as far as the genesis of the aspergilloma? Second, would you have waited 3 years or would you have operated 3 years ago? We eventually operated because of the increased dimensions.

**Dr Al-Kattan:** Number one, in all our patients they needed either a second course of chemotherapy or bone marrow transplantation, and actually 6 of those groups proceeded to bone marrow transplant. Once you are going to induce neutropenia again, you cannot leave such an aspergilloma. They will definitely progress into invasive aspergilloma, which carries 50 to 70% mortality. Now, you can win with a silent Aspergillus fungal ball, but I don’t think this should be the case because a mortality will not justify waiting, and we know in that group of patients, the lobectomy, morbidity and mortality is almost nil. So you have to compare the risk, and I would advise not to leave such a lesion.