REVIEW ARTICLE

Aspergilloma and the surgeon

Loven Moodley[1], Jehron Pillay[1], Keertan Dheda[2]

[1]Chris Barnard Division of Cardiothoracic Surgery, [2]Division of Pulmonology, Groote Schuur Hospital, University of Cape Town, South Africa

ABSTRACT

Aspergillus fungus is a ubiquitous saprophyte that is the causative organism for the development of an aspergilloma. The most common species causing an aspergilloma is the Apergillus fumigatus. An aspergilloma is a conglomeration of mucus, inflammatory cells and altered blood elements. Aspergillomas typically form in pre-existing lung pathology, most notably and commonly in old healed tuberculosis cavities. They are classified into simple and complex types that have clinical relevance. Symptoms are very variable and it is not uncommon to incidentally find a lung aspergilloma. In most case series, the most common presenting symptom is haemoptysis which varies from mild to catastrophic bleeds. Given the limited information about the natural history of the disease, there is unfortunately no recognised factor or variable which can predict how an aspergilloma will manifest itself, hence the manner of treatment is a still a topic of debate among treating physicians. The mainstay of treatment is surgical intervention and medical options although disappointing at the current stage, require further investigation in light of the newer available anti-fungal agents. The need for surgical intervention is however not as clear-cut as one would like, since many patients have multiple co-morbidities and other diffuse or focal lung pathology, making the decision process indeterminate in certain instances. In this review, we focus on the different surgical options available for the management of aspergilloma across variable clinical settings, and we propose an approach to its management.

KEYWORDS

Aspergilloma; clinical course; surgical management

Introduction

The aspergillus fungus is responsible for many clinical entities or a wide spectrum of pathology in the human body. Lung manifestations are quite diverse and include:

(I)   Pulmonary aspergilloma;
(II)   Allergic bronchopulmonary aspergillosis;
(III) Chronic necrotizing pulmonary aspergillosis;
(IV)   Invasive aspergillosis (1).

This article focuses on pulmonary aspergilloma and the surgical management thereof.

Aspergilli are saprophytes and are present worldwide. Most human infections (95%) are caused by the species aspergillus fumigatus (2).

Thoracic aspergillomas

Most pulmonary aspergillomas are found in the lung tissue. Being saprophytes, they infest a pre-existing cavity in the lung. These cavities may be the result of previous pathology including tuberculosis, healed abscesses, sarcoidosis, pneumoconiosis or cystic fibrosis (3-7).

An unusual presentation of aspergilli infection is endo-bronchial aspergilloma (1,8,9). This is simply the fungus found endo-bronchially and it may occur with or without pulmonary involvement (1).
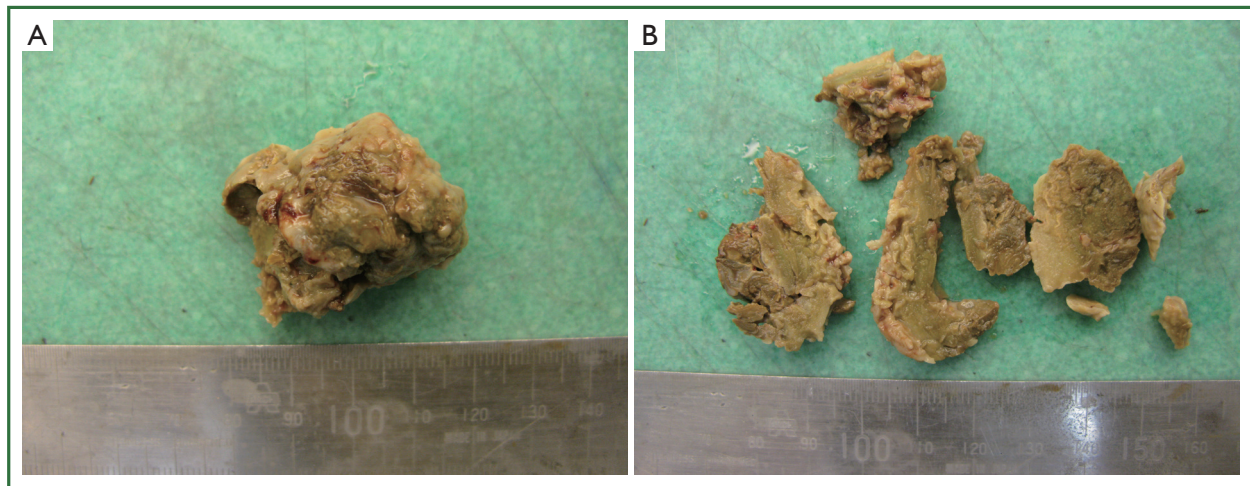
Pleural aspergillomas are usually found in the scenario of chronic empyemas, where the suppuration produces a conducive environment for the colonisation of the aspergillus (10).

Figure 1. Gross picture of a Mycetoma. (A) Intact specimen; (B) Cross section.
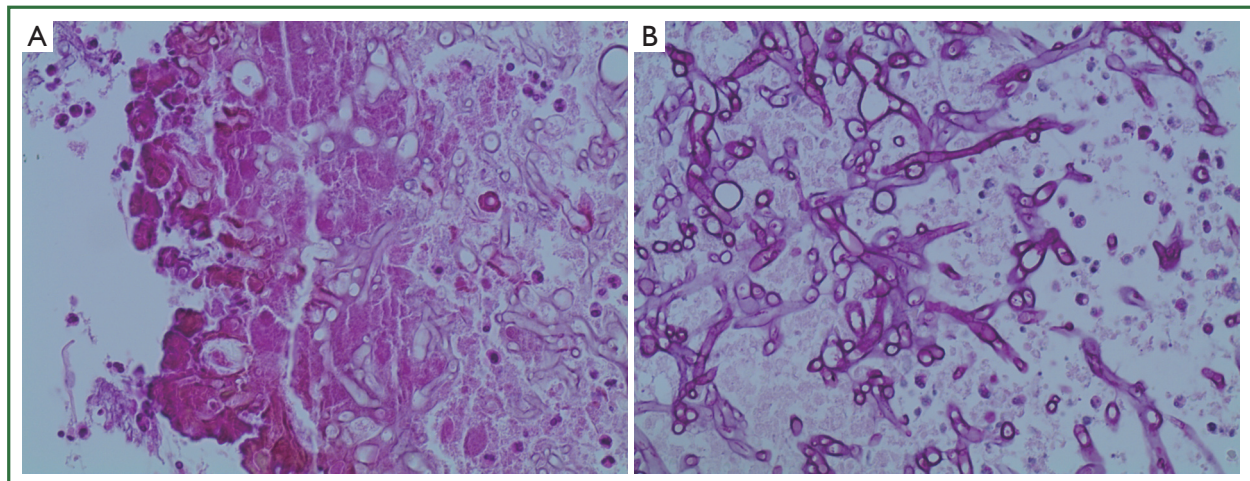
Figure 2. Histology of aspergilloma. (A) Microscopic features of the aspergilloma; (B) Magnified slide to show the acute angulations and the septated hyphae of the aspergillus fungus.

Anatomy

Macroscopically

The aspergillus fungus colonizes a cavity in the lung (mostly upper lobes) (11) and forms a mass of varying size. It is also known as a fungus ball or a mycetoma. Grossly it appears as a clay ball with rough edges (Figure 1A,B).

Microscopically

Classically the fungus has septated hyphae with acute angulations (Figure 2A,B).

Encompassed in the conglomerate mass is fibrin, inflammatory cells and other altered blood elements (12).

## Classification

It is important in the management of aspergillomas to understand the classification fashioned by Belcher and Plummer (13,14) as it has important clinical ramifications.

They divided pulmonary aspergillomas into simple and complex types.

Simple aspergilloma

Here the aspergilloma develops in a thin-walled cavity that has adjacent normal lung parenchyma (Figure 3A-C). Herein
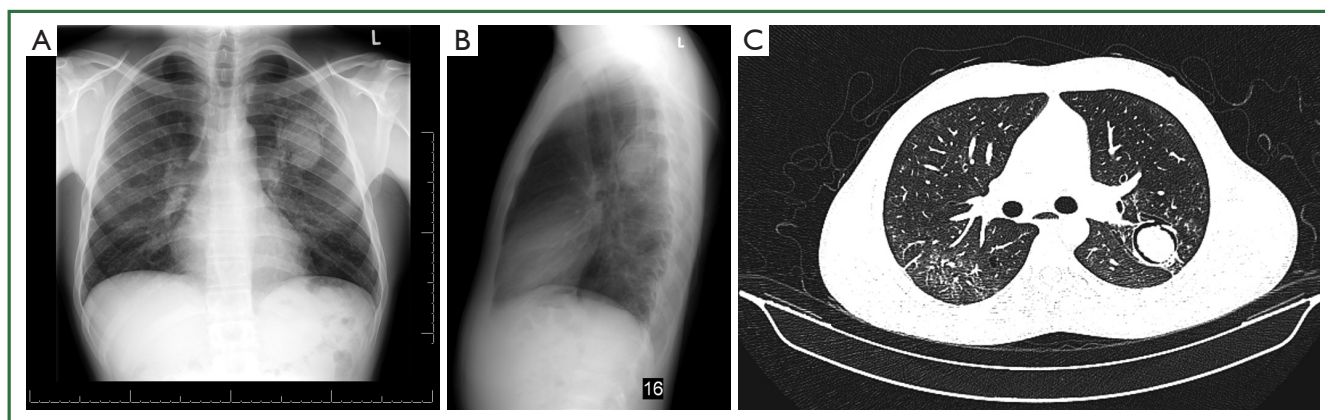
Figure 3. Radiology of a simple aspergilloma. (A) PA chest x-ray; (B) Lateral view. Note the air-crescent sign; (C) CT picture of the same aspergilloma.

the disease process is much more localized. The pleura is not involved in the disease process (3,14-16).

Complex aspergilloma

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 aspergillus fungus has merely colonised this unhealthy destroyed tissue. The lung and pleural pathology is usually due to pre-existing disease processes (most commonly tuberculosis) (3,17) (Figure 4A-D). 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.

Pathophysiology

The aspergillus fungus is commonly found in sputum cultures (11). They invade the lung through the respiratory tract and colonize the pre-existing cavity which has a direct communication to a bronchiole (18). There may be tissue invasion of the lung causing the more invasive and aggressive forms of pulmonary aspergillosis or a chronic necrotizing form (19).

Predisposing conditions

The most common preceding lung lesion is an open healed TB cavity. The incidence of cavitatory TB being affected by aspergilloma formation is 11-17% (3,20). Other conditions include sarcoidosis, abscesses, cysts, bronchiectasis, cavitatory tumours and bullae (3,18,21,22).

Chen *et al.* (22) found that the interval between the diagnosis of TB and aspergilloma development varied from less than a year to up to 30 years. They quoted an average of 9.2 years to aspergilloma development.

It is also reported that aspergillomas may develop in healthy lungs, whereby the aspergilli fungi secrete a digestive enzyme in the surrounding lung to create a space for its colonisation (2,23).

Aspergilli can proliferate and easily colonize a cavity as phagocytosis is hindered in cavities found in the lung.

Clinical course of aspergillomas

The natural history has been poorly studied. Moreover, the underlying disease process may confound the natural history of an aspergilloma (21,24,25). There is no consistent variable that can predict the outcome of an aspergilloma (14,22).

Aspergillomas can be extremely variable in its course, ranging from undergoing spontaneous lysis (7-10%) to causing severe haemoptysis (22,26,27).

Up to 30% of patients with minor haemoptysis may go on to develop life-threatening haemoptysis (28).

It is also reported that the severity of haemoptysis is not related to the size, the number of aspergillomas nor to the underlying lung disease, erythrocyte sedimentation rate, eosinophil count or to the response to skin prick tests (29).

Jewkes *et al.* reported a recurrence of aspergillomas post-surgery to be in the region of 7% (29,30).

Symptomatology

This can be diverse ranging from patients being asymptomatic to experiencing life-threatening haemoptysis.

Many-a-times patients present with symptoms related to the
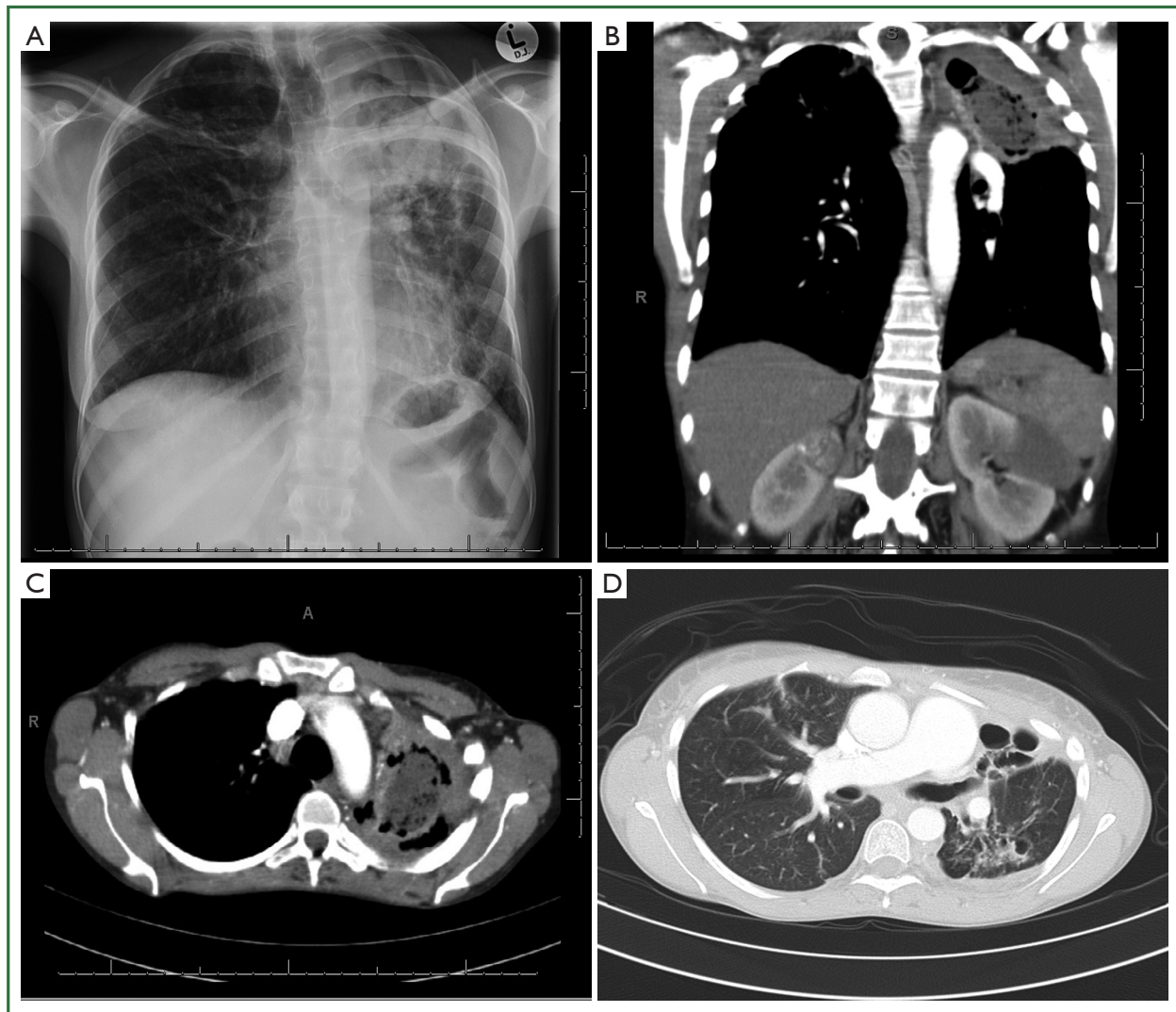
Figure 4. Radiology of a complex aspergilloma. (A) PA chest x-ray showing a complex aspergilloma in the left upper lobe; (B) Coronal CT scan of the complex aspergilloma; (C) Axial CT picture of the complex aspergilloma; (D) CT scan of the same patient showing the diffuse bronchectasis and cavitation involving the lingula and superior segment of the left lower lobe.

underlying diseased lung.

Most patients present with a productive cough containing either mucus, pus or blood (2). Dyspnoea is usually due to primary lung disease (3,31).

Most series report haemoptysis as being the most common symptom with an incidence of around 80% (21,32).

What causes haemoptysis?

The likelihood of massive haemoptysis in a patient with an aspergilloma is unpredictable, in part because of the lack of prospective data about the natural history of the condition.

The size, complexity of the aspergilloma or a sentinel bleed

cannot predict if patients will progress to massive haemoptysis (11).

Possibilities as to the cause of haemoptysis are (2,13,29,33):

(I)   Erosion (local invasion) of adjacent vessels;
(II)   Mechanical irritation of exposed vasculature in the cavity;
(III) The release of an endotoxin and trypsin like proteolytic enzyme from the fungus;
(IV)   Presumed acute superimposed bacterial infection.

Radiological signs

The radiological signs are variable and classically the mycetoma is surrounded by a crescent of air in the cavity, but this really depends on how large the aspergilloma is within the cavity. The

Table 1. Early surgical intervention irrespective of symptoms.

Proponents	Opponents
1. Risk of massive haemoptysis (up to 30%) if conservative approach is adopted	1. As symptoms are variable, it is better to offer surgery only if complications manifest
2. No identifiable variable predicting complications	2. Surgery very difficult and fraught with morbidities
3. Better to operate under elective conditions rather than emergent conditions when patients may be more clinically unstable	

walls of the cavity can be either thin or thick walled.

The radiological appearance of an aspergilloma forms a differential diagnosis of a "ball-in-a-hole" which also includes lung abscesses, cavitatory carcinomas, and ruptured hydatid cysts, to name a few.

When the cavity is much larger than the aspergilloma, it is seen to be mobile and it assumes different positions in the cavity depending on positional change of the patient. This change of position is gravity dependent.

Additional pleural and lung parenchymal changes dictate whether the aspergilloma is of a simple or complex type.

Treatment

The treatment for aspergillomas remains controversial and there is no consensus amongst the treating physicians. This is mainly because of the variability of the underlying lung disease process. The optimal treatment strategy is unknown.

Medical management

The medical management of aspergillomas has a complementary role and has been fairly disappointing, although there are still ongoing investigations into its role (11).

Anti-fungal agents, whether systemic or intra-cavitatory have showed no consistent success.

Likewise bronchial artery embolization appears to be a temporary measure and vascular collaterals tend to develop quite soon after embolization.

Surgical management

There is also no consensus regarding the timing of surgery and the type of surgery needed.

Many earlier reports showed a high mortality and morbidity rate (60%) (13,14,26,34-36) after surgical intervention for aspergilloma. This has obviously influenced the bias towards a more conservative and medical management of this condition.

Newer studies from the year 2000 onwards show much

more favourable results with surgical intervention. Akbari *et al.* showed an operative mortality of 3.3% and a 33.3% morbidity (13,37).

Park *et al.* reported a 0.9% operative mortality and 23.6% morbidity in their series of 110 patients (38).

Lee *et al.* (13) recommended surgery for all patients with an aspergilloma and having adequate pulmonary reserve, even if asymptomatic.

Since the current risk of surgery is less than the risk of a massive bleed, the scale seems to be tilting towards early surgical intervention on suitable candidates diagnosed with an aspergilloma. This however positions the role of surgical timing to be debatable (Table 1) (13,22,34,39).

The predicament arises in patients with unsuitable lung function precluding any pulmonary resection. In these cases, one has to carefully balance the risk benefit ratio and in this subset of patients, the more conservative operative procedures come to the fore. These surgical interventions are offered to prevent massive and disastrous haemoptysis from occurring.

Indications for surgical intervention

Assuming patients are functionally optimal for surgery:
- (I)   Symptomatic patients with aspergillomas;
- (II)   Indeterminate lesions with a high suspicion of lung malignancy;
- (III) Asymptomatic aspergilloma (still controversial).

Types of surgery

(I)   Wedge or segmentectomy.
  (II)   Anatomical resections—lobectomy or pneumonectomy.
  (III) Cavernostomy and thoracoplasty.

Wedge/segmentectomy (26)

Usually reserved for simple aspergilloma that is small and either peripheral (wedge) or lies locally within a segment (segmentectomy).

Video 1. Cavernostomy, removal of aspergilloma and thoracoplasty for an apical aspergilloma.

Since a simple aspergilloma is a relatively benign disease and if the whole aspergilloma can be removed by lesser resections, then lung conserving surgery can be undertaken.

Anatomical resection (lobectomy or pneumonectomy)

These operations are usually reserved for a large simple aspergilloma occupying almost the whole lobe or for complex aspergillomas. It is undesirable to leave diseased lung behind if the patient can functionally tolerate anatomical lung resection.

Sometimes the disease process may bridge the fissure and partly occupy the adjacent lobe. This may then require tailoring the lobectomy to include a wedge of the adjacent lobe.

The same principles are adhered to as for the resection of inflammatory diseased lung. The usual precautions when attending this pathology must be applied and respected. Most morbidities and mortalities of case series arise from operating upon complex aspergillomas and many surgeons have been humbled by complications. Some reasons for these complexities include: obliterated pleural space, very stuck hilum and mediastinal surface, increased collateral circulation and patients that are nutritionally disadvantaged.

Cavernostomy and limited thoracoplasty

This type of procedure is reserved for high risk patients with complex aspergillomas, namely patients who functionally would not be able to tolerate anatomical resection. Whether this operation can be extended to other patients, namely those with good lung functions and simple aspergillomas, is still contentious

and is in need of more evidence. At present anatomical resection remains the gold standard.

The goal of this operation is to remove the culprit lesion namely the aspergilloma, close off the communicating bronchioles, collapse down the cavity (via an apicolysis) and perform a limited thoracoplasty to obliterate the resultant space.

It must be stated that this operation is much less tedious than anatomical resections.

It is based on the assumption that the ongoing haemoptysis is most likely due to the aspergilloma and hence this procedure is concentrated only on removing the inciting lesion (aspergilloma) and leaving the rest of the diseased lung *in situ*.

The steps for an apical lung aspergilloma are:
(I)   Tailored high thoracotomy as for a thoracoplasty operation;
(II)   Pleural space entered and lung cut into, to open the cavity;
(III) Aspergilloma removed in total and cavity washed out;
(IV)   All bronchial communications sutured closed;
(V)   Apicolysis of cavity or lung to be able to collapse the cavity;
(VI)   Cavity sutured closed. One may introduce intercostal muscles into the cavity;
(VII) Tailored thoracoplasty to collapse the chest wall, and obliterate the resultant space left by the aspergilloma removal. During the thoracoplasty, the first rib may be left intact;
(VIII) Apical area drained with an intercostal drain;
(IX)   Wound closed in layers (Video 1).

This procedure is a modification of that reported by Daly *et al.* (40,41), wherein a myoplasty was done. Others have described atrophy of the muscles used, due to inactivity (42,43). Some authors have recommended a 2-stage procedure but we recommend it be done in a single setting (40).

A complementary thoracoplasty is advocated to obliterate the space resulting from collapsing of the cavity. This allows one to refrain from the arduous task of freeing the remainder of the lung in the hope that it will fill the space (3). A thoracoplasty may not be required if the aspergilloma is not located apically.

This operation has to be tailored according to size and location of the aspergilloma.

Surgical approach to different clinical scenarios (Figure 5)

If a symptomatic patient has bilateral disease, then it is advisable to perform a bronchoscopy to confirm the site of bleeding, before performing surgery.

If patients are deemed non-surgical candidates, even with the slightest of surgical interventions, then conservative medical treatment has to be adopted.
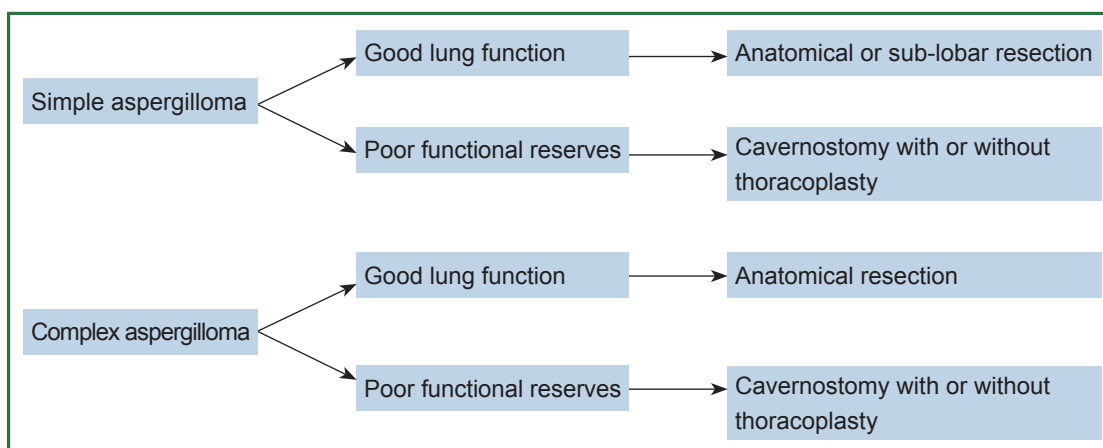
Figure 5. Simplified surgical approach to aspergillomas.

Surgical complications

Surgery for inflammatory lung disease is fraught with morbidity and mortality, hence the earlier, more dated opinion of being conservative with patients having aspergillomas.

Daly *et al.* (41) reported a mortality of 25% and morbidity (including excessive bleeding, residual pleural space, broncho-pleural fistulae and empyema) up to 60%.

Later reports are more favourable (13,28,44).

Summary

Aspergilloma is a result of a saprophytic infection of a diseased lung. The course and prognosis of this subset of patients cannot be predicted with certainty.

There are many surgical options, but one has to carefully choose and tailor the procedure according to the functional stability of the patient (28) (Figure 5).

Acknowledgements

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