

Pulmonary aspergilloma: from classification to management

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Abstract

Pulmonary aspergilloma is a form of aspergillosis characterized by the colonization of a preexisting pulmonary cavity, most often of tuberculosis origin. Clinical symptoms are predominately hemoptysis that can be life-threatening, and thoracic computed tomography can distinguish simple from complex pulmonary aspergilloma. The best therapeutic option remains surgery which allows surgical resection of the mycetoma and the underlying cavity. Nonsurgical treatment is performed in inoperable patients because of severe respiratory failure or a poor general condition.

Keywords

Aspergillosis, hemoptysis, lung diseases, fungal

Introduction

Pulmonary aspergilloma (PA) is the colonization and development of a fungal ball secondary to *Aspergillus fumigatus* in a preexisting pulmonary cavity, most commonly of tuberculosis origin.¹ According to Denning and colleagues,² PA represents the simple form of a group of diseases called chronic pulmonary aspergillosis (CPA). PA can be life-threatening by causing severe hemoptysis related to the formation of systemic and bronchial hypervascularization. Hypervascularization can be treated in the acute phase by an endobronchial technique with injection of several products (terlipressin, adrenaline), but this remains of insufficient efficiency. The best option in the acute phase of massive hemoptysis is endovascular treatment, especially bronchial artery embolization in the majority of cases (more than 90%) and vaso-occlusion of the pulmonary artery in less than 10% of cases.³ Surgery is the best therapeutic option for PA but it is associated with high morbidity and mortality rates due to severe pleural adhesions and infection in the underlying lung. There is general agreement that surgery is indicated in all symptomatic patients, while in patients without clinical manifestations, surgical intervention is not universally indicated.

Classification

Classification of Belcher and Plummer

Belcher and Plummer⁴ introduced a classification of PA into two subtypes: simple and complex, according to clinical and radiological criteria. This classification, described in 1960, is still used to decide on the treatment of PA, especially in the surgical literature. In simple PA, patients are clinically asymptomatic, in a good general condition, and have no respiratory function disorder or malnutrition. On imaging, there is a peripheral parenchymal cavity with thin edges, without lung fibrosis or pachypleuritis. In contrast, patients with complex PA are most commonly in poor general condition, malnourished, and usually present with serious hemoptysis, with or without bronchorrhea.^{5,6}

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On thoracic computed tomography (CT), it is characterized by single or multiple thick-edged excavations associated with perilesional pulmonary parenchymal fibrosis and pachypleuritis.

PA can be categorized into three groups: allergic bronchopulmonary aspergillosis, CPA, and invasive pulmonary aspergillosis.⁷ Allergic bronchopulmonary aspergillosis and invasive pulmonary aspergillosis have been excluded from this review because they respond to initial medical treatment. Concerning CPA, recent guidelines were published in December 2015 on behalf of the European Society for Clinical Microbiology and Infectious Diseases and the European Respiratory Society.² These societies have classified CPA into four forms. Chronic cavitary pulmonary aspergillosis, formerly called complex aspergilloma, is the most common form of CPA, and can progress if untreated to chronic fibrosing pulmonary aspergillosis. Chronic cavitary pulmonary aspergillosis is characterized by one or more pulmonary cavities, possibly containing regular or irregular intraluminal material, in association with pulmonary and systemic symptoms and raised inflammatory markers over a period of at least 3 months. Chronic fibrosing pulmonary aspergillosis, often the end result of untreated chronic cavitary pulmonary aspergillosis, is characterized by extensive fibrosis and destruction of at least two lobes, leading to a major loss of lung function. Serological or microbiological evidence implicating *Aspergillus* is required for diagnosis, and one or more aspergillomas may be present. Simple aspergilloma is a single pulmonary cavity containing a single fungal ball with serological or microbiological evidence implicating *Aspergillus* in a nonimmunocompromised patient, with minor or no symptoms and no radiological progression over at least 3 months of observation. *Aspergillus* nodule is a less common manifestation of CPA, characterized by one or more nodules (<3 cm), which may mimic other diseases (carcinoma of the lung, tuberculoma), without tissue invasion, and can only be diagnosed on histology. Subacute invasive aspergillosis, formerly called chronic necrotizing or semi-invasive pulmonary aspergillosis, occurs over 1 to 3 months in a mildly immunocompromised patient, with variable radiological features (cavitation, nodules). In this review, by PA we mean all aspergillosis lung diseases that respond initially to surgical management and not to medical treatment.

Epidemiology and predisposing factors

PA can develop at any age but most often in elderly subjects, probably because of the aging of patients with post-tuberculosis lung lesions. Most commonly, authors report a median age ranging between 34 and

65 years.⁸⁻¹⁰ PA can affect both sexes, but many authors have reported a male predominance.⁸⁻¹² Development of PA is most often in underlying lung lesions where local immunodeficiency is found. Parenchymal sequelae and cavities secondary to tuberculosis are the most frequent predisposing lung factors driving the colonization by *Aspergillus*, especially in countries where tuberculosis is an endemic disease.¹¹ The average delay between tuberculosis and the occurrence of PA varies in different series from 9 to 14 years.¹² Other common predisposing lung lesions are bronchiectasis, emphysematous bullae, sarcoidosis, evacuated lung abscess, necrotic lung cancer, pulmonary fibrosis, a pulmonary cavity after radiotherapy, and a post-traumatic cavity.^{11,13,14} However, a pre-existing cavity is not mandatory because *Aspergillus* causes enzymatic secretions that lead to destruction of the lung parenchyma, particularly if it is weakened by anterior radiotherapy or semi-invasive aspergillosis.^{15,16}

Clinical diagnosis

Clinical suspicion is based on a history of tuberculosis or one of the aforementioned predisposing lung diseases. PA can remain asymptomatic for several years. Hemoptysis is the most frequent symptom reported in most series,^{8,9,11} and may be simple recurrent hemoptoic sputum or life-threatening hemoptysis. Hemoptysis is the result of erosion of adjacent vessels secondary to systemic hypervascularization, leading to hypertrophied bronchial arteries and neovascularization through the parietal arteries. There is no parallel between the abundance of hemoptysis and the size of PA or the condition of the underlying lung, and hemoptysis is an important sign taken into account in the decision for surgery. Chest pain is caused by peripheral PA which comes into contact with the pleura. Bronchorrhea and dyspnea are observed mainly in patients with PA associated with destroyed lung. In this setting, a poor general condition and fever can be also present. Fortuitous discovery of PA is possible during routine thoracic imaging, or in the setting of follow-up of pulmonary tuberculosis, or after an anatomopathological study of a surgical specimen. Physical examination is generally unhelpful in PA.

Paraclinical diagnosis

Chest radiography and thoracic computed tomography

The different phases of development of PA in a pre-existing cavity are responsible for different radiological appearances.¹⁷ Initially, PA can manifest on thoracic

imaging as a simple cavity or an excavated lesion with thick walls. Later, when the fungus ball develops in the cavity, it manifest with the typical appearance of PA: opacity surmounted by an air crescent. This appearance can also be seen in necrotic lung cancer, hydatid cyst, or even a foreign body in the lung.¹⁸ When the fungus ball fills the entire cavity, imaging findings are either a pulmonary nodule or a parenchymal mass, depending on the size of the lung cavity. Thoracic CT in the lateral decubitus position can be helpful when the diagnosis is in doubt, by demonstrating mobilization of the fungus ball. Thoracic CT also allows differentiating between simple and complex PA by identifying the condition of the cavity walls, presence or absence of pachypleuritis, and the condition of the surrounding pulmonary parenchyma. For inoperable pulmonary aspergillomas, thoracic CT can plan percutaneous treatment by injection of antifungal products,¹⁹ or allow percutaneous biopsy of the lung lesion when the diagnosis is not yet established. Lastly, it is important to remember that PA is more often found in the upper lobes of the lung and upper segments of the lower lobes where tuberculosis is more likely to develop.

Fiberoptic bronchoscopy

Fiberoptic bronchoscopy can aid in the diagnosis of PA. Direct visualization of the fungus ball on fiberoptic bronchoscopy was reported for the first time in 1987 by Smith and colleagues.²⁰ In addition, fiberoptic bronchoscopy allows a bronchoalveolar lavage to look for *Aspergillus* or *Mycobacterium tuberculosis* in a microbiological study. Fiberoptic bronchoscopy can permit a biopsy of the bronchial tree in case of doubt in the diagnosis, and can also identify the origin of bleeding in cases of hemoptysis, especially in the setting of bilateral hemoptysis, and stop active bleeding by instilling hemostatic agents.²¹

Antibody diagnosis

The use of anti-aspergillus antibodies in diagnosis and the type of antibody that must be chosen depend on the clinical form of PA. According to Denning and colleagues,² all patients having chronic or subacute invasive aspergillosis should be tested for *Aspergillus fumigatus* immunoglobulin G antibody or precipitins. In our setting, this is not routinely carried out.

Surgical treatment

Surgery for PA remains the best therapeutic option despite high rates of mortality and morbidity. Surgery allows eradication concurrently of the fungus ball,

underlying cavity, and surrounding unhealthy parenchyma. The goals of surgery are to avoid a life-threatening hemoptysis and the development of an invasive clinical form, pulmonary fibrosis, or renal amyloidosis due to chronic inflammation.²¹

Before deciding the surgical procedure, it is mandatory to assess whether the patient is operable or not and to anticipate various postoperative complications by evaluation of respiratory function and comorbidities. Respiratory function is assessed by measuring the forced expiratory volume in 1 s and diffusion capacity for carbon monoxide. A value lower than 80% of at least one of these parameters leads to the next stage of the assessment for lung parenchyma resection, established by the patient's exercise capacity (peak oxygen consumption).²² The predicted postoperative value of forced expiratory volume in 1 s can be calculated by knowledge of the number of resected lung segments on thoracic CT.²³ Other tests may be required for underlying comorbidities.

To reduce postoperative complications, anemia secondary to recurrent hemoptysis may require a preoperative blood transfusion, and infection is managed with antibiotics. Smoking cessation contributes to a reduction of respiratory complications (atelectasis, pneumonia).²⁴ The patient must be prepared for surgery by explaining the surgical procedure, the various complications after the intervention, and beneficial respiratory physiotherapy. Surgery for PA is associated with hemorrhagic complications due to severe pleural adhesions and calcified lymph nodes that make dissection of bronchial and vascular elements challenging. To protect the healthy lung against spillage of secretions, the anesthetic procedure should be performed with a double-lumen endotracheal tube.

Approaches

A posterolateral thoracotomy is the usual approach in open surgery, allowing direct visualization of the lesions, manual palpation of the lung parenchyma, and quick control of vessels in case of massive bleeding.⁹ Extrapleural dissection is mandatory to ensure pleuropulmonary release and avoid opening of the lesions in the pleural cavity.¹¹ It must be taken into account that muscles involved in the thoracotomy (especially latissimus dorsi and serratus anterior muscles) can be useful for a subsequent transposition muscle flap in the case of bronchopleural fistula or empyema, and these muscles should be preserved.⁸ The main drawback of a posterolateral thoracotomy is the intense postoperative pain that can lead to complications such as atelectasis and pneumonia. The pain is more severe if rib resection is performed because of retraction of the intercostal spaces.

Video-assisted thoracic surgery (VATS) has undergone a significant evolution and has now been extended to technically challenging procedures. This technique is mainly dedicated to localized PA, with no severe pulmonary or pleural scarring, a healthy surrounding lung parenchyma, and the absence of lymph nodes near vessels.²⁵ VATS can also be carried out for complex PA in selected patients with a low risk of complications. Some authors advocate VATS because it offers several advantages to patients by decreasing postoperative complications, reducing chest pain, allowing rapid recovery, and ensuring a short hospital stay.²⁵⁻²⁷ Disadvantages are mainly the non-palpation of the lung parenchyma and the risk of conversion to a thoracotomy.

Surgical procedures

The ideal surgical treatment consists of an anatomical lung resection that allows excision of the mycetoma and underlying cavity associated with unhealthy lung parenchyma. The choice of surgical procedure is balanced between complete resection of the lesion to avoid recurrence and preservation of a maximum amount of lung parenchyma. Lobectomy is performed most frequently according to several series.^{11,28,29} Pneumonectomy is associated with high rates of mortality and morbidity and must be carried out only in selected patients such as those with PA associated with destroyed lung, or for urgent hemostasis. Sublobar resection can be performed for simple PA and in selected patients with complex PA, with no difference in long-term outcomes.²⁹ Other minor surgical techniques have been reported in the literature, such as speleostomy which consists of a simple procedure allowing a permanent aperture between the cavity and the skin, but this is poorly accepted by patients. Also, excision of the fungal ball can be carried out in very complex PA to the apical region because of difficulties in release of the adhesions. After surgery, antifungal treatment is indicated especially when there is excess opening of lesions in the pleural space, to decrease the risk of contamination.

Nonsurgical treatment

When surgery is not indicated because of poor respiratory reserve or other comorbidities, medical treatment (by intravenous injection or direct injection into the PA guided by percutaneous CT or endobronchial injection) or bronchoscopic removal can be proposed as therapeutic alternatives. Antifungal treatment has not shown effectiveness because of the avascular character of PA, and currently, no randomized trial has been performed in this setting.²⁸ Probably, this treatment (most commonly voriconazole or itraconazole) is used in patients who cannot benefit from a surgical

procedure to minimize clinical symptoms. Also, techniques of intracavitary instillation of antifungal agents have been proposed, including percutaneous CT that was firstly described by Krakówka and colleagues³⁰ and has become more popular due to the wide use of CT. The fungal ball is destroyed and the risk of hemoptysis and infection is reduced with a rate of recurrence estimated at 20%. The rate of complications is less in peripheral lesions, and mainly consist of pneumothorax, subcutaneous emphysema, and hemoptysis.³¹ However, these techniques have been reported in retrospective studies with a small number of patients, making it difficult to conclude recommendations.³²

Bronchoscopic removal of PA has been described in cases of a pulmonary cavity with development of fungal ball, and the goal is eradication of the fungal ball. This procedure is preferably started by virtual bronchoscopy reconstruction and ultrathin bronchoscopy to identify airways leading into the pulmonary cavity.³² Endobronchial removal of PA is performed under general anesthesia with a double-lumen endotracheal tube (to prevent spillage into the contralateral lung), with flexible or rigid bronchoscopy, with or without antifungal therapy.^{33,34}

Discussion

PA remains quite frequent in our country because of endemic tuberculosis. The diagnosis is based mainly on the presence of already treated tuberculosis, hemoptysis that constitutes the most commonly reported symptom, and radiological manifestations. The volume of hemoptysis must be assessed, and in urgent cases, bronchial artery embolization should be performed in the acute phase; it is appropriate and a minimally invasive technique to allow hemostasis. Surgery is the best option beyond the acute phase of massive hemoptysis that must be treated especially by bronchial artery embolization. A posterolateral thoracotomy is the standard approach because of severe pleural adhesion and calcified lymph nodes. A few recent articles have highlighted the benefit of VATS in simple PA. Lobectomy is the main surgical procedure, and segmentectomy or wedge resection can be performed in small peripheral simple PA. Bleeding is the most frequent complication after surgery for PA. Antifungal treatment is indicated in non-operated patients, or when there is contamination of the pleural space during surgery on opening the lesion.

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