Chronic pulmonary aspergillosis - longterm follow-up over 20 years, a case report

Henry Marshall¹, Simon Jones², Alan Williams³

1. Department of Thoracic Medicine, The Prince Charles Hospital, Brisbane, Australia
2. Department of Radiology, The Royal Bournemouth Hospital, Bournemouth, United Kingdom
3. Department of Thoracic Medicine, The Royal Bournemouth Hospital, Bournemouth, United Kingdom

* Correspondence: Dr. Henry Marshall, Department of Thoracic Medicine, The Prince Charles Hospital, Brisbane, Queensland, Australia (Henry.Marshall@health.qld.gov.au)

ABSTRACT

We describe a case of chronic pulmonary aspergillosis complicated with a slowly growing aspergilloma followed for two decades without specific intervention. It developed with no background of local or systemic immune dysfunction in a middle aged female. The case illustrates many features of this disease as well as uniquely documenting the natural radiological evolution from a small non-specific cystic lesion to a massive aspergilloma. The aspergilloma subsequently autolysed and the patient's condition changed to an allergic phenotype with development of widespread bronchiectasis and pulmonary fibrosis. We briefly discuss the range of disease aspergillus can cause in humans, its differential diagnosis and treatments.

CASE REPORT

A 65 year old lady presented with nine months lassitude, intermittent night sweats and mild chest discomfort without cough or haemoptysis. She was an ex-smoker with 15 pack-years history, normal spirometry (FEV1 103 % predicted, FVC 94 % predicted, FEV1/FVC ratio 88%) and no past medical history except for hypertension. Physical examination was normal; body mass index (BMI) was 26 kg/m2. A Chest radiograph showed patchy airspace shadowing in the left mid-zone (Figure 1)

Linear tomography demonstrated a cystic lesion (Figure 2). Bronchoscopic washings failed to grow fungi, acid-fast bacilli or show any features to suggest malignancy.

Over the next eighteen months the lesion remained stable. A non-contrast computed tomogram (CT) of the chest (10/10mm axial sections to carina followed by 10/15mm sections to base) revealed a normal mediastinum and a single small calcified left hilar lymph node. The apical left lower lobe segment contained an area of consolidation contiguous with the left descending pulmonary artery and extending to the pleural surface. The rest of the lung parenchyma was normal (Figure 3). The lesion gradually increased in size over the subsequent years (Figure 4). She suffered intermittent haemoptysis in relation to intercurrent lower respiratory tract infections. She lost weight. At five years a CT scan (non-contrast, 10/10mm axial sections) found the lesion was now an ill-defined, lobulated soft tissue mass extending from the left pulmonary artery to the pleural surface (Figure 5).

The lesion continued to grow slowly. Intermittent symptoms continued as before. Repeat CT at nine years showed the mass to be far more complex with multiple cavities and flecks of calcium (Figure 6). It had grown to 50mm maximum diameter and was in contact with the pleura. The air
crescent sign was positive; multiple aspergillomata were diagnosed. Aspergillus precipitins were strongly positive.

Over the next two years the aspergillomata coalesced into a single large fungus ball (Figure 7) reaching a maximum width of 130mm on the chest radiograph (Figure 8). During this time (thirteen years after presentation) she suffered a spontaneous left sided pneumothorax which resolved with intercostal drainage (Figure 9 and Figure 10). A few months after this episode the aspergilloma started to spontaneously lyse, a fluid level becoming apparent (Figure 11).

Four months after the start of lysis the patient developed wheeze; a new symptom. She responded well to oral prednisone 20mg daily which was continued for six months. After a total of seven months the aspergilloma had completely lysed, leaving a large fluid-filled cavity (Figure 12). CT in 2005 (multi slice noncontrast protocol with both supine and prone imaging) showed extensive bilateral fibrosis and traction bronchiectasis (Figure 13). Aspergillus precipitins were now negative but aspergillus-specific IgE remained elevated at 189 kU/L. Spirometry showed FEV1 61% predicted; FVC 57% predicted and FEV1/FVC ratio 87%. BMI was stable at 17 kg/m2. A small amount of fluid remained in the cavity (Figure 14, Figure 15).

The patient died of unrelated causes in 2008, 20 years after her initial presentation.

**DISCUSSION**

**The spectrum of Aspergillus disease**

Over one hundred species of the ubiquitous saprophytic mould genus aspergillus have been characterized. The bulk of human disease is caused by A. fumigatus, A. flavus, A. terreus and A. niger. The most common organ affected by the airborne spores is the lung. The spectrum of disease depends on host factors, such as underlying local (eg COPD) or systemic disease (eg diabetes, steroid use, alcohol excess), and the host immune response. Up to 20% of cases have reportedly normal lungs (1). Pulmonary manifestations range from allergic bronchopulmonary aspergillosis (ABPA) and hypersensitivity pneumonitis (HP) with a hyperimmune host response through to aspergilloma, chronic necrotizing pulmonary aspergillosis (CNPA) and invasive aspergillosis (IA) with a normal, attenuated or deficient host immune response respectively.

**Chronic pulmonary aspergillosis**

Chronic pulmonary aspergillosis (CPA) is rare and has only been reported as isolated cases or small series thus a true incidence cannot be ascertained. CPA has also been known as 'chronic necrotizing pulmonary aspergillosis', 'semi-invasive aspergillosis' or 'chronic cavitatory aspergillosis' and was highlighted by Gefter et al and Binder et al in the 1980s although they were not the first to describe it (2, 3).

Typically the patient presents with more than one symptom - the most common being constitutional (weight loss, malaise) or organ specific (productive cough, haemoptysis, chest pain).

Initial radiographic features are that of a slowly enlarging, generally apical, ill-defined infiltrate. Over time this may form one or several cavities with thin or thickened walls. Fungal ball(s) occur in 50% of cases. Cavity expansion occurs over months to years. Pleural thickening can be an associated finding. Mild immunosuppression or underlying lung disease is often, but not always, present.

Early radiological findings are non-specific which can result in delayed diagnosis. The features may mimic mycobacterial infection, histoplasmosis, coccidioidomycosis, bacterial abscess, wegener's granulomatosis or neoplasm. Diagnosis can be made on histopathological and/ or clinical grounds but also requires the exclusion of other potential diagnoses.

In one of the larger case series to date (n=18) Denning (4) proposed a subclassification of chronic pulmonary aspergillosis into three forms:
1. Subacute invasive/chronic necrotizing pulmonary aspergillosis, (subacute IPA/CNPA), characterized by the evolution of a single thin-walled cavity and fungus ball over weeks to months often on the background of mild immune compromise
2. Chronic cavitatory pulmonary aspergillosis, (CCPA), often on the background of chronic obstructive pulmonary disease, characterized by slowly-growing, multiple cavities with surrounding inflammation, the cavities may coalesce and may or may not contain fungal balls
3. Chronic fibrosing pulmonary aspergillosis, (CPF), the potential final outcome of untreated CCPA with a unilateral or lobar pulmonary fibrosis.

In contrast, simple aspergilloma is a non-progressive colonization of a pre-existing cavity. Radiological progress over time is thus helpful in distinguishing CCPA from simple aspergilloma.

Microbiological culture of aspergillus is not specific or sensitive: only 50% of patients grow aspergillus from sputum or bronchoalveolar lavage. In other clinical contexts positive cultures may simply reflect colonization.

Serological tests are helpful: the majority of patients are positive for aspergillus precipitins (IgG antibody) although the titre may vary over time. Two-thirds of patients also have a raised aspergillus-specific IgE or positive skin-prick test. After surgical resection the IgG levels become undetectable. Inflammatory markers are raised (5).

Denning et al proposed the following diagnostic criteria for enrolment into clinical trials demonstrated in table 1 (4).

Histopathological specimens of CNPA generally show a chronic granulomatous process with fungal hyphae. Other features such as necrotizing pneumonia, bronchiectatic cavities
Chronic pulmonary aspergillosis (CPA) is a difficult diagnosis to make, mimicking other more common disease, often leading to diagnostic delay. Proposed diagnostic criteria require the correlation of clinical, radiological and microbiological results. Treatment with oral antifungals is a long term requirement and produces disease stability or improvement in most cases. Surgical resection can be considered in selected cases.

**REFERENCES**


**FIGURES**

**Figure 1.** 65 year old female with the early stages of chronic pulmonary aspergillosis. May 1989. Presenting plain chest radiograph showing an area of consolidation within the apical segment of the left lower lobe.

**Figure 2 (left).** 65 year old female with the early stages of chronic pulmonary aspergillosis. June 1989. Linear tomogram of chest showing a complex, cystic lesion in the apical segment of left lower lobe.

**Figure 3.** 66 year old female with chronic pulmonary aspergillosis. October 1990 Computed tomogram of thorax showing early cavitation and adjacent inflammatory reaction in the apical segment left lower lobe. The surrounding lung parenchyma appears normal.

**Figure 4 (top).** 71 year old female with chronic pulmonary aspergillosis. Plain chest radiograph November 1995. The slowly growing lesion is apparent in the apical segment of the left lower lobe.

**Figure 4 (bottom).** 71 year old female with chronic pulmonary aspergillosis. Plain chest radiograph November 1995. The slowly growing lesion is apparent in the apical segment of the left lower lobe.
Thoracic Radiology: Chronic pulmonary aspergillosis - longterm follow-up over 20 years, a case report

Figure 5. 70 year old female with chronic pulmonary aspergillosis. Computed tomogram of thorax on lung windows. November 1994. Within the left lower lobe, contiguous with the left descending pulmonary artery and extending out to the pleural surface is an ill-defined, lobulated soft tissue mass representing multiple small aspergillomata. This lesion had gradually increased in size over the previous five years.

Figure 6. 75 year old female with chronic pulmonary aspergillosis. Computed tomogram of thorax performed in the prone position on lung windows. Within the apical segment of the left lower lobe there is a complex lobular soft tissue mass of mixed density. This extends from the origin of the left lower lobe bronchus to contact the pleura laterally and measures approximately 5cm in diameter. Several flecks of calcification are noted. The mass contains air density (air-crescent sign) but no fluid level. No mediastinal mass or adenopathy is noted. Adjacent inflammatory changes extend to the pleura. Although the mass contacts the chest wall, there is no sign of chest wall abnormality.

Figure 7. 76 year old female with chronic pulmonary aspergillosis. Plain chest radiograph September 2000 showing a large aspergilloma within a left lower lobe cavity and a smaller aspergilloma medial to this.

Figure 8. 78 year old female with chronic pulmonary aspergillosis. Plain chest radiograph October 2002. The aspergilloma within its cavity demonstrating the air-crescent sign.
Thoracic Radiology: Chronic pulmonary aspergillosis - longterm follow-up over 20 years, a case report

Figure 9. 78 year old female with chronic pulmonary aspergillosis. Plain chest radiograph April 2002 demonstrating spontaneous left pneumothorax. Note smaller air-fluid levels medial to main cavity probably representing lysis of the smaller aspergilloma.

Figure 10. 78 year old female with chronic pulmonary aspergillosis. Plain chest radiograph April 2002 (taken 4 days after figure 9). Left-sided chest drain in situ. Partial re-expansion of lung is seen with small rim of pneumothorax still present. Incidental subcutaneous emphysema is seen around left axilla.

Figure 11. 79 year old female with chronic pulmonary aspergillosis. Plain Chest radiograph November 2003 showing air-fluid level within the large left lower lobe cavity. The large aspergilloma has reduced in size and the smaller medial aspergilloma is no longer apparent. Note reticular-nodular changes in the lung fields and volume loss in the right hemithorax.

Figure 12. 80 year old female with chronic pulmonary aspergillosis. Plain chest radiograph June 2004 after complete lysis of aspergilloma. Increasing fibrotic changes are seen in both lungs. The large cavity, with an air-fluid level, is seen at the left base.
Figure 13. 80 year old female with chronic pulmonary aspergillosis. Multislice non-contrast computed tomogram of thorax September 2005 showing left lower lobe cavity and background fibrotic and bronchiectatic changes. The thick-walled cavity measures approximately 12cm in maximum AP dimension. A few flecks of calcification are present in the wall posteriorly.

Figure 14. 82 year old female with chronic pulmonary aspergillosis. Plain chest radiograph February 2006. The large cavity with an air-fluid level persists at the left base. Extensive bilateral fibrotic changes are seen.

Figure 15. 82 year old female with end-stage chronic pulmonary aspergillosis. HRCT chest December 2006. Both lungs show marked fibrosis with widespread bibasal honeycombing and bronchiectasis which has progressed since the previous scan in Sept 2005. There is extensive volume loss in the right hemithorax. There is a large thick-walled cavity in the left lower lobe. A 2.7cm diameter area of soft tissue density lies anterior to the cavity. This may represent dependent debris within a cyst or bronchiectatic airway, or possibly a small 'daughter' aspergilloma. There is patch of pleural calcification in the left chest wall. Multiple small volume nodes are seen in the mediastinum.

ABBREVIATIONS

FEV1 = Forced expiratory volume in 1 second
FVC = Forced vital capacity
BMI = Body mass Index
CT = computed tomography/ tomogram
COPD = chronic obstructive pulmonary disease
ABPA = allergic bronchopulmonary aspergillosis
HP = hypersensitivity pneumonitis
IA = invasive aspergillosis
CNPA = chronic necrotizing pulmonary aspergillosis
CPA = Chronic pulmonary aspergillosis
CCPA = Chronic cavitatory pulmonary aspergillosis
CFPA = Chronic fibrosing pulmonary aspergillosis
IgE/G = immunoglobulin class E/G

KEYWORDS
Aspergillosis, chronic lung disease, aspergilloma, pneumothorax, adult, pulmonary, computed tomography
### Proposed enrolment criteria for prospective clinical studies of chronic pulmonary aspergillosis (CPA).

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Chronic pulmonary or systemic symptoms (duration 3 months) compatible with CPA, including at least 1 of the following symptoms: weight loss, productive cough, or haemoptysis</td>
</tr>
<tr>
<td>2</td>
<td>Cavitary pulmonary lesion with evidence of paracavitary infiltrates, new cavity formation, or expansion of cavity size over time</td>
</tr>
<tr>
<td>3</td>
<td>Either positive serum <em>Aspergillus</em> precipitins or isolation of <em>Aspergillus</em> spp. from pulmonary or pleural cavity</td>
</tr>
<tr>
<td>4</td>
<td>Elevated levels of inflammatory markers (C-reactive protein, plasma viscosity, or erythrocyte sedimentation rate)</td>
</tr>
<tr>
<td>5</td>
<td>Exclusion of other pulmonary pathogens that are associated with similar disease presentation, including mycobacteria and endemic fungi (especially <em>Coccidioides immitis</em> and <em>Histoplasma capsulatum</em>)</td>
</tr>
<tr>
<td>6</td>
<td>No overt immunocompromising conditions (e.g., HIV infection, leukaemia, chronic granulomatous disease)</td>
</tr>
</tbody>
</table>

**NOTE.** All criteria must be met to be enrolled; for criterion 3, one or the other condition must be met.

### Table 1:
Proposed enrolment criteria for prospective clinical studies of chronic pulmonary aspergillosis by Denning et al (4).

---

**Online access**

This publication is online available at:


**Interactivity**

This publication is available as an interactive article with scroll, window/level, magnify and more features. Available online at www.RadiologyCases.com

Published by EduRad

www.EduRad.org