Allergic Bronchopulmonary Aspergillosis and Aspergilloma*

Long-term Follow-up without Enlargement of a Large Multiloculated Cavity

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A 47-year-old man with a history of mild asthma presented with hemoptysis attributed to a large multiloculated cavity mycetoma. Peripheral blood eosinophilia of 43 percent led to the diagnosis of allergic bronchopulmonary aspergillosis (ABPA). Treatment of ABPA with prednisone led to resolution of an upper lobe infiltrate and a dramatic reduction in the total serum IgE level. Evaluation over a two-year period did not demonstrate enlargement of the cavity or disseminated aspergillosis.

Pulmonary mycetomas are considered to result from saprophytic growth of mycelia within pre-existing cavities. Histologically, the cavities contain masses of tangled mycelia, fibrin, and cellular debris, but there is no tissue necrosis or invasion of blood vessels. The emergence of pulmonary aspergillosis in patients with allergic bronchopulmonary aspergillosis (ABPA) is infrequent. Safirstein et al. did not identify any patients with a mycetoma in a five-year retrospective review of 50 patients with ABPA. However, they did report separately one patient with ABPA who developed a mycetoma. Of 111 patients with ABPA evaluated by McCarthy et al., mycetomas were present in seven patients. Information regarding natural history or effect of therapy for ABPA on the status of the mycetoma were not reported. We describe a patient with a long history of asthma who presented with hemoptysis and was found to have a large multiloculated mycetoma. The presence of peripheral blood eosinophilia led to the diagnosis of ABPA. Follow-up information over a two-year period is presented and suggests that corticosteroid therapy necessary for ABPA did not lead to enlargement of the cavity or disseminated aspergillosis.

CASE REPORT

A 47-year-old black man was admitted to the University of Chicago Hospital in April, 1981 because of six weeks of hemoptysis. The patient had smoked 50 pack-years of cigarettes until stopping in September, 1980. He had been employed in a foundry for the past three years cleaning mold and sand casts. Other occupations included maintenance and utility work for residences. For seven months prior to admission, he had produced approximately ¼ cup of yellow to brown sputum daily. He described malaise and a 15-pound weight loss during this time. Since childhood, he had experienced episodes of wheezing dyspnea that in adulthood were treated with theophylline 130 mg, ephedrine 25 mg, phenobarbital 8 mg (Teldral). Although occasionally he required epinephrine injections for attacks of asthma, corticosteroids were never administered. He had seasonal allergic rhinitis and asthma from June through October and noted dyspnea when exposed to cats, house dust, damp areas, and smoke-filled rooms.

The patient denied episodes of pneumonia or chest radiographic abnormalities. There was no history of tuberculosis or known exposures. Five siblings and his mother had asthma.

Physical examination revealed a thin black man in no acute distress. Vital signs were normal. Nasal mucosa were erythematous and without polyps. The chest examination revealed normal diaphragmatic excursion, percussion hyperresonance and bilateral expiratory rhonchi. Cardiac examination demonstrated a non-displaced apical impulse, physiologic splitting of S2, S4 gallop, and a grade 1/4 ejection murmur at the left sternal border. There was no cyanosis or clubbing of digits. Chest radiograph (Fig 1) demonstrated a large multiloculated cavity in the superior segment of the right upper lobe with an ovoid density at the inferior margin of the cavity. Infiltrates radiating from the right hilum to the cavity and in the left upper lobe were present along with ring shadows. The cavity mass changed position on lateral decubitus films. Sputum examination revealed no eosinophils or hyphae, but fungal cultures yielded growth of Aspergillus flavus and Aspergillus glaucus. Stains and cultures for mycobacteria were negative as was purified protein derivative skin test. Total white blood cell count in peripheral blood was 11,900 with 43 percent eosinophils. Pulmonary function measurements included vital capacity, 2.77 L (68 percent predicted);
FEV₁, 0.83 L (27 per cent); and MMF, 0.20 L/sec (6 per cent) without
significant bronchodilator response. FBC by plethysmography was
5.85 L (185 per cent); RV, 2.70 L (153 per cent); and DCO, 13.3
mL/min/mm Hg (49 per cent). Immunoglobulin concentrations (IgA,
IgM, IgG) were within normal limits. Total serum IgE was elevated
dramatically at 28,730 ng/ml (normal mean 300 ng/ml).

Skin testing for immediate cutaneous reactivity demonstrated
wheals and flares to giant and short ragweed, Penicillium, cat, dog,
dust, Dematiaceae and Aspergillus by prick test (antigens 1:10 or 1:20
weight/volume, Hollister Stier, Spokane, Washington). Serum IgE
and IgG antibodies to Aspergillus fumigatus were elevated compared
with asthmatic subjects who were prick skin-test-positive to
Aspergillus, but who did not have other evidence for allergic
bronchopulmonary aspergillosis (ABPA). Precipitating antibody was
present to Aspergillus fumigatus.

The patient was considered to have sufficient criteria for a
diagnosis of ABPA in that he had: 1) asthma; 2) proximal bronchiec-
tasis; 3) peripheral blood eosinophilia; 4) elevated serum IgE; 5)
precipitating antibodies to Aspergillus fumigatus; 6) immediate cutane-
ous reactivity to Aspergillus; and 7) elevated serum IgE and IgG
antibodies to Aspergillus fumigatus. The total serum IgE of 28,730
ng/ml at the time of diagnosis decreased to 15,875 ng/ml after two
weeks of therapy with prednisone. Within three months, the IgE
was 8,622 ng/ml. Use of corticosteroids was tapered and discon-
tinued. Serial measurements of IgE over the next 18 months ranged
from 3,150 to 4,875 ng/ml. Episodes of dyspnea were reduced greatly
with corticosteroids, but irreversible obstruction of flow rates
remained. Chest radiographs in March, 1983 (Fig 2) demonstrated
clearing of the left upper lobe infiltrate and persistence of the
depicted right upper lobe cavity.

DISCUSSION

Aspergillus-associated pulmonary diseases consist of IgE-
mediated asthma, ABPA, aspergilloma (fungus ball), invasive
aspergillosis, hypersensitivity pneumonitis, and chronic
necrotizing pneumonia. Our patient met criteria for ABPA,
although we are unaware of a past history of transient
pulmonary infiltrates. Although an aspergilloma can develop
in bronchiectatic lung in patients with ABPA, in a five-year
follow-up of 50 patients with ABPA wherein 926 radiographs
were reviewed, no mycetoma was identified. Safirstein et al
described a separate patient with ABPA who developed a
mycetoma. Treatment consisted of intracavity instillation of
pinimaricin, an antifungal agent. Some reduction in the size of
the cavity occurred, but apparently new ABPA infiltrates
were noted on two subsequent occasions.

Ein et al reported two patients with a history of tuber-
culosus who had nearly simultaneous onset of a mycetoma
and an ABPA-like illness. Neither patient had a history of
asthma or allergic diseases and long-term followup after
initiation of corticosteroid therapy is not described. Other
reports have emphasized dissemination of aspergillosis in
three patients with ABPA and mycetoma with the possibil-
ity that systemic and/or aerosolized corticosteroids contrib-
uted to the dissemination.

Our patient is the first described with ABPA and asper-
gilloma who was followed-up for two years after initiation
of corticosteroid treatment. Neither increase in size of the large
multiloculated mycetoma nor disseminated aspergillosis oc-
curred in spite of this patient's irreversible obstructive
pulmonary disease and corticosteroid ingestion. The dra-
matic fall in total serum IgE with corticosteroid therapy is
consistent with the diagnosis of ABPA. We are uncertain
whether ABPA preceded the onset of aspergilloma, but in
view of his long history of asthma, this seems likely as
opposed to the patients described by Ein et al who had
simultaneous onset of ABPA and aspergilloma. In those
patients, mycetoma was felt to be secondary to old tuber-
culosus cavities. A remotely possible explanation for the
cavitary lesion in this patient might be undiagnosed old
sarcoidosis, but extensive fibrosis in other lung fields was
not present on chest radiographs. An occupationally induced
disease causing cavitation seems unlikely unless his many
years of maintenance (janitorial) activities in moldy base-
ments could have led to insidious lung damage from ABPA.

The presence of Aspergillus glaucus and Aspergillus flavus
is interesting. We do not have results of mycetoma culture, as
needle aspiration was not considered essential. These fungi
could have colonized the mycetoma or damaged the bronchi.
The possibility that these species caused ABPA cannot be
excluded.

The optimal therapy for management of pulmonary asper-
gilloma remains controversial, although nonsurgical treat-
ment or no specific therapy may be indicated in the absence
of exsanguinating hemoptysis. Our patient did not have
significant further hemoptysis once corticosteroid therapy
was initiated for ABPA. Because of the few patients described
in the literature with ABPA and aspergilloma, the natural
history of these combined entities is unknown. The course of
our patient over a two-year period suggests that conservative
medical management with treatment of underlying ABPA is
advisable.

REFERENCES
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FIGURE 2. PA radiograph of March 5, 1983 demonstrates resolution
of left upper lobe infiltrate and unchanged size of right upper lobe
cavity.
Pulmonary Melanoma

Primary vs Metastatic

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We report one of the few cases of apparently primary pulmonary melanomas documented by both clinical and autopsy examination. The possibility of spontaneous regression of a melanoma primary in another site after metastasis has occurred may explain some of these cases.

Of the ten cases of presumably primary melanoma of the lung reported in the English literature, most cannot be accepted without some reservation. We report one of the few cases in which absence of a primary extrapulmonary melanoma was documented by both clinical and autopsy examination. Nevertheless, the existence of a primary pulmonary melanoma remains somewhat equivocal because of the remote possibility of spontaneous regression of a primary melanoma of the skin or other site after a pulmonary metastasis has occurred.

Case Report

The patient was an 80-year-old previously healthy white man who was found to have a coin lesion of the right middle lobe on routine chest x-ray examination during an admission work-up for diagnosis of lower GI bleeding. (Discharge diagnosis was bleeding hemorrhoids.) A month follow-up chest x-ray film showed enlargement of the lesion to 1.5 cm diameter, and he was admitted with a diagnosis of probable carcinoma of the lung. He underwent exploratory thoracotomy with excisional biopsy of the lesion which was located in the fissure between the right upper and middle lobes.

The specimen consisted of a 1.5 cm firm, black tumor mass with attached rim of lung parenchyma. Microscopic examination showed a pleomorphic malignant neoplasm containing dark brown pigment granules (Fig 1). Fontana-Masson stain of the granules was positive for melanin, and electron microscopy showed melanosomes within the tumor cells (Fig 2). A right hilar lymph node was negative for metastatic disease.

Extensive examinations for primary melanoma in the skin, scalp, nail beds, genital and anal regions, and eyes were repeatedly performed; however, no lesion was found. There was no lymphadenopathy. The patient had several cutaneous squamous cell carcinomas excised in the mid-1970s, but there was no history of other skin lesions. There was no clinical evidence of involvement of any other organ, and CT scan of the brain, liver-spleen scan and bone scan were negative.

The patient received a two-month outpatient course of radiotherapy to the chest, totaling 5,000 rads. He developed increasing dyspnea on exertion and was found to have increased opacity of the lungs in the distribution of the radiation fields. He was readmitted with a diagnosis of probable radiation pneumonitis and pneumonia. His dyspnea worsened to the point that mechanical ventilation was required, and he became hypotensive and died 11 days after admission.

At autopsy, careful examination of the skin showed no evidence of melanoma. Dissection was restricted to the chest. A microscopic 2 mm focus of metastatic melanoma was present in the left upper lobe; otherwise, the thoracic organs were free of tumor. Diffuse radiation...