The Formation of Pulmonary Mycetomata

CHARLES PRZYJEMSKI, MD,* AND ROBERTO MATTII, MD†

Pulmonary mycetomata appeared in the previously normal lung of a patient being treated for acute leukemia. The roentgenographic progression from normal lung through poorly defined infiltrates to well developed mycetomata was quite rapid, about two weeks, and coincided with recovery from prolonged leukopenia. The mycetomata were removed soon after their formation and microscopic study revealed that the lesions were autoamputated spheres of lung tissue containing hyphae. This is the first report demonstrating that mycetomata may be primarily "lung balls" rather than "fungus balls." Cleavage of infected from adjacent healthy lung tissue is apparently accomplished through leukocyte enzymatic activity. The appearance of mycetomata in a preexisting pneumonic infiltrate may herald improved host resistance with conversion of a deeply infiltrating process to relatively extrinsic surface colonization and specific treatment may be unwarranted.


The consensus of reviews of pulmonary mycetomata is that preexisting lung disease is nearly always present. Pulmonary cavities caused by chronic bronchiectasis, lung cysts, carcinoma, and granulomatous disease apparently provide nurseries for growth of fungi into spherical masses. In this report, we describe the development of multiple pulmonary aspergillomata from presumptive aspergillus bronchopneumonia in the previously normal lung of a patient receiving chemotherapy for acute granulocytic leukemia.

Case Report

The patient, a 34-year-old woman, sought treatment because of a cough, sore throat, and low-grade fever; she received a course of penicillin treatment on an outpatient basis. Symptoms persisted and further evaluation demonstrated acute leukemia (Auer-rod-positive). Baseline skin testing revealed negative reactions to purified protein derivative (PPD) and candida, 20-mm erythema to mumps, and 20-mm erythema with 5-mm induration to SKSD. Remission was induced with arabinocide and daunorubicin, resulting in severe leukopenia and thrombocytopenia. The total leukocyte count fell from 12,800/mm³ to 250/mm³ over six days and remained in the 200–1,000/mm³ range for 35 days (Fig. 1). Chest x-rays obtained three weeks and one week (Fig. 2A) before the rise in leukocyte count were normal. However, concomitant with the rise in leukocyte count, a poorly defined right upper lobe infiltrate was seen on x-ray (Fig. 2B) and five days later, when the leukocyte count had climbed to 3,000/mm³, numerous right upper lobe cavities containing rounded densities consistent with mycetomata appeared (Fig. 2C). Ten days later, a right upper lobectomy was performed, revealing spheroidal mucoid greyish-tan masses within cavities in the substance of the lung (Fig. 3). The walls of the cavities were indurated, but the tissue between the cavities and the pleura appeared to be normal. The masses averaged 2 cm in diameter.

Histologic examination showed that (Fig. 4A) the masses consisted of lung parenchyma, showing coagulation necrosis, diffusely infiltrated by septate, branched hyphae consistent with Aspergillus species. A few vessels within the masses contained fibrin thrombi and hyphae. The margin of fungus balls and the rim of the cavities contained masses of degenerating polymorphonuclear leukocytes (Fig. 4B). Adjacent lung tissue contained chronic inflammatory infiltrates, but no fungi or other organisms were demonstrated by staining. There was no evidence of bronchiectasis. Cultures of the mycetomata were negative, but serum sent to the CDC Mycology-Immunology Laboratory revealed precipitins to Aspergillus flavus.

Discussion

With the introduction of chemotherapy and associated leukopenia, deep invasion by saprophytic fungi has become common. This association seems to have been first described by Craig and Farber in 1953 while analyzing the effects of chemotherapy on childhood leukemia. A subsequent report confirms the high frequency of invasive Aspergillosis in treated adult
leukemia. In a recent review of Aspergillus lobar pneumonia, it is pointed out that preexisting lung disease is not necessarily present as opposed to mycetoma formation which apparently requires a preexisting cavity. In 1 case of a series reported by Meyer et al. a pneumonia progressed to mycetoma formation in association with leukemic remission, but examination of resected lung tissue demonstrated that the cavity was lined by epidermoid epithelium, suggesting that the formation of the cavity antedated that of mycetoma.

The present case suggests that mycetomata may arise in foci of Aspergillus bronchopneumonia and that the presence of polymorphonuclear leukocytes is essential for the conversion. Alternate theories do not seem entirely adequate. First, there was no evidence of preexisting cavities. Second, the mycetoma did not consist of a simple aggregate of hyphae displacing lung parenchyma, but showed a framework of necrotic pulmonary parenchyma throughout the lesion. Finally, simple intravascular fungus growth with occlusion would be expected to cause wedge-shaped lesions extending to the pleura as seen in pulmonary embolism. The mycetomata in the present case were buried within the lung parenchyma with unaffected lung tissue separating the lesions from the pleural surface. In addition, although there was radiologic evidence of right upper lobe pneumonia for over a week, conversion of the process to discrete mycetomata coincided with the return of mature granulocytes to the circulation. Polymorphonuclear leukocytes are known to be the source of potent enzymes capable of digesting lung tissue. The development of mycetomata as granulocytes became available and the presence of a continuous band of degenerating acute inflammatory cells at the interface of mycetoma and cavity suggests that leukocyte enzyme release digested a spherical band of lung tissue resulting in a sequestrum of infected lung tissue. The nodule was thus primarily a lung ball rather than a fungus ball. The apparent restriction of the lytic process might be related to impaired circulation deep within the fungal infiltrate, and the intense polymorphonuclear chemotaxis could be explained by an Arthus phenomenon with immune complex formation between fungal antigens and the specific agglutinins identified in the patient’s serum resulting in activation of chemotactic complement factors. A similar pathogenesis has been proposed for necrobiotic lung nodules which form in response to dirofilariasis.

Dirofilariasis presents as a coin lesion on chest radiographs where it simulates carcinoma and it is often excised. The resected nodule is well demarcated and usually separated from the pleura by normal lung tissue. Microscopically, the nodules show coagulative necrosis of pulmonary tissue with ghost-like outlines of alveolar walls, blood vessels, and respiratory passages. At the center of the mass, within a branch of the pulmonary artery, is a variably viable round worm with features characteristic of Dirofilaria immitis. Apparently, lung sequestra do not form in dirofilariasis, although peripheral fibrosis and central cavitation may occur. Possibly the delayed, abrupt appearance of polymorphonuclear leukocytes in the present case favored peripheral dissolution of infected lung tissue and sequestrum formation. As in the present case, dirofilariasis nodules are a result of localized, rounded lung infarction without the characteristic wedge shape of purely embolic pulmonary embolism suggesting immunologic and/or inflammatory influence on the extent of the infarction.
Progression of pneumonic infiltrate to mycetoma could indicate improved host defense mechanisms with conversion of a deeply infiltrating fungus growth to relatively “extrinsic” surface colonization, and the failure of appropriate cultures to grow the organism from the fungus ball suggests that the organisms were rendered nonviable by the time of lobectomy—an apparently common event. Furthermore, in the present case, those mycetomata which were not excised showed roentgenographic evidence of slow resolution. For these two reasons, operative or antibiotic treatment of mycetomata, especially those arising in an area of pneumonia, may be unwarranted. Instead, attention should be directed to treatment of the underlying disease with correction of leukopenia and immune deficiencies.
ADDENDUM

The patient died in early 1980. Leukemic relapse accompanied by Pseudomonas pneumonia and sepsis were terminal events. At autopsy, residual pulmonary mycetomata were encountered. Microscopically the lesions consisted of multiple concentric layers of hyphae elements. A background of necrotic pulmonary parenchyma could no longer be appreciated.

REFERENCES