Disseminated Aspergillosis, Cushing's Syndrome, and Oat Cell Carcinoma of the Lung*

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Disseminated aspergillosis is a known complication of neoplastic disease; however, it is usually associated with neoplasms of the hematopoietic or lymphoreticular systems or with immunosuppressed states. We describe the previously unreported association of disseminated aspergillosis and Cushing's syndrome secondary to a corticotropin-secreting oat cell carcinoma of the lung, and we review the current literature on disseminated aspergillosis complicating neoplastic disease.

Disseminated aspergillosis is a known complication of neoplastic disease and is usually associated with neoplasms of the hematopoietic or lymphoreticular systems or with immunosuppressed states.1 We were unable to find a previous report describing the association of disseminated aspergillosis and Cushing's syndrome related to a corticotropin-secreting oat cell carcinoma of the lung.

CASE REPORT

A 47-year-old white man sought admission to David Grant USAF Medical Center, Travis Air Force Base, California, because of increasing weakness and numbness of both legs for 11 days. He had been well until three months earlier when he developed lethargy and malaise associated with a 19 kg (42 lb) loss of weight. Two months later, the patient had noted polyuria and polydipsia. Fifteen days before admission, he had experienced the onset of a productive cough, but he denied having hemoptysis, pain in the chest, fever, or chills.

On physical examination the patient was afebrile and mildly tachypneic but was not ill-appearing. His body habitus was typical of that seen in Cushing's syndrome, with marked facial and truncal obesity. Rales and wheezes were heard throughout both pulmonary fields. The liver was enlarged to 18 cm, and there was marked muscular wasting of the limbs, with obvious pedal edema.

The hemoglobin level was 13.0 gm/100 ml. The leucocyte count was 11,600/cu mm, with 74 percent neutrophils, 8 percent band cells, and 20 percent lymphocytes. The level of glucose in the blood was 164 mg/100 ml. The serum levels of electrolytes were as follows: sodium, 150 mEq/L; potassium, 1.9 mEq/L; chloride, 80 mEq/L; and bicarbonate, 40 mEq/L. While breathing room air, the patient had an arterial oxygen pressure of 82 mm Hg, arterial carbon dioxide tension of 41 mm Hg, and arterial pH of 7.50. The 24-hour urinary level of 17-ketosteroids was 102.3 mg/day (normal range, 10 to 25 mg/day). The 24-hour urinary level of free cortisol was 121 mg/day (normal, less than 100 mg/day). The plasma level of ACTH was 812 pg/ml (normal, less than 150 pg/ml). Six cultures of blood were negative for aerobic and anaerobic bacteria. Smears and cultures of sputum for pathogenic bacteria, including Mycobacterium tuberculosis, were negative. Cutaneous tests were negative for M tuberculosis and coccidioidomycosis. The chest roentgenogram showed a right hilar mass, enlargement of right tracheobronchial lymph nodes, a patchy consolidation in the right upper and left lower lobes (Fig 1).

On the fifth day of hospitalization, the patient experienced several episodes of hemoptysis, and a repeat chest roent-

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Figure 1. Posteroanterior (A, upper) and lateral (B, lower) chest x-ray films, showing right hilar mass, enlarged right tracheobronchial lymph nodes, patchy consolidation in right lower lobe, and ill-defined densities in right upper and left lower lobes.
genogram revealed progressive consolidation of the right upper and right lower pulmonary zones, with several areas of cavitation. A fiberoptic bronchoscopic procedure with transbronchial biopsy of the lung yielded pulmonary parenchyma showing necrotic tissue containing branching septate hyphae. Cultures of sputum grew Aspergillus sp. Cytologic studies of the sputum were nondiagnostic. Examination of the bone marrow showed metastatic oat cell carcinoma. On the seventh day of hospitalization, intravenous therapy with amphotericin B was begun. On the eighth day of hospitalization, the patient was hypotensive and unresponsive. He died on the ninth day of hospitalization.

At necropsy oat cell carcinoma was found adjacent to the right upper lobe bronchus. The paratracheal nodes and liver contained metastatic nodules. Throughout both pulmonary fields, there were areas of consolidation which, on microscopic examination, showed extensive areas of hemorrhage and necrosis containing septate branching hyphae. Microabscesses with hyphae were also found in the myocardium, thyroid gland, kidney, and brain.

**DISCUSSION**

Aspergillosis of the lung may occur in several ways: (1) allergic bronchopulmonary aspergillosis, a process in which the Aspergillus involves the superficial mucosa of the bronchial wall, with symptoms of asthma, eosinophilia, and fleeting pulmonary infiltrates; (2) intracavitary mycetoma, a disease in which the Aspergillus colonizes a preexisting pulmonary cavity, forming a mass of mycelia radiographically visible as a fungus ball, with symptoms of hemoptysis; (3) pneumatic aspergillosis; and (4) disseminated aspergillosis. The last two types have been reported most commonly in populations of patients whose defenses have been altered by hematopoietic or lymphoreticular neoplasms or by immunosuppressed states. The increasing importance of fungal disease in this group has been well documented in several recent series.

This case is typical of other reported cases of disseminated aspergillosis in many respects, including the distribution of involvement and the pulmonary parenchymal process consisting of a hemorrhagic necrotizing bronchopneumonia; however, our case is unusual in that there has been a predominance of hematopoietic and lymphoreticular malignant neoplasms in large series of aspergillosis, and only rarely has primary cancer of the lung been reported. Although disseminated aspergillosis is known to be associated with corticosteroid therapy, its occurrence with a corticotropin-secreting oat cell carcinoma of the lung has not, to our knowledge, been reported.

The administration of corticosteroids has been shown to be an important predisposing factor to the development of aspergillosis in animals. Phagocytized spores remain dormant or degenerated in normal macrophages, whereas those in macrophages from animals treated with corticosteroids show evidence of germination. It thus is likely that the development of disseminated aspergillosis in this patient with florid Cushing's syndrome was related to the markedly increased endogenous production of corticosteroids, rather than the more direct effects of the malignant process.

**REFERENCES**


**Loculated Pericardial Effusion in Acute Pericarditis**

**Diagnosis by Combined Echocardiographic and Radioisotopic Techniques**

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A young man with a typical clinical presentation of acute pericarditis, on M-mode echocardiography, was repeatedly found to have a relatively echo-free area posterosuperior to the left ventricle, disappearing as the left ventricular apex was scanned. A radioisotopic "pericardial scan" revealed pericardial fluid lateral and inferior to the heart but not at the apex. This represents an additional type of M-mode echocardiographic presentation of loculated pericardial effusion.

Loculation of pericardial fluid in pericardial disease may result in inability to aspirate pericardial contents either for diagnosis or relief of compression (tamponade). In cases of acute pericarditis with effusion requiring surgical intervention, adhesions between the visceral and parietal layers of the pericardium are almost invariably found at operation, regardless of the etiology of the disease.

Despite the frequent presence of adhesions in acute pericarditis, no specific echocardiographic criteria for loculated pericardial effusions have been developed, as indicated in a number of currently popular texts and atlases, although case reports have appeared in the literature.

The patient presented appears to have had a pericardial effusion loculated to the superior aspect of the left ventricle posteriorly with none present at the left ventricular apex. Confirmation of the M-mode echocardiographic findings was made by a radioisotopic scanning technique. The ultrasonic findings in this individual comprise yet another echo pattern that may be found in this condition.

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