tumors such as lung carcinoma are less susceptible, accounting for 2 to 13 percent of IPA cases.1,3 Meyer and associates have described that patients with solid tumors who had Aspergillus infections had at least two of the following features in common: corticosteroid treatment, cytotoxic therapy or leukopenia <4,000/cu mm. Patients with necrotizing bronchial aspergillosis are less severely compromised than those with other forms of IPA. Young and associates1 have reported that bronchial aspergillosis developed in patients with mild leukopenia, some of whom had been treated with corticosteroids or antineoplastic drugs. The patient reported here had mild leukopenia (3,300/cu mm) as the result of neoadjuvant chemotherapy at the time of operation; IPA is a rare complication after pulmonary surgery.2 In our patient, there may be some abnormalities in pulmonary defense mechanisms related to lung resection. Impairment of mucociliary function and tissue damage produced by surgical manipulation, particularly lymph node dissection, may have been significant factors leading to endobronchial proliferation of Aspergillus in the early post-operative period. The development of bronchial aspergillosis in our patient also was probably facilitated by neoadjuvant chemotherapy in association with granulocytopenia; IPA should be noted as a pulmonary complication after surgery and neoadjuvant chemotherapy for lung carcinoma.

The clinical diagnosis of IPA is difficult because of the nonspecific nature of its symptoms and the lack of reliability of microbiologic, serologic, and radiographic findings.1,4 Sputum cultures are positive on more than one occasion in less than 10 percent of IPA cases.1,5 In our patient, the diagnosis of Aspergillus infection was suspected because repeated sputum examinations proved positive. This was confirmed by the biopsy specimens obtained during FBS; FBS played a useful role for early diagnosis. At the present time, amphotericin B is considered the treatment of choice for life-threatening IPA in an immunocompromised host. We used itraconazole, a new orally active triazole, to treat the less severely compromised patient for the limited invasive infection. It was effective and did not have significant side effects.

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Adamantinoma of the Tibia with Pulmonary Metastases and Hypercalcemia*

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Adamantinomas of long bones are rare primary malignant bone tumors. A case of a woman who died of pulmonary metastases of an adamantinoma of the tibia is presented. A unique feature of this case is the association with hypercalcemia. The association of hypercalcemia, hypophosphatemia, decreased parathyroid hormone levels and increased urinary cAMP excretion suggests a humorally mediated hypercalcemia. Histologic and ultrastructural analysis of the pulmonary metastases demonstrated that the tumor was composed of a heterogeneous cell population with mesenchymal and epithelial differentiation.

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cAMP = \text{cyclic adenosine 5'}-\text{monophosphate; GF = glomerular filtrate; PTH = parathyroid hormone}
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Adamantinomas are rare primary neoplasms of bone which account for about 0.3 to 0.5 percent of all malignant bone tumors.1,2 Up to 1989, about 265 cases had been reported.1,3 The tibia was involved in about 85 percent of the patients reported by Moon and Mori.2

CASE REPORT

The patient was admitted to the hospital in 1959 when she was

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FIGURE 1. Chest radiograph showing multiple nodules in the parenchyma of both lungs and a pleural effusion on the right.

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13 years old with a pathologic fracture of the left tibia. Histologic material was not available for review. The diagnosis of adamantinoma was made in 1984, following curettage of a local recurrence.

In April 1987, she developed hemoptysis. A chest radiograph showed nodular densities in both lungs and a right-sided pleural effusion (Fig 1). Bronchoscopy revealed endobronchial lesions with histologic confirmation of adamantinoma in the bronchial biopsy specimens. A radionuclide bone scan was normal.

At that time, a chronic hypercalcemia up to 16 mg/dl (normal range: 8.5 to 10.5 mg/dl), in association with hypophosphatemia, was diagnosed. The urinary cAMP excretion was increased to 11.6 nmol cAMP/100 ml GF (normal range: 1.8 to 4.5 nmol/100 ml GF). Parathyroid hormone levels were decreased.

In April 1988, a bone scan showed a hot spot in the seventh rib on the right.

The patient died on January 1, 1989, from respiratory insufficiency. At autopsy, the parenchyma of both lungs and the right pleural surface were to a great extent replaced by tumor nodules. A solitary skeletal metastasis was found in the right seventh rib. At light microscopy, the tumor tissue displayed the picture of an adamantinoma of long bones. The epithelial component was less obvious than in the primary bone tumor; the lesion displayed a predominant spindle cell pattern (Fig 2, A). The cells of the stromal component stained with antibodies against vimentin. The epithelial component of the tumor stained with antibodies directed against high-molecular weight cytokeratins. The epithelial nature of some of the tumor cells was confirmed by the presence of a network of pre-keratin filaments in their cytoplasm (Fig 2, B). There was no ultrastructural evidence of secretory activity.

**Discussion**

This case history illustrates the typical clinical course of an adamantinoma of the tibia. Metastatic spread occurred to the lungs and the skeleton, the localizations most frequently cited in the literature.

The patient ultimately died 24 years after the diagnosis of adamantinoma was made, illustrating the protracted evolution and the late occurrence of metastases.

Curettage and local excision are inadequate treatment and often lead to local recurrence and metastatic disease. Although large series of documented cases are not available for review, most authors now recommend wide surgical excision or amputation. The development of late metastases is not unusual in inadequately treated patients; they even have been described 16 years after primary amputation.

Pulmonary metastases are the most common metastases. In the series of Keeney et al (85 cases), they were noted in 13 patients (15 percent), an average of 8.2 years after the initial diagnosis. They were found in 70 percent of all deceased patients in the review by Moon and Mori. The pulmonary metastases appeared as solid masses of varying size and number in the lung parenchyma and the pleura. In some cases, as in our patient, endobronchial metastases were reported. A spontaneous pneumothorax was reported as the first indication that pulmonary spread had occurred.

The histologic appearance of the adamantinoma is remarkable for its variability in different areas of the same tumor and from case to case. The typical appearance is that of small epithelial islands in a fibrous stroma. The pulmonary metastases of our patient showed a predominant spindle cell pattern without obvious epithelial differentiation; in some areas, however, a basaloид pattern with peripheral palisading was found. In addition, there may be differences in histologic pattern between the primary bone tumor and its metastases; this also was the case in our patient, where epithelial islands easily were recognizable in the primary tibial lesion.

The histogenesis of the tumor still is controversial, but many authors, using ultrastructural and immunohistochemical techniques, believe it is of epithelial origin. Weiss and Dorfman, however, interpret the lesion as a neoplasm, capable of differentiating along epithelial as well as mesenchymal lines. In our patient, the biphasic nature of the pulmonary metastases was confirmed using ultrastructural and immunohistochemical techniques. As far as we are aware, this is the first report on the electron microscopy of pulmonary metastases from adamantinoma. It confirmed the epithelial nature of some of the tumor cells.

The unique feature of this case is the association of the adamantinoma with hypercalcemia. The hypercalcemia was
diagnosed in April 1987; at that moment the radionuclide bone scan was normal. One year later, the bone scan showed a solitary hot spot in a rib. At autopsy, this rib lesion was the only skeletal metastasis. Therefore, we do not think that bone lysis by skeletal metastases is the explanation for the patient’s hypercalcemia. Moreover, the association of hypercalcemia, hypophosphatemia, decreased PTH levels and increased urinary cAMP excretion in our patient suggests the action of an adenylate cyclase stimulating factor (a PTH-like peptide?), causing a humorally mediated hypercalcemia.

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Heimlich Valve Treatment of Pneumocystis carinii-Associated Pneumothorax

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Two patients were treated for AIDS-associated bilateral pneumothoraces which persisted despite prolonged chest tube drainage. Heimlich flutter valves were used to facilitate the outpatient management of these patients.

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Numerous reports have appeared in the past few years of spontaneous pneumothoraces occurring in patients with the acquired immunodeficiency syndrome and Pneumocystis carinii pneumonia.1-3 Pneumothorax and bronchopleural fistula are believed to occur as a result of lung destruction by Pneumocystis organisms.1 Like many other complications of AIDS, pneumothorax can have devastating physical and psychologic consequences, since prolonged hospitalization and chest tube drainage may be required. Standard surgical approaches for the treatment of refractory or recurrent spontaneous pneumothoraces may not be advisable in AIDS patients, especially when the pneumothoraces occur bilaterally. We describe two patients with P carinii-associated bilateral pneumothoraces where Heimlich valves were used to maintain lung inflation in an outpatient setting.

Case Reports

Case 1

The patient was a 31-year-old man with a two-year history of AIDS. He had complications of P carinii pneumonia and cytomegalovirus retinitis. The patient was doing well on prophylactic aerosolized pentamidine, 100 mg every two weeks, when he suddenly developed shortness of breath and chest tightness. A chest x-ray film demonstrated large bilateral pneumothoraces and bilateral airspace disease. Bilateral chest tubes were inserted and connected to suction. Pneumocystis carinii organisms were isolated from bronchoalveolar lavage fluid. Pentamidine, 250 mg intravenously once a day, was administered. After two weeks of pentamidine therapy, pulmonary infiltrates resolved and pentamidine was changed to aerosolized therapy with 60 mg given once a week. When the pneumothoraces failed to resolve with prolonged chest drainage, pleurodesis with tetracycline was attempted bilaterally three times over a five-week period without success. Bilateral pneumothoraces recurred on each occasion after suction was discontinued. Pleural fluid drainage averaged 10 to 20 mL/day from each chest tube. Surgical intervention was considered but was not recommended. Finally, after ten weeks of hospitalization with chest tube drainage, the patient requested discharge from the hospital. The chest tubes were then attached to Heimlich valves with drainage bags and the patient was discharged. Very small apical pneumothoraces were present on a chest roentgenogram taken prior to discharge (Fig 1). One week after discharge, the patient was readmitted for treatment of a small empyema in the left chest. Pneumothoraces were not present on a chest roentgenogram at that time. Pleural fluid cultures were positive for Staphylococcus aureus, Proteus mirabilis, and Morganella morganii. The empyema resolved with appropriate antibiotic therapy. The left chest tube was successfully removed three weeks and the right chest tube six weeks after placement of the Heimlich valves. No further pneumothoraces have occurred over the subsequent nine months.

Case 2

The patient was a terminally ill 33-year-old man with a two-year history of AIDS complicated by P carinii pneumonia, cytomegalovirus retinitis with blindness, and severe weight loss. Four months prior to admission, he developed a right spontaneous pneumothorax which resolved without chest tube drainage. The patient continued on treatment with prophylactic pentamidine aerosol therapy. The patient developed a paroxysm of coughing followed by sharp right chest pain and shortness of breath. A chest roentgenogram revealed a large right pneumothorax with small bilateral pleural effusions. Pulmonary parenchymal abnormalities were not observed. The patient was hospitalized and a chest tube was inserted and attached to a Heimlich valve. The pneumothorax persisted but was smaller. Three days after admission, a large left pneumothorax was discovered and a chest tube was inserted in the left chest. Despite insertion of an additional chest tube on the right, small bilateral pneumothoraces persisted despite suction drainage with a pressure of ~30 cm H2O. He refused to have bronchoscopy, and empirical therapy for Pneumocystis pneumonia was started and consisted of aerosolized pentamidine, 600 mg/day, dapsone, and trimethoprim. When no resolution of the pneumothoraces occurred after five days of antibiotic therapy and 27 days of chest tube drainage, the patient requested discharge from the hospital. Heimlich valves and drainage bags were then attached to the ends of the chest tubes, and the patient was discharged. A chest roentgenogram taken prior to discharge showed small bilateral pneumothoraces. This is shown in Figure 1, right. The patient did well at home for one week following discharge until excessive pleural fluid drainage interfered with function of the Heimlich valves. The patient refused further medical

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