Pneumocystis carinii Pneumonitis in Patients with Lung Cancer*

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Pneumocystis carinii pneumonia was histologically documented in five patients with bronchogenic carcinoma. All patients had been treated with combination antineoplastic chemotherapy. Two patients received no corticosteroids, two received no chest radiotherapy, and one received neither radiotherapy nor corticosteroids. This suggests that as more patients with lung cancer are treated with intensive chemotherapy, pulmonary infection with P carinii may become an important differential diagnostic consideration in the presence of pulmonary infiltrates.

Pneumonitis due to Pneumocystis carinii is recognized as an important differential diagnostic consideration in patients with pulmonary infiltrates and certain abnormalities of their immune defense mechanisms. Most clinicians are aware of P carinii pneumonitis occurring in malignant and nonmalignant diseases of the lymphoreticular tissues, congenital immuno-deficiency disorders, and in premature and debilitated malnourished infants. The other large category of associated predisposing factors includes those disorders which have required the use of various immunosuppressive agents, the most important of which appear to be the corticosteroids. Large reviews of the subject of Pneumocystis infection have included only sporadic cases of Pneumocystis pneumonia occurring in patients with solid tumors such as ovarian cancer, neuroblastoma, and carcinoma of the breast or bladder.

However, of the thousands of reported cases of P carinii pneumonia reported, the occurrence of this infection in the presence of lung cancer has been casually noted in only two patients; once in 1972 and once in 1979.

The following five cases, seen over a two-year period, treated with intensive combination chemotherapy at the NCI/VA Medical Oncology Branch illustrate that P carinii must be considered among the etiologic possibilities of pneumonitis in patients with carcinoma of the lung, even in the absence of preceding or concomitant corticosteroid therapy.

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CLINICAL SUMMARY

All patients were men and ranged in age from 49 to 67 years old. All patients had carcinoma of the lung; two had small cell carcinoma and one each had adenocarcinoma, mixed small cell and adenocarcinoma, and mixed adenosquamous carcinoma.

Three patients were being treated with sequential three-drug combination chemotherapy consisting of six-week alternating regimens of cyclophosphamide, methotrexate, and lomustine or vincristine, doxorubicin hydrochloride (Adriamycin), and procarbazine. The details of this therapy are described elsewhere. One patient was treated with high dose intravenous methotrexate, with folinic acid rescue and one received, sequentially, methotrexate, cis-dichorodiamine platinum II, pentamethylmelamine, and a combination of doxorubicin and mitomycin C. In addition to chemotherapy, three patients had been treated with radiotherapy to the primary lung lesion. Three of the five patients had also received systemic therapy with dexamethasone for symptomatic relief of proven or suspected cerebral metastases concomitant, in two instances, with brain radiotherapy. In each of these three instances, the corticosteroid was either being reduced in dosage or had been discontinued just prior to the diagnosis of P carinii pneumonia. The salient features of patient therapy are summarized in Table I.

The presenting symptoms and signs, as in most cases of P carinii pneumonia, were nonspecific and included dyspnea, cough, fever, and arterial hypoxemia. All patients had chest roentgenograms that demonstrated diffuse interstitial infiltrates.

The diagnosis was established in three cases by open lung biopsy, in one by transbronchial lung biopsy, and in one by examination of lung tissue obtained at autopsy.

In spite of therapy with pentamidine, a combination of sulfadiazine and pyrimethamine, or trime-
thoprim-sulfamethoxazole, three of the patients died. One expired within 12 hours of hospital admission, and had received no therapy.

**DISCUSSION**

In recent years, chemotherapy for carcinoma of the lung has become much more intense and is frequently associated with the use of multiple chemotherapeutic drugs as well as radiotherapy. As a result, it is perhaps surprising that *P. carinii* pneumonia has not yet been reported to occur in increasing frequency in patients with underlying primary lung tumors.

Although there is a dearth of information in the medical literature about *P. carinii* infection in patients with lung cancer, the cases of Pneumocystis pneumonia reported here illustrate that the infection does occur in patients with this disease in association with antineoplastic chemotherapy. Recent studies also suggest that this disease may increase in frequency in patients with nonlymphoproliferative solid tumors who are treated with more intensive and immunosuppressive chemotherapy. The occurrence of *P. carinii* pneumonia has not been documented in patients with other solid tumors at this institution. However, patients with lung cancer are the only ones with solid tumors who are receiving intensive chemotherapy here. In addition, as shown in Table 1, it should be stressed that this infection can appear in patients with lung cancer who have received neither corticosteroids (cases 1 and 2) nor chest radiotherapy (cases 1 and 3).

Since pulmonary infiltrates in patients receiving therapy for lung cancer may result from radiation therapy, antineoplastic chemotherapy, lymphangitic dissemination of tumor, or uncommon infectious agents such as *P. carinii*, various treatment modalities that might be contraindicated could be administered if the clinical diagnosis were incorrect. Therefore, it is imperative that, in the setting of interstitial pneumonic infiltrates in patients receiving chemotherapy for lung cancer, a definitive diagnosis, using all clinically feasible methods, must be established through early examination of the involved lung tissue.

### Table 1—Summary of Therapy Administered to Five Patients with Lung Cancer and Pneumocytosis

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<th>Case</th>
<th>Intensive Chemotherapy</th>
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References