Giant Cell Carcinoma of the Lung*
Clinical and Roentgenographic Manifestations

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Giant cell carcinoma of the lung is an unusual form of pulmonary malignancy that follows an extremely aggressive clinical course. We report the clinical and roentgenographic manifestations of 14 patients with pathologically proven giant cell carcinoma of the lung, and compare our data to other reports in the literature. Our patients often presented with or developed constitutional or nonthoracic symptoms. This neoplasm was characterized by early evidence of widespread metastases. However, extension of tumor to the chest wall was not as frequent in our series as has been previously described. The survival from the time of diagnosis was extremely short. Any hope of successful treatment of this neoplasm depends on prompt, early diagnosis. Pulmonary giant cell carcinoma should be included in the differential diagnosis of large, round or oval, sharply outlined peripheral lung masses.

Pulmonary giant cell carcinoma is one of the most highly malignant lung neoplasms. Although the histogenesis of pulmonary giant cell carcinoma remains uncertain, it is presently classified as large cell undifferentiated bronchogenic carcinoma. However, it is generally regarded as a distinct entity based on its unusual histologic features and its extremely aggressive clinical course. Only one previous study has emphasized the roentgenographic features of this neoplasm.1 The present report describes the clinical, roentgenographic, and pathologic findings in 14 patients with pulmonary giant cell carcinoma.

Clinical Material and Findings

Fourteen patients with pathologically proven pulmonary giant cell carcinoma were collected from the files of the University of Alabama at Birmingham Hospitals, the Birmingham Veterans Administration Hospital, and the Massachusetts General Hospital during a 12-year period from 1968 to 1980. The ages of the patients ranged from 21 to 82 years. The peak incidence occurred in the sixth decade (six patients), and the average age was 54.2 years. Thirteen patients were men and one was a woman. The diagnosis was established by bronchoscopy in two patients, by thoracotomy in six patients, and only by autopsy in six patients.

The chief symptoms which led to hospitalization were as follows: cough (seven patients), hemoptysis (four patients), dyspnea (nine patients), loss of weight (11 patients), and chest pain (five patients). Neurologic symptoms such as headache, seizures, and stroke were manifested in seven patients. Two patients had no symptoms referable to the chest despite huge lung tumors (8 × 6 cm in one patient and 15 × 14 cm in the other). Five of the patients were nonsmokers and nine were smokers (20 to 50 pack-years).

Death occurred within 11 months from the onset of symptoms in ten of the 14 patients. Three of the patients were lost to follow-up. Only two patients survived more than one year following diagnosis. The average survival of the 11 patients who were followed was 7.4 months from the time symptoms first developed and 4.2 months from the time of diagnosis. Six patients were treated with a combination of chemotherapy and radiation therapy. There was no difference in the survival time of the treated vs the untreated groups. Autopsies were performed in seven patients. Extension of the tumor into the chest wall, diaphragm, or mediastinum was observed in three patients. All seven patients had lymph node metastases. Metastases were found in the adrenals (six patients), the brain (four patients), the liver (three patients), the opposite lung (three patients), the heart (two patients), the pancreas (two patients), the kidney (two patients), the small intestine (one patient), the skin (one patient), and the vertebra (one patient).

Roentgenographic Features

The lesions were located in the right upper lobe (four patients), the right middle lobe (one patient), the right lower lobe (four patients), the left upper lobe (three patients), and the left lower lobe (two patients). The tumors were either oval or round and rather smooth in contour with sharply defined borders (Fig 1 and 2). On initial chest roentgenograms, the tumor was greater than 5 cm in at least one dimension in 11 of the patients (79 percent). One patient had massive lobar consolidation involving the right upper lobe. Metastases to the hilar or paratracheal nodes were evident in eight patients. One lesion became cavitated. One patient had pleural effusion.

Discussion

Bronchogenic carcinoma is one of the top three causes of cancer deaths in middle aged and older adults. Prognosis for bronchogenic carcinoma is highly dependent upon histologic type. Chest radiology is important in initial recognition of the presence of pulmonary malignancy and radiologic criteria may help provide the clinician with probability information regarding the most likely type of neoplasm. Although pulmonary giant cell carcinoma is an unusual form of bronchogenic carcinoma, recognition of it is important because of its very poor prognosis.

Pulmonary giant cell carcinoma was initially de-
scribed as a distinct histologic entity by Nash and Stout in 1958. Its light microscopic features include predominance of very pleomorphic multinucleated giant tumor cells (Fig 3). These giant cells may contain other cannibalized cells (eg, polymorphonuclear leukocytes) within their cytoplasm. Wang et al6 considered that this phenomenon was due to migration of the smaller cells into the aging tumor giant cells (termed "emperipolesis") rather than phagocytosis by the tumor cells. The giant cells may be within a background of smaller spindle-shaped cells. The overall appearance can resemble rhabdomyosarcoma, but no cross-striations should be seen.

Ozello and Stout4 demonstrated the epithelial nature of pulmonary giant cell carcinoma by tissue culture technique. Some investigators have considered this neoplasm to be a poorly differentiated adenocarcinoma.6-8 However, ultrastructural studies have shown that true giant cell tumors of lung are devoid of adenocarcinomatous features.18 Currently, giant cell...
Giant-cell Carcinoma of the Lung (Shin et al)

FIGURE 3. Tumor biopsy specimen from the patient in Figure 1 demonstrates a highly anaplastic carcinoma, characterized by marked pleomorphism and hyperchromatism which contains large numbers of bizarre multinucleated giant cells. Cannibalized cells are present within some of the tumor giant cells (original magnification x 220).

carcinoma is considered to be a type of large cell undifferentiated carcinoma by both the World Health Organization and the Armed Forces Institute of Pathology classifications of bronchogenic carcinomas.13 Of all large cell bronchogenic carcinomas, the giant cell variety carries the poorest prognosis.13 Some reports on pulmonary giant cell carcinoma have included cases of otherwise typical squamous cell carcinoma or adenocarcinoma that have sparse numbers of giant cells;14 this has led to an overestimate of the incidence of pulmonary giant cell carcinoma. The true incidence of this neoplasm is probably under 4 percent of all bronchogenic carcinomas.14-16

In most previous series of pulmonary giant cell carcinomas, the patients are predominantly male and their age is slightly below the usual ages of patients with bronchogenic carcinoma. Thirteen of our 14 patients were men, but our patient population was biased, because about half of the patients were hospitalized in a Veterans Administration facility. The average age of our patients (54 years) is consistent with most other reports.15,17 It should be noted, however, that this neoplasm can occur in adults of practically any age. Our series includes four patients below 40 years of age. The report of Kallenberg and Jaquès15 emphasizes the occurrence in an older age group than previously recorded. Our study agrees with other studies of pulmonary giant cell carcinoma in the very aggressive behavior of this neoplasm. Most reports in the literature show average survival times of only five or six months.7,14-16 In our patients in whom adequate follow-up was available (11 patients), average survival time was 7.4 months from the time of initial symptoms, and only 4.2 months from the time of diagnosis. In addition, in the seven patients on whom autopsies were performed, there were widespread lymphatic and hematogenous metastases; an average of more than four organs were involved with metastases in this group. Regional lymph nodes, adrenal glands, and brain were the most common sites of involvement. Also, local extension into the chest wall, mediastinum, and diaphragm was quite common. The effectiveness of therapy for this neoplasm is unknown largely because such small groups of patients have been assembled that a prospective controlled trial is impossible. Razuk et al17 suggested that resection and radiation may extend survival time. We cannot reach a conclusion in this regard from our data. One of our patients survived 18 months after resection and another was still alive with brain metastases two years after resection and radiation therapy.

The chest roentgenograms in our patients showed peripheral location of the tumors. Location by lobe was similar to that of most bronchogenic carcinomas.19 Roentgenographic features in our series included a sharp round or oval outline without lobulation. Theros reported that sharp borders were present in 43 percent of large cell bronchogenic carcinomas. We did not observe tumor cavitation or pleural involvement in as high a frequency as did Gajaraj et al.1 Several of the patients in our series demonstrated extremely rapid tumor growth. One patient (Fig 1) had a clear chest roentgenogram only four months prior to presentation with a very large peripheral lesion. This rapid growth rate, along with the peripheral location of the tumor, emphasizes the difficulty of establishing the diagnosis at a stage when therapy can be beneficial.

In summary, the clinical, roentgenographic, and pathologic features of 14 patients with giant cell carcinoma of the lung are presented. Chest radiographic films, while not diagnostic of this rare neoplasm, can have highly suggestive features. Unfortunately, this diagnosis carries an extremely poor prognosis.

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