Pulmonary Lymphangitic Carcinomatosis: Chronicity of Radiographic Findings in Long-Term Survivors

OBJECTIVE. Long-term survival after development of pulmonary lymphangitic carcinomatosis is considered unusual. However, modern chemotherapy can result in surprising stability or only gradual progression of lymphangitic carcinomatosis. We evaluated the course of radiographic findings in 10 patients with chronic lymphangitic carcinomatosis.

MATERIALS AND METHODS. Ten patients met our criterion of having lymphangitic carcinomatosis for at least 6 months. The primary tumor was a carcinoma of the breast in six cases, the ovary in two, the pancreas in one, and the skin in one. Serial radiographs (all cases) and CT scans (eight cases) were analyzed retrospectively.

RESULTS. Survival with lymphangitic carcinomatosis ranged from 11 to 30 months (median, 13 months). With chemotherapy, the radiographic abnormalities and pulmonary symptoms initially regressed in six patients, progressed in two, and remained unchanged in two; the radiographic findings of lymphangitic carcinomatosis were progressing at the time of death in four patients. All patients had periods of at least 4 months of relative stability or slow progression of pulmonary radiographic abnormalities. Serial transbronchial biopsies in one case confirmed persistent lymphangitic carcinomatosis despite therapy, and autopsy disclosed persistent lymphangitic tumor in two others.

CONCLUSION. Stability or slow progression of radiographic findings can occur in some patients with lymphangitic carcinomatosis. Therefore, chronicity of radiographic findings should not be taken as evidence against lymphangitic carcinomatosis as the cause of an interstitial abnormality in a patient with cancer.

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Long-term survival after development of pulmonary lymphangitic carcinomatosis from extrathoracic cancers (principally breast carcinomas) has been considered unusual. For instance, before the introduction of modern chemotherapy for metastatic breast cancer, about half of affected patients died within 3 months and only 15% of patients survived beyond 6 months [1]. Even with modern chemotherapy, lymphangitic carcinomatosis of the lung has proven responsive in only a few series [2].

These and similar statistics initially led us to discount lymphangitic carcinomatosis as the cause of chronic interstitial pulmonary infiltrates in cancer patients under surveillance in our clinics. However, in the last eight years, we have observed ten cases of proven lymphangitic carcinomatosis in which radiographs showed remarkable persistence and relative stability or slow progression of the infiltrate. We present these cases to demonstrate that chronicity of an interstitial infiltrate in a cancer patient should not be taken as evidence against lymphangitic carcinomatosis as its cause.

Materials and Methods

At each of the two contributing institutions, the same group of radiologists reviews the surveillance chest radiographs for all oncology patients. Thus, every case is known to at least one of us. Cases showing features consistent with lymphangitic carcinomatosis lasting several months have been tabulated over an 8-year period beginning in July 1986. We chose 6 months as the criterion for considering lymphangitic carcinomatosis to be chronic. The 10 such cases for which there was confirmation of lymphangitic carcinomatosis constitute the study population. There were eight women and two men; ages ranged from 29 to 59 (mean, 40.2) years at diagnosis.
All patients had serial chest radiographs available, and eight had CT scans of the chest. For each case, the entire film record was reviewed by at least one chest radiologist. The onset date of radiographic evidence of lymphangitic carcinomatosis (i.e., linear, micronodular, or reticulonodular interstitial opacities) was noted. Subsequent fluctuations in the extent and intensity of the infiltrates and the presence, progression, or regression of any associated findings such as pleural effusion, lymphadenopathy, and skeletal metastasis were also noted. Available thoracic CT scans were evaluated along with the plain radiographs.

Of the eight patients, six had primary carcinomas of the breast, two of the ovary, one of the pancreas, and one of the skin. Four of the patients with breast cancer presented with localized disease; they underwent resection of the primary tumor, and three of the four also had adjuvant radiation therapy and chemotherapy. One patient with ovarian cancer presented with localized disease and underwent surgical debulking followed by chemotherapy. The patient with pancreatic cancer initially was thought to have nasopharyngeal carcinoma because at presentation he had poorly differentiated carcinoma in the nasopharynx and paranasal sinuses. He was initially treated with radiation and chemotherapy, but widespread metastasis ensued, and autopsy revealed a primary pancreatic carcinoma.

The interval from diagnosis of cancer to detection of lymphangitic metastasis ranged from 0 to 52 months (mean, 18.5 months). Two patients, one with breast carcinoma and one with ovarian carcinoma, had lymphangitic carcinomatosis at the time their cancers were initially diagnosed.

Lymphangitic carcinomatosis was confirmed by transbronchial biopsy in eight cases and by lavage or sputum cytology in two. A second transbronchial biopsy was performed in one case, confirming that the persisting interstitial abnormality was indeed still lymphangitic carcinoma. Autopsy confirmation of persisting lymphangitic carcinomatosis was obtained in two other cases. All but one patient had evidence of metastasis to sites other than the lungs.

**Results**

The radiographic features of lymphangitic carcinomatosis were linear, micronodular (i.e., less than 3 mm), or reticulonodular interstitial infiltrates (Figs. 1 and 2). A few larger nodules (up to 1 cm) were present in five patients but were not the dominant finding in any of the cases. Pleural effusions occurred in seven patients and lymphadenopathy was identified in five.

The duration of the radiographic findings of lymphangitic carcinomatosis ranged from 6 to 30 months (median, 13 months). Survival with lymphangitic metastasis exceeded the period of radiographic observation in two patients: one had radiographic evidence of lymphangitic carcinomatosis for 14 months but survived 16 months, and the other had radiographic evidence for 6 months but survived 12 months, and persistent lymphangitic tumor was verified at autopsy. Median survival was 13 months.

![Fig. 1.—50-year-old woman with infiltrating ductal carcinoma of the breast.](helsenet.info)

A, Chest radiograph obtained at time of initial diagnosis of breast cancer shows lymphangitic carcinomatosis as ill-defined nodular and linear interstitial infiltrate.

B, Photomicrograph of specimen from transbronchial lung biopsy reveals tumor deposits (arrow) in lymphatic channels.

C, Chest radiograph obtained after 3 months of chemotherapy shows substantial resolution but persistence of some interstitial infiltrate.

D, Thin-section (1.5-mm) CT scan made at same time as C shows peripheral nodular metastases, thickening of secondary lobular septa, and bronchovascular bundles.

E, Chest radiograph obtained 13 months after C shows only slight worsening of lymphangitic carcinomatosis.
The radiographic findings initially regressed with chemotherapy in six patients, progressed in two, and remained unchanged in two. Eight of the patients had periods of at least 4 months of relative stability of the radiographic manifestations of lymphangitic carcinomatosis; one had only minimal changes (initial slight regression followed by slight progression) over the course, and one had only slow progression throughout the course. Radiographic findings of lymphangitic carcinomatosis were progressing at the time of death in four patients.

Discussion
The term "lymphangitic carcinomatosis" is potentially misleading because it implies that the tumor spreads to the lungs via the lymphatics [3]. In most cases the tumor disseminates hematogenously to the lungs and only secondarily penetrates vessel walls and invades the surrounding interstitium. Although tumor is indeed present in the lymphatic vessels, most of the radiographically visible tumor is in the interstitium around the lymphatics [3].

In our practice, breast cancer is the tumor that most often causes lymphangitic carcinomatosis. However, even in cases of breast cancer, lymphatic involvement occurs in 9% or less [4, 5]. In ovarian cancer it occurs in less than 1% [6].

The typical radiographic finding in lymphangitic carcinomatosis is an interstitial infiltrate that is usually coarse and patchy but may be diffuse and symmetric [1, 4, 5, 7, 8]. There may be accompanying hilar or mediastinal lymphadenopathy and pleural effusion. Differential diagnostic considerations include pulmonary edema, opportunistic infection, radiation fibrosis, and drug-induced lung disease [9]. False-negative [5, 10–12] and false-positive [4] radiographic diagnosis of lymphangitic carcinomatosis is not uncommon. CT is more sensitive than plain radiography [13, 14].

Lymphangitic carcinomatosis traditionally has carried a poor prognosis. All 24 patients reported by Harold [15] died within 3 months after the onset of dyspnea. Of the 60 patients reported by Yang and Lin [1], half died within 3 months and only one seventh survived beyond 6 months. Greenspan [2] found survival to be 15% at 1 year and 2–4% at 2 years. A more recent paper showed that only 38% of patients with lymphangitic carcinomatosis responded to chemotherapy [16]. Median response duration and survival were both less than 1 year.

However, the introduction of combined chemotherapy for metastatic breast cancer has induced objective regression and prolonged survival in some cases [2, 5, 9, 17–22]. Greenspan [2] reported one patient who survived more than 4 years after diagnosis of lymphangitic metastasis. Creech et
al. [17] reported a patient who had complete regression of lymphangitic metastasis for 15 months. Almost all of such cases manifested complete clearing of the lung abnormalities, but the radiographic findings and their evolution with therapy were not described in detail.

We observed radiographic evidence of lymphangitic carcinomatosis lasting from 6 to 30 months, with survival ranging from 11 to 30 months. Survival exceeded radiographic follow-up for two reasons: first, two patients stopped having radiographs in the last weeks or months of their lives; second, one patient had acute lung disease terminally that made it impossible to evaluate lymphangitic carcinomatosis on radiographs.

Radiographic abnormalities suggesting lymphangitic carcinomatosis but persisting after chemotherapy could reflect tumor-induced interstitial fibrosis rather than viable tumor. However, three of our cases had evidence that lymphangitic carcinomatosis did indeed persist. Carcinoma was detected on a second transbronchial biopsy in one case and on postmortem examination in the two others.

In conclusion, despite proven, radiographically visible lymphangitic carcinomatosis, survival ranged from 11 to 30 months in 10 patients; radiographic manifestations persisted from 6 to 30 months, and all cases manifested at least 4 months of relative stability or slow progression of the pulmonary radiographic abnormalities. These cases illustrate that modern chemotherapy can result in surprising stability or slow progression of lymphangitic carcinomatosis. Such stability, therefore, should not dissuade the radiologist from considering lymphangitic carcinomatosis as the cause of a chronic interstitial lung abnormality in a patient with an extrathoracic carcinoma with the potential for lung metastasis.

REFERENCES