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Pulmonary Lymphangitic Carcinomatosis From Renal Cell Carcinoma

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A B S T R A C T

Lymphangitic carcinomatosis, the presence of tumor within the pulmonary lymphatics, occurs in the setting of malignant tumors and is associated with a poor prognosis. Here we describe a case of lymphangitic carcinomatosis in the setting of renal cell carcinoma and review the radiological manifestations of this disease.

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Introduction

Pulmonary lymphangitic carcinomatosis is a less common radiographic manifestation of metastatic disease to the lungs that carries a poorer prognosis. Much of the published literature describing lymphangitic carcinomatosis is combined with tumor embolism; however, Soares et al. studied 222 autopsies of cancer cases and found that arterial tumor embolism and lymphangitic carcinomatosis are clinically similar presenting disease that are different pathophyiologically.[1] There is a lack of published literature dedicated solely to pulmonary lymphangitic carcinomatosis. It is important to differentiate lymphangitic carcinomatosis from other causes with similar imaging appearance, such as edema or infection, that may also occur in cancer patients as carcinomatosis has staging and prognostic implications.

Case Report

A 49-year-old man presented to the emergency department shortness of breath and 1 day of left-sided pleuritic chest pain. He also had been experiencing progressive short of breath with exertion for 1 month. He denied any fevers, chills, myalgias, hemoptysis, recent sick contacts, or recent travel. His past medical history was significant for renal cell carcinoma with spinal and right lower lobe lung metastasis with partial right nephrectomy and T8 partial corpectomy 2 years ago followed by radiation therapy to his T8 lesion and stereotactic body radiation therapy to his lung lesion. Most recently he received systemic, palliative chemotherapy with daily cabozantinib. On examination, he had a blood pressure of 111/63 mm Hg, sinus heart rate of 81 beats/min, a respiratory rate of 21 breathes/min, and was afebrile. He required 2 L/min via nasal cannula to maintain oxygen saturation above 88%. Physical examination revealed a cachectic male with diffuse inspiratory crackles on chest auscultation with no chest wall tenderness, normal cardiac physical examination, and trace bilateral lower extremity pitting edema. Laboratory studies showed no leukocytosis, a normal basic metabolic panel, and a normal level of B-type natriuretic peptide.

A chest radiograph (Fig 1) demonstrated diffuse bilateral interstitial prominence, left upper lobe cavitary lesion, and right upper lung airspace disease. Computed tomography of the chest (Figs 2 and 3) showed a combination of smooth and nodular interlobular septal thickening that was bilateral and asymmetric. There are bilateral small pleural effusions, including fluid tracking into the fissures, as well as mediastinal lymphadenopathy, and bilateral lung masses (Figs 2 and 3). The combination of these imaging findings, particularly the nodular appearance of the interlobular septal thickening (Fig 2, arrow), and his known history of metastatic renal cell carcinoma makes lymphangitic carcinomatosis is the likely diagnosis. A tissue biopsy for confirmation was not pursued due to patient comorbidities and little benefit to the patient's management.

The patient was admitted to the hospital and underwent drainage of his pleural effusion with significant symptomatic relief but no alleviation of his oxygen requirement. Pleural studies were notable for tumor cells, and upon reaccumulation of fluid an intrapleural catheter was placed for palliative support. He was discharged on supplemental oxygen, and despite systemic, palliative chemotherapy he had progression of his disease and died.

Discussion

Lymphangitic carcinomatosis, also called lymphangitis carcinomatosa, is the presence of tumor within the pulmonary lymphatic system. Any malignant tumor may develop lymphangitic carcinomatosis; however, tumors originating from the breast, lung, esophagus, stomach, and renal cell carcinoma are more frequently reported.[2] The pathophysiology is poorly understood, but access to the lymphatic system is thought to be by direct invasion, lymphatic circulation, or hematogenously spread followed by invasion of the

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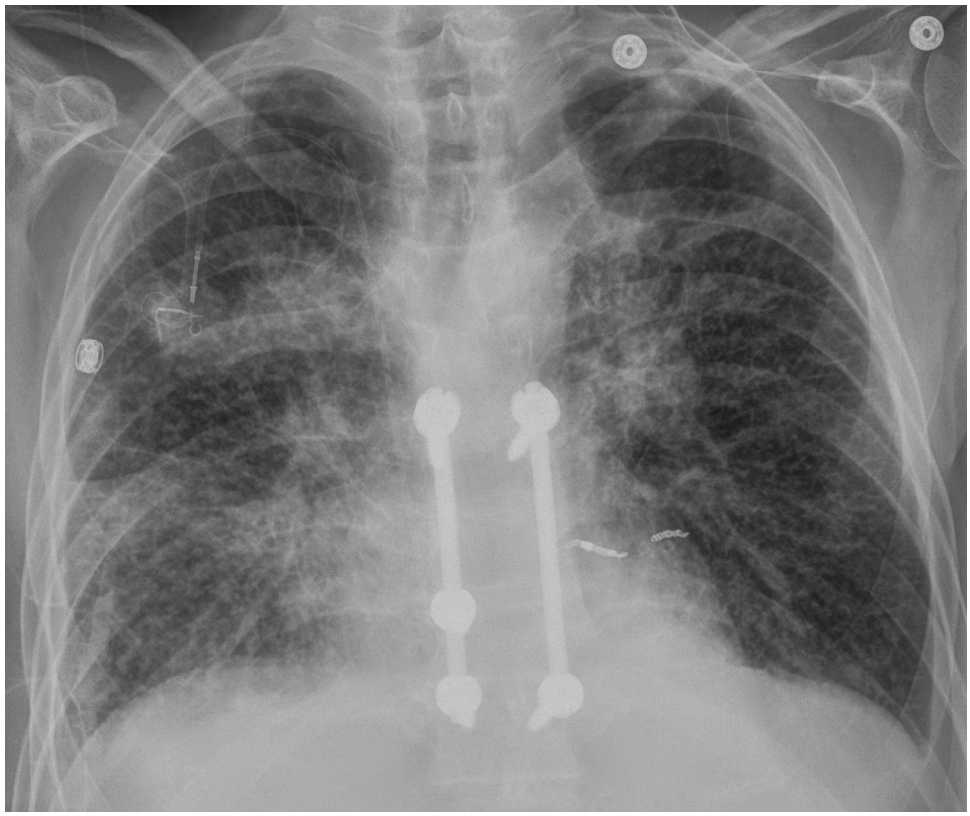

FIG 1. Chest radiograph with posteroanterior view diffuse bilateral interstitial prominence, left upper lobe cavitary lesion, and right upper lung airspace disease.

adjacent interstium.[3,4] After embedding in the pulmonary lymphatic system, it is hypothesized that trapped tumor cells create an obstructive process leading to local edema and lymphatic fluid accumulation.[3] This is supported by the classic histologic appearance of obstruction and distention of the lymphatics by tumor cells.[3,5,6]

Lymphangitic carcinomatosis commonly has a nonspecific presentation of progressive shortness of breath.[2,7] Other symptoms are usually associated with the underlying malignancy, which include cough, hemoptysis, pleuritic chest pain, fatigue, and/or weight loss. Respiratory symptoms are part of the initial presentation in 46% of patients and frequently represent advanced disease.[3] Chest radiograph appearance ranges from normal to diffuse reticular or nodular infiltrates, pleural effusions, and coarse bronchovascular markings.[4,7]

The hallmark of pulmonary lymphangitic carcinomatosis on chest computed tomography is irregularly thickened interlobular septa, bronchi, and pulmonary vasculature, which is thought to be a result of perilymphatic edema and fluid accumulation.[4,5,8] Interlobular septa comprise the outline of the hexagonal or polygonal secondary pulmonary lobule and are made up of a venous and lymphatic systems.[9,10] A bronchiole and an artery are located centrally in the

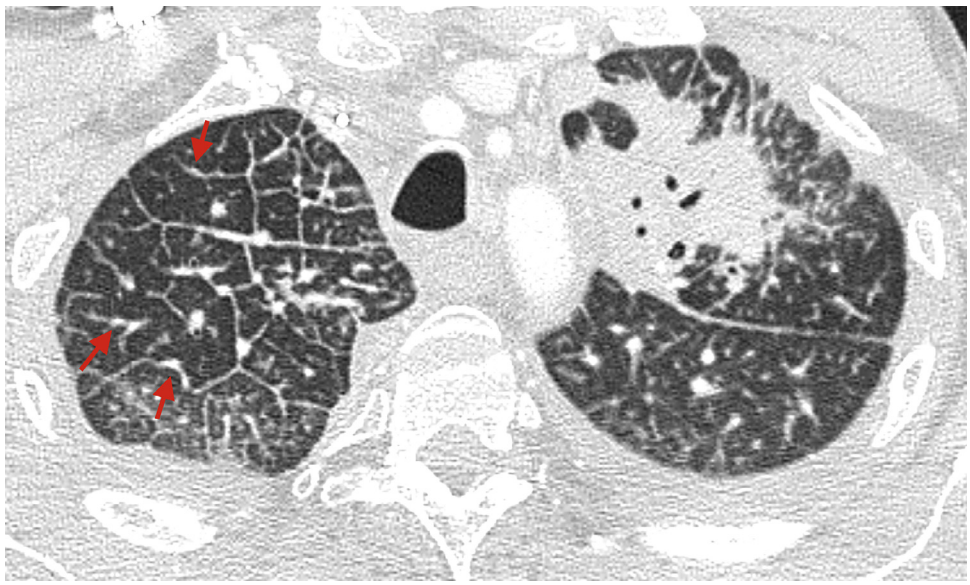

FIG 2. Contrast enhanced computed tomography scan of the chest shows a left upper lobe mass, bilateral pleural effusions, along with thickened, somewhat nodular interlobular septa.

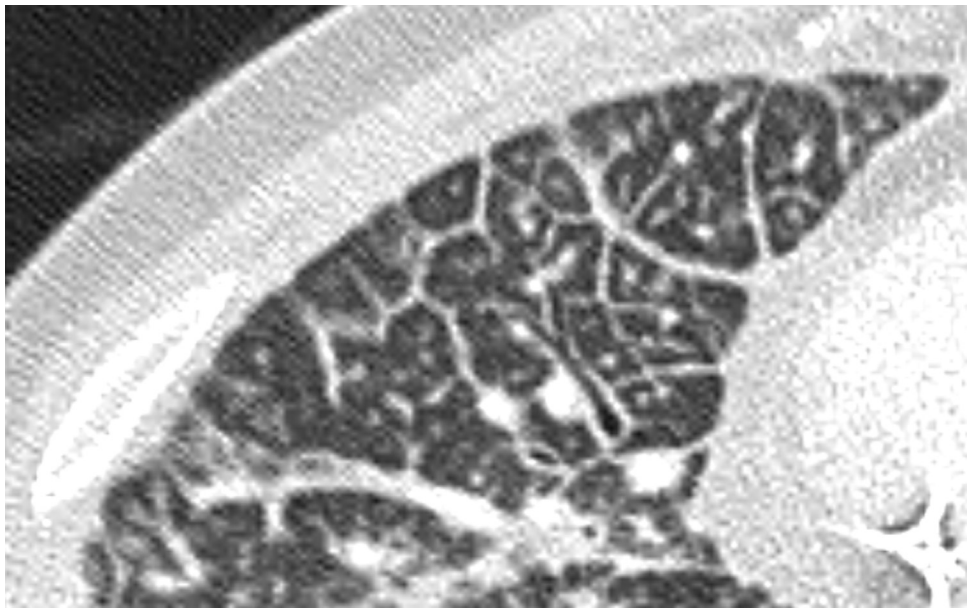

FIG 3. Contrast enhanced computed tomography scan of the chest better demonstrates thickened and nodular interlobular septa in the right middle lobe.

secondary pulmonary lobule.[9,10] Thickening of the interlobular septa appears as short lines extending perpendicularly to the peripheral pleura or may appear surrounding secondary pulmonary lobules more centrally, becoming more visible when there is pathologic insult to either the lymphatic or venous system.[9,10] The thickened interlobular septa may appear smooth, nodular, or irregular and have a focal, diffuse, asymmetric, or symmetric pattern of distribution throughout the chest.[9,10] Observing these findings in the presence or absence of a lung mass, hilar or mediastinal lymphadenopathy, and pleural effusions, may help to narrow the differential as well. Smooth septal thickening may be secondary to pulmonary venous congestion from heart failure, or pulmonary veno-occlusive disease.[8,11] Heart failure in particular will have a lower lobe predominance that is usually symmetric and more centrally located.[8] There are often findings of pleural effusions, ground-glass opacities, and cardiomegaly in the setting of heart failure.[8] Lymphatic etiologies of a smooth septal appearance include congenital lymphangiectasis, pulmonary lymphangiomatosis, and Erdheim-Chester disease.[8,12-14] A nodular appearance may be seen in sarcoidosis, lymphangitic carcinomatosis, pulmonary amyloidosis, silicosis, or asbestosis.[8,15-17]

A definitive diagnosis of lymphangitic carcinomatosis is made after biopsy and histopathologic confirmation. However, in many cases the presumptive diagnosis is made by clinical evaluation and radiographic findings, since patients may have comorbidities precluding biopsy or additional tissue specimens provide no further guidance to management. Laboratory studies are usually nonspecific. Bronchoalveolar lavage and washings are described in some reports to yield cytology of approximately 75%.[18] Currently, transbronchial biopsy is considered the initial approach due to patient tolerance and presumed high yield but published sensitivity or specificity is lacking.[19-21] Surgical lung biopsy and transthoracic lung biopsy are alternative approaches.

Treatment of lymphangitic carcinomatosis is largely supportive and centers on treating the primary malignancy for systemic involvement with chemotherapy, radiation, and for the primary site potential surgical intervention.

Conclusions

Pulmonary lymphangitic carcinomatosis has nonspecific clinical presentation and potential indolent course. The presentation with interlobular septal thickening, most often with an irregular pattern is diagnostic on CT. Interlobular septal thickening can be seen in a number of pathologies, but with a closer evaluation of the presence or absence of other radiographic findings can narrow the differential diagnosis. Lung biopsy with transbronchial biopsy followed by surgical or transthoracic approaches may assist with making the diagnosis; however, these procedures may not be tolerated well by the cancer patient. The identification of lymphangitic carcinomatosis confers poorer prognosis, due to higher stage of disease, and treatment is focused on the primary malignancy and improving the patient's quality of life.

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