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## CLINICAL VIGNETTE

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# Lymphangitic Carcinomatosis and Pulmonary Tumor Emboli Presenting as Waxing and Waning Pulmonary Infiltrates

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### *Introduction*

Antemortem diagnosis of pulmonary tumor emboli or lymphangitic carcinomatosis is rare, with diagnoses more often made on autopsy. We present a patient with lymphangitic carcinomatosis and pulmonary tumor emboli that presented as waxing and waning shortness of breath. Pulmonary infiltrates on imaging were diagnosed with cryobiopsy on navigational bronchoscopy.

### *Case Presentation*

A 56-year-old female with a history of right breast cancer underwent right lumpectomy and sentinel lymph node biopsy at an outside hospital. Pathology showed a Grade 3 1.6 cm invasive ductal carcinoma with 12 of 16 lymph nodes involved and with negative CT chest. The tumor was ER (-), PR (-), HER2 (-) with a Ki 67 of 60%. She received adjuvant chemotherapy with doxorubicin, cyclophosphamide, and nanoparticle, albumin bound paclitaxel followed by radiation therapy. Approximately 7 months later while traveling, she developed fever, dry cough, chest pain and shortness of breath. CT chest showed new multifocal consolidations with differential diagnosis of infection or medication induced pneumonitis. COVID19 testing was negative. Her adjuvant capecitabine was held due to these symptoms. She completed a course of appropriate antibiotics with improved symptoms. However, a few weeks later symptoms worsened and continued to wax and wane. Expecterated mucous cultures were negative for bacterial, fungal and acid fast bacilli. Repeat CT chest showed waxing and waning multifocal peripheral ground glass and airspace consolidation. Differential diagnosis was infectious or non-infectious organizing pneumonia, from drug toxicity (Figure 1a-b). She underwent robotic assisted navigational bronchoscopy with bronchoalveolar lavage (BAL) and biopsies in the right upper lobe. BAL was negative for infectious studies. BAL cell count was predominantly alveolar macrophages with no eosinophils. Forceps biopsy and cryobiopsy showed necrotic tissue most consistent with infarcted lung and infarcted tumor within a vessel. Additional biopsy showed a small focus of carcinoma within the lymphovascular space with breast primary. This was thought to be within an artery (Figure 2a-d).

Given this pathology, we suspected her waxing and waning respiratory symptoms and peripheral pulmonary infiltrates were due to lymphangitic carcinomatosis and pulmonary tumor

emboli causing pulmonary infarcts. This was the first presentation of metastases for this patient. Diagnosis led to treatment adjustments and early involvement of palliative care.

### *Discussion*

Pulmonary tumor emboli and lymphangitic carcinomatosis are rare, end-stage manifestations of malignancy that have a poor prognosis. The terms are often used interchangeably because they often occur together and are evaluated and treated similarly. However, they are morphologically distinct.<sup>1</sup> Tumor may invade nearby vessels directly or tumor fragments may be released into the tumor's neovasculature or neolymphatics. Pulmonary tumor emboli refers to identification of tumor within the pulmonary blood vessels on pathologic lung sample. Occasionally, tumor embolization is associated with pulmonary hemorrhagic infarction distal to the occlusion.<sup>1</sup> Lymphangitic carcinomatosis refers to the presence of tumor within pulmonary lymphatics leading to thickened bronchovascular bundles and interstitial septae. These are both distinct from solid metastases which invade all components of pulmonary parenchymal tissue.

Intrathoracic metastases occur in 30-40% of patients with malignant disease with 6-8% of these having lymphangitic carcinomatosis. The most common underlying primary tumors are breast (33%), gastric (29%), and lung (17%).<sup>2</sup> Autopsy series estimate the incidence of pulmonary tumor embolism between 3% and 26% in patients with solid tumors.<sup>3</sup> Pulmonary lymphangitic carcinomatosis and pulmonary tumor emboli are rare manifestations of cancer with non-specific symptoms. Most patients present with non-specific dyspnea and dry cough,<sup>2-4</sup> and the diagnosis often remains unsuspected until autopsy.

CT chest findings characteristic of lymphangitic carcinomatosis include thickened interlobular septa with nodular appearance and some cases associated ground glass opacities that represent interstitial edema.<sup>4</sup> CT pulmonary angiography findings characteristic of tumor emboli include a dilated, beaded or tree in bud appearance of the pulmonary arteries.<sup>5</sup>

In patients with cancer, dyspnea and abnormal chest imaging, bronchoscopy with bronchoalveolar lavage and transbronchial

biopsy is the diagnostic test of choice to evaluate for multiple possible differential diagnoses. These include the more common etiologies of infectious disease, interstitial lung disease and toxicities of chemotherapeutic agents, as well as less common diagnoses of lymphangitic carcinomatosis and pulmonary tumor emboli. Antemortem diagnosis of pulmonary tumor embolism or lymphangitic carcinomatosis is rare and diagnosis more often made on autopsy.

Prognosis for pulmonary tumor embolism and lymphangitic carcinomatosis is poor. There are no specific treatments for pulmonary tumor embolism and lymphangitic carcinomatosis other than the treatments directed at the primary tumor. Approximately half of patients die within two months of symptom onset. A recent review reported observed better survival in patients identified between the years 2000 and 2018 compared to earlier patients from 1970 through 1999.<sup>4</sup> These are rare conditions with non-specific symptoms and diagnosis

is often delayed or not made until autopsy. Earlier diagnosis may prolong survival time and reduce patient suffering. In our patient, the early diagnosis led to alteration to treatment and early involvement of palliative care.

### **Conclusion**

Patients with cancer, dyspnea and abnormal chest imaging, have a broad differential diagnosis. They include the more common infections, interstitial lung disease and chemotherapy toxicities, as well as the less common lymphangitic carcinomatosis and pulmonary tumor emboli. It is reasonable to initiate evaluation with conservative measures and treat empirically with antimicrobials. If symptoms and abnormal chest imaging persist, a definitive diagnosis should be sought with bronchoscopy, BAL and biopsy when clinically feasible.

### **Figures**

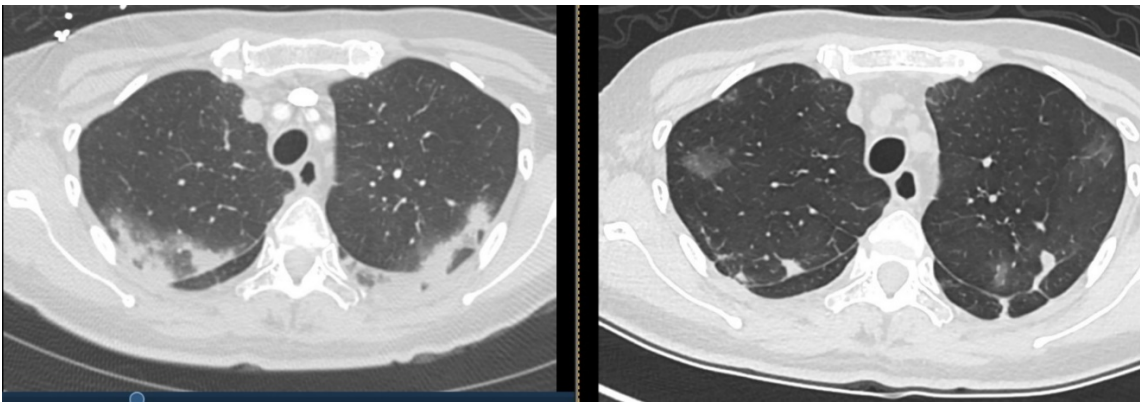


Figure 1a. Left - initial CT chest with right upper lobe and left upper lobe infiltrates. Right - subsequent CT chest with improvement to right upper lobe and left upper lobe infiltrates.

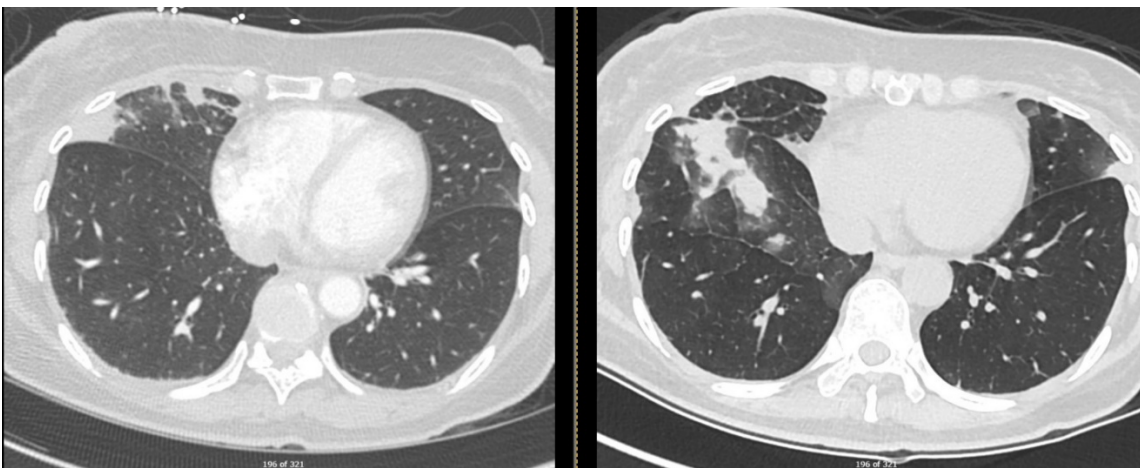


Figure 1b. Left - initial CT chest with right middle lobe infiltrate and without right lower lobe infiltrate. Right - subsequent CT chest with improvement to right middle lobe infiltrate and new right lower lobe infiltrate.

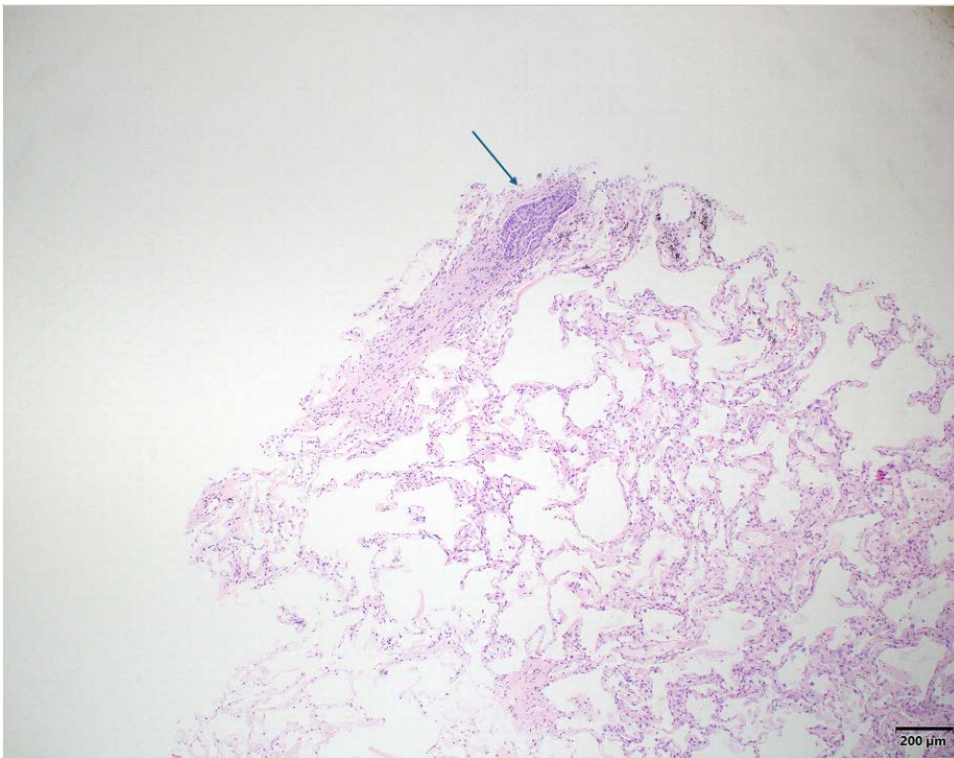


Figure 2a. Surgical pathology of right lung cryobiopsy showing tumor embolus in artery

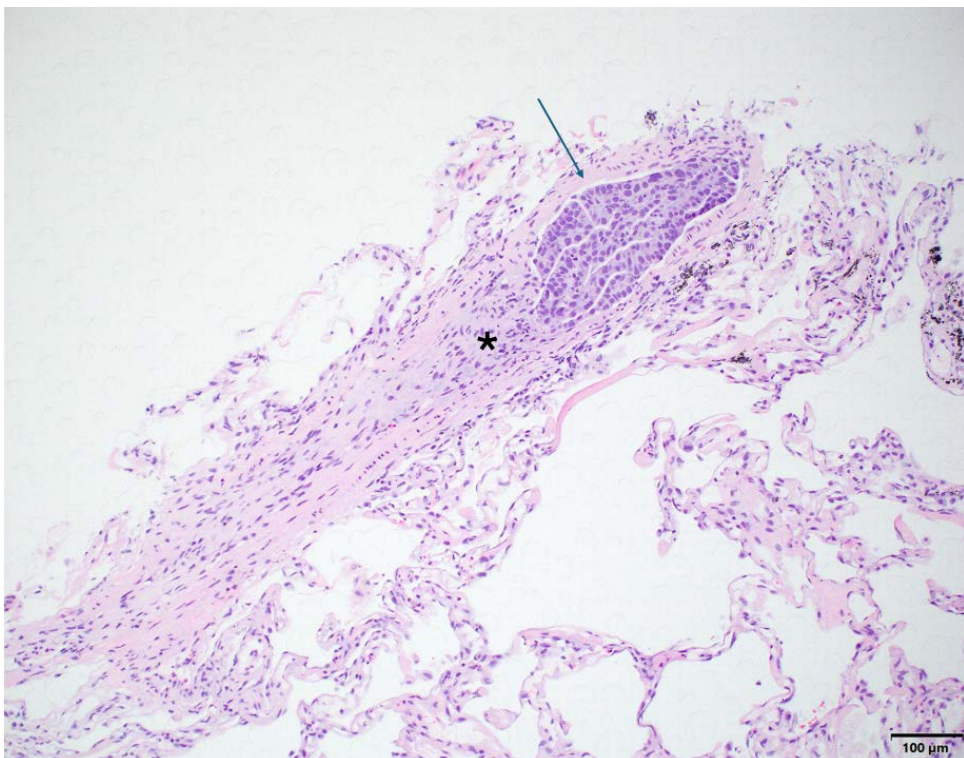


Figure 2b. Surgical pathology of right lung cryobiopsy with arrow showing tumor embolus in artery and star showing organized thrombus adherent to tumor

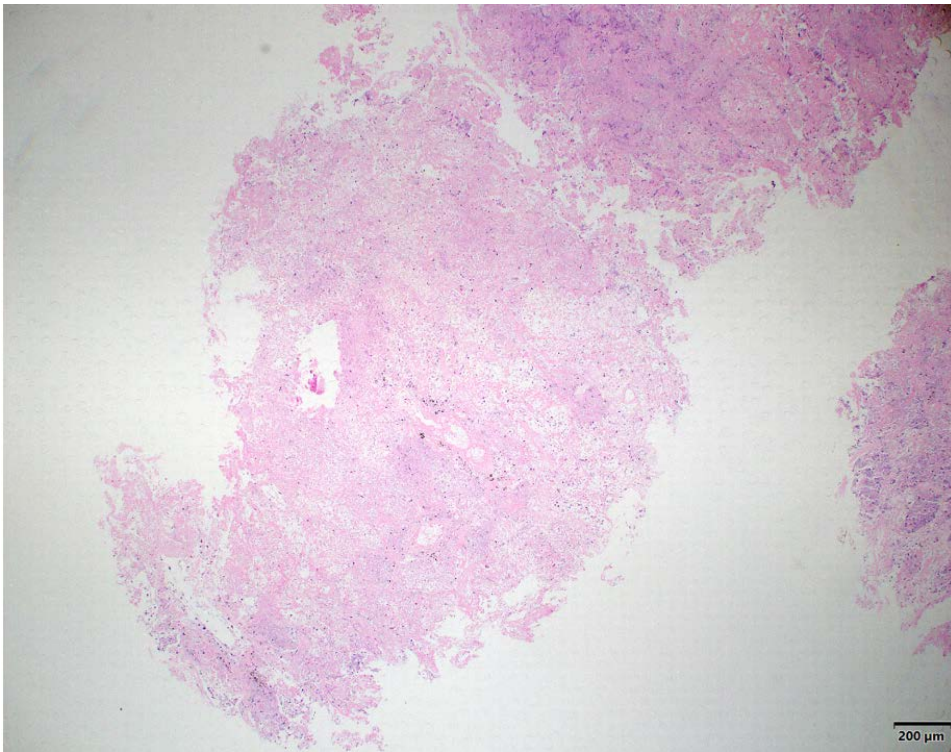


Figure 2c: Surgical pathology of right lung cryobiopsy showing necrotic tissue

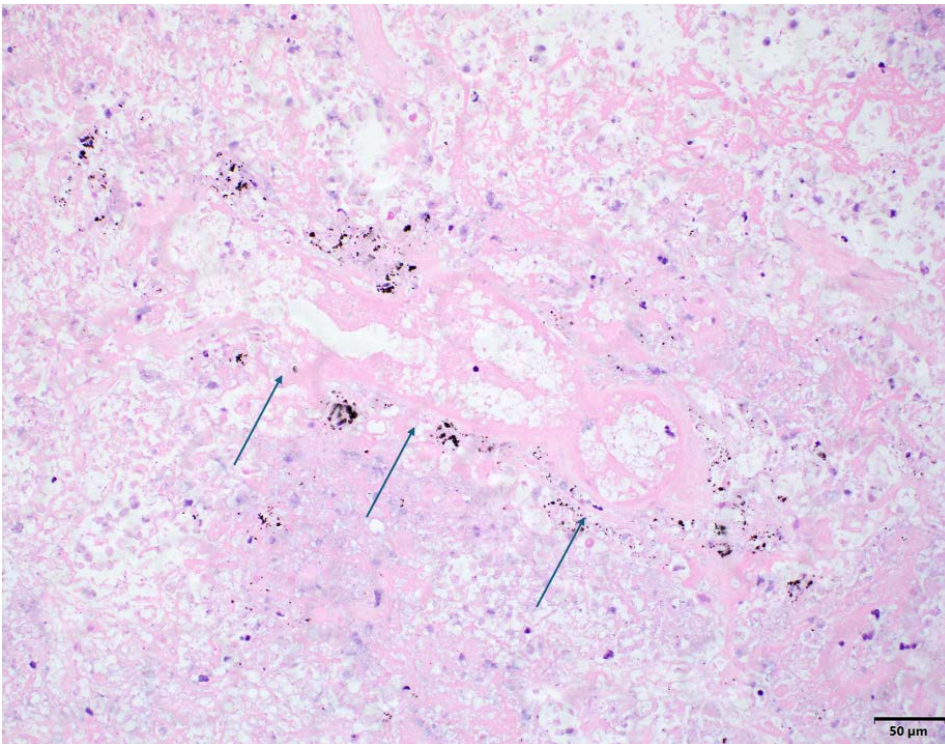


Figure 2d: Surgical pathology of right lung cryobiopsy at higher power showing there is a devitalized artery surrounded by anthracotic (black) pigment, suggesting the necrotic tissue is infarcted lung

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