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Rapidly Progressive Pulmonary Nodules and Mass-Like Opacities: A Case Report of Pulmonary T-Cell Lymphoma

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Abstract

Pulmonary involvement by T-cell lymphoma is rare. Its radiographic features - consolidation, ground-glass opacities, nodules, and pleural effusions - overlap substantially with infectious, inflammatory, and other neoplastic processes, often leading to diagnostic delay. An elderly immunocompetent woman who was initially hospitalized for suspected community-acquired pneumonia developed progressive respiratory failure after which robotic-assisted bronchoscopy with transbronchial biopsy revealed T-cell lymphoma. This case highlights the diagnostic challenge of pulmonary lymphoma, which can closely mimic pneumonia and other common pulmonary conditions. Progressive pulmonary opacities refractory to antimicrobial therapy should prompt early consideration of lymphoma and timely tissue biopsy. Prompt diagnosis and initiation of chemotherapy can lead to favorable outcomes, even in patients with advanced respiratory failure.

Keywords: T-cell; Lymphoma; Pulmonary; Nodules; Masses

Introduction

T-cell lymphoma involvement of the lungs is rare. Lymphoma with pulmonary involvement is more often of the B-cell type. The rapid progression of pulmonary nodules and mass-like opacities over weeks is more suggestive of an infectious etiology. We review a case of an immunocompetent patient who developed progressive dyspnea and hypoxia without improvement on antibiotics and rapidly progressive radiographic abnormalities with the ultimate diagnosis of peripheral T-cell lymphoma.

Case Presentation

A 62-year-old female with no significant past medical history was referred to the Emergency Department (ED) from urgent care for tachycardia and presumptive community-acquired pneumonia. She presented to the ED with a productive cough with white sputum of 3 weeks duration. She denied fever, chills, hemoptysis, pleuritic chest pain, or lower extremity swelling. Initial vitals were notable for tachycardia to 130 beats per minute. She was afebrile and without hypoxia.

Physical examination revealed right lower lung inspiratory crackles and was otherwise unremarkable. Computed tomography (CT) chest imaging showed a dense right lower lobe consolidation with surrounding ground glass in addition to multiple bilateral mixed density nodules measuring up to 1.7 cm, and a moderate right pleural effusion (Figure 1A). The patient was admitted for treatment of presumed community acquired pneumonia. She received several days of intravenous antibiotics with ceftriaxone and vancomycin and was sent home to complete a 10-day course of antibiotics with oral amoxicillin-clavulanic acid. The pulmonary team was consulted and arranged a follow up appointment outpatient.

The patient returned to the ED nine days post-discharge with progressively worsening shortness of breath and productive cough, and new hypoxia requiring high flow nasal cannula (HFNC). She reported having completed the full course of oral antibiotics but had been unable to make it to her outpatient pulmonary appointment. Repeat CT chest showed significantly progressed multiple extensive mixed density mass-like opacities throughout both lungs, significant progression of the right lower lobe opacity with extensive lucency and less air bronchograms, and mediastinal and right hilar adenopathy which appeared more prominent and more densely enhancing than 12 days prior (Figure 1B). A broad infectious workup was sent. Infectious workup included galactomannan, fungitell, Interferon Gamma Release Assay, HIV antigen/antibody test and HIV viral load, Haemophaelis influenza B IgG, Mycoplasma pneumoniae IgM/IgG, Chlamydia psitacci IgM/IgG, Brucella IgG, Coxiella IgM/IgG, Bartonella henselae and Bartonella quintana IgM/IgG, EBV, coccidioides IgM/IgG, hepatitis B and C, all of which resulted as negative. Autoimmune workup for vasculitis with C-ANCA and P-ANCA were both negative. Empiric antibiotics were started with vancomycin, piperacillin/tazobactam, and azithromycin; additionally, she received 6 days of methylprednisolone (60 mg) followed by 2 days of prednisone (30 mg) for treatment of severe pneumonia versus organizing pneumonia. Thoracentesis was performed and revealed an exudative pleural effusion, with cytology and culture resulting negative. The patient continued to have increasing oxygen requirements on HFNC. Repeat CT chest was obtained on day 8 of hospitalization (Figure 1C).

CT revealed worsening bilateral nodular and ground glass opacities throughout the lungs with persistent right lower lobe consolidation. She was transferred to the medical intensive care unit and intubated in preparation for robotic assisted bronchoscopy with transbronchial biopsy. Bronchoalveolar lavage (BAL) was performed, and biopsy was taken from a mass in the posterior right upper lobe. The BAL specimen was positive for malignant cells, which demonstrated an aberrant T or NK cell immunophenotype by flow cytometry (CD45+, surface CD3-, cytoplasmic CD3+, CD2 dim+, CD7 bright+, CD5-, CD4-, CD8+, CD10-, CD25-, CD56-, TCRγδ-). The tissue biopsy showed features consistent with T-cell lymphoma, showing an extensive infiltrate of predominantly small to medium-sized T-lymphocytes, with an intraepithelial component; by immunohistochemistry the atypical lymphocytes were CD3+, CD2+ (weak to moderate), CD7+, CD5-, CD8+, CD4-, CD25-, FOXP3-, CD34-, TdT-, CD1a-, Granzyme B-, CD30 weak+ in small subset, with Ki67 proliferation index of approximately 60% (Figure 2). In situ hybridization stain for EBV-encoded small RNA (EBER) was negative. Serological assays for Human T Lymphocyte Viruses 1 and 2 were negative. The patient was transferred to a higher-level care facility within the hospital system for initiation of chemotherapy. On day 18 of hospitalization, treatment was initiated with brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone (BV-CHP). A tracheostomy was placed on day 19 of hospitalization and rapid ventilator weaning to trach collar was initiated on day 24.

Follow-up CT chest imaging nearing hospital discharge was notable for a decrease in the size and number of mixed solid and ground glass opacities throughout the bilateral lungs (Figure 1D). These imaging findings correlated with clinical improvement as the patient was able to be weaned rapidly from the ventilator and the tracheostomy was de-cannulated prior to hospital discharge to acute rehabilitation.

Two months later, the patient's course was complicated by spread of lymphoma to the brain and leptomeninges, severe malnutrition, and overall deterioration. Five months after initial diagnosis, the patient decided to pursue comfort care and passed away shortly thereafter.

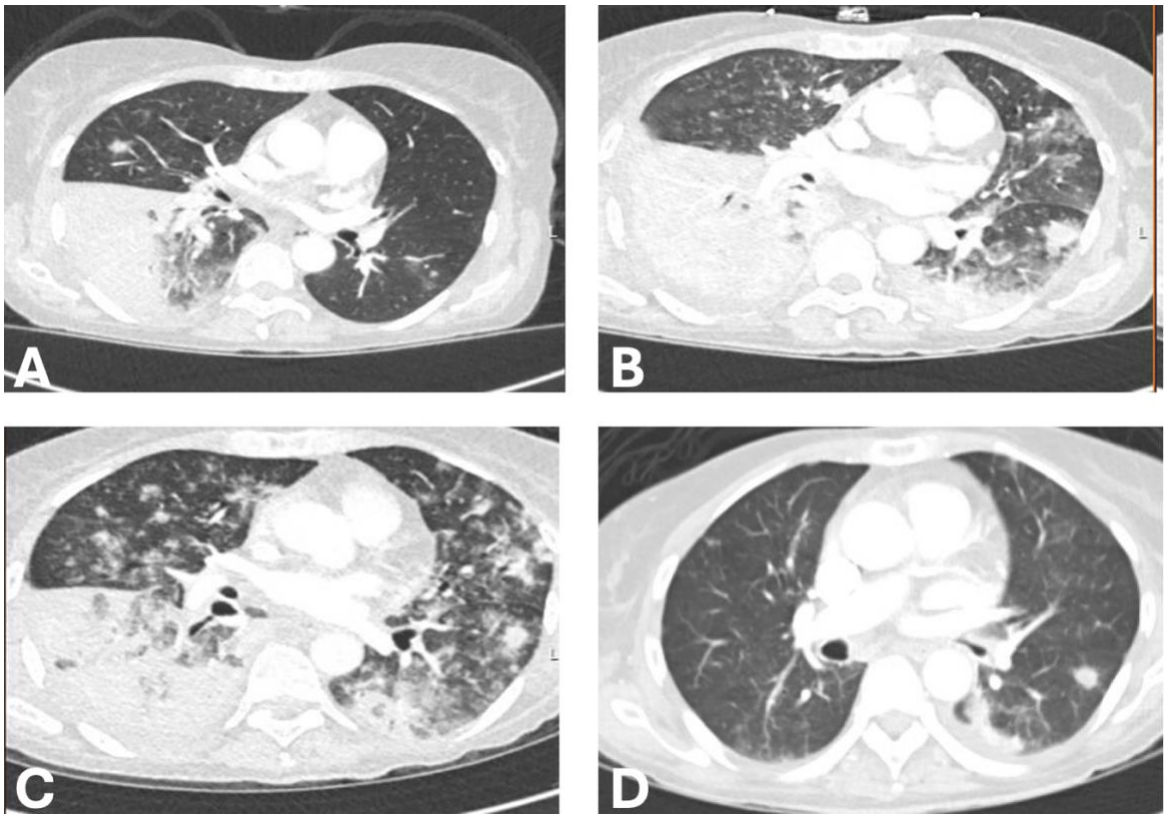

Figure 1: CT Chest Imaging showing progression of lung opacification over time.

(A) CT Chest from day 1, on initial presentation

(B) CT Chest on readmission, obtained 12 days after image A

(C) CT Chest follow up, obtained 20 days after image A

(D) CT Chest after 2 cycles of chemotherapy

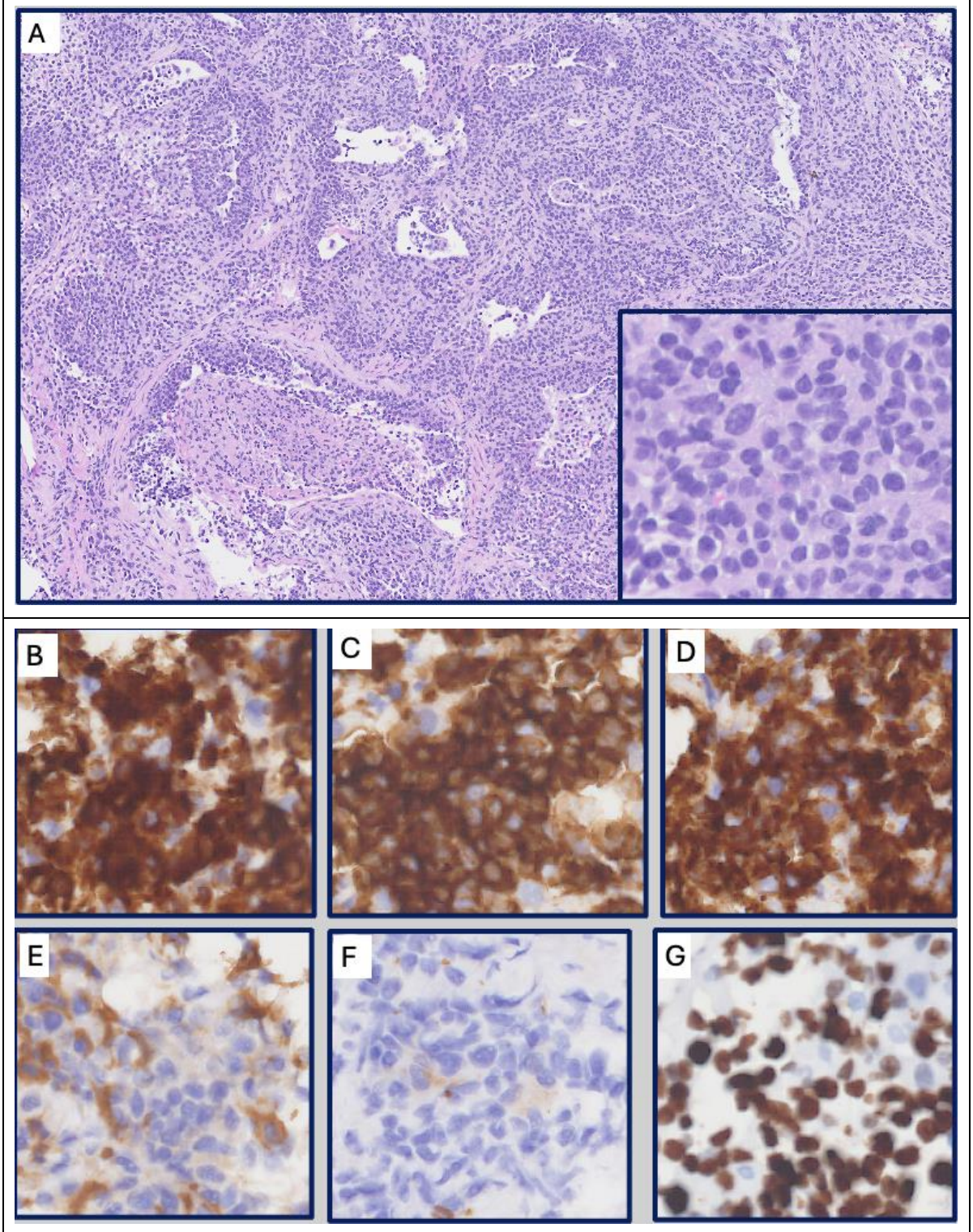

Figure 2: Morphological and immunophenotypic features of the lung cryobiopsy. (A) Haematoxylin & eosin stain showing lung with extensive infiltration by variable-sized atypical lymphocytes throughout the interstitium, and with an intraepithelial component. (B-G) By immunohistochemistry, the atypical cells express CD3 (B), CD7 (C), CD8 (D), are negative for CD4 (E), with aberrant loss of CD5 (F), and Ki67 proliferation index of approximately 60%. A, x100 (inset x400); B-G, x400.

Discussion

The incidence of peripheral T-cell lymphoma (PTCL) has been increasing in the United States. Abouyabis et al. reported that the annual incidence rose from 0.2 to 0.9 cases per 100,000 population between 1992 and 2005, with higher rates observed among Black individuals [1]. Among PTCL subtypes, one of the most common is peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS), which encompasses T-cell lymphomas that do not meet criteria for more specifically defined categories in the World Health Organization classification. Pulmonary involvement is relatively uncommon but has been reported in approximately 2–8% of PTCL-NOS cases [2,3].

Pulmonary manifestations of lymphoma are heterogeneous. A review of CT findings in patients with non-Hodgkin lymphoma demonstrated that the most frequent abnormalities included mass or mass-like consolidation larger than 1 cm (56%), small pulmonary nodules under 1 cm (56%), and peribronchial thickening (69%) [4]. Additional findings such as pleural-based masses, mediastinal adenopathy, and pleural effusions have also been reported in pulmonary lymphoma. These radiographic features contribute to the diagnostic challenge of PTCL-NOS, as the imaging patterns often overlap with many common pulmonary diseases.

The radiographic presentation of pulmonary T-cell lymphoma can mimic a wide spectrum of infectious, inflammatory, and neoplastic processes. Dense consolidation with surrounding ground-glass attenuation, as seen in our patient, often raises concern for bacterial pneumonia or aspiration, particularly when accompanied by systemic signs of infection. However, these conditions typically demonstrate interval improvement with appropriate antimicrobial therapy, whereas lymphoma often progresses or remains unchanged. The presence of mixed-density nodules introduces additional diagnostic considerations. Angioinvasive fungal infections such as aspergillosis or mucormycosis may produce nodules with surrounding ground-glass halos (“halo sign”) [5], a pattern also observed in eosinophilic pneumonia, septic embolism, vasculitis, and certain metastatic malignancies [6].

Inflammatory conditions can closely resemble pulmonary lymphoma. Organizing pneumonia frequently presents with peripheral or peribronchial consolidations with ground-glass components and may appear mass-like [7]. Granulomatosis with polyangiitis and other pulmonary vasculitides can produce multifocal nodules, sometimes cavitary, along with ground-glass opacity due to hemorrhage or capillaritis, making distinction from lymphoma difficult without biopsy [8]. Sarcoidosis may also mimic pulmonary lymphoma by demonstrating nodular thickening along bronchovascular bundles and interlobular septa, and may progress to conglomerate opacities or mass-like lesions in advanced stages [9]. Diffuse alveolar hemorrhage (DAH) represents another important mimic, as it often produces patchy ground-glass opacities or consolidation with rapid radiographic fluctuation [10]. Furthermore, metastatic disease, particularly from angiosarcoma, melanoma, or carcinoma, can produce hemorrhagic or mixed-attenuation nodules that closely resemble lymphomatous lesions. Given the substantial overlap among these entities, no single CT pattern reliably distinguishes pulmonary lymphoma from its mimics, reinforcing the necessity for early histopathologic confirmation [11].

BAL remains useful as an initial screening tool when combined with clonality analysis for detecting monoclonal B-cell populations, as in extranodal marginal zone (MALT) lymphoma, or other B-cell lymphomas [12]. However, BAL has limited sensitivity or specificity for most other types of pulmonary lymphoma, including T-cell lymphoma [13]. Definitive diagnosis of pulmonary lymphoma most often requires tissue biopsy (e.g. transbronchial lung biopsy (TBLB), transbronchial lung cryobiopsy (TBLC) or surgical biopsy). The key advantage of specimen biopsy is the ability to obtain intact tissue architecture required for lymphoma subtyping, immunohistochemistry, and molecular characterization. Several studies have compared the diagnostic yield and accuracy of TBLB vs TBLC, as these are less invasive diagnostic approaches compared to a surgical approach for specimen collection.

Cryobiopsy is a technique that yields specimens that are larger in size, with less crush artifact, and with more viable lung tissue compared to those obtained by TBLB with forceps [14,15]. In a study by Kinoshita et al, 100 patients underwent TBLB, TBLC, and cytology brushings; diagnostic yield was compared between these modalities. The study found no significant difference between TBLB and TBLC overall, though when stratified by biopsy site, they found that TBLC was significantly superior to TBLB for specimen collection specifically in the lower lung lobes [16]. Another study by Atkas et al, found that cryobiopsy yielded a diagnosis significantly more often than transbronchial forcep biopsy for the diagnosis of lung cancer [14]. A meta-analysis comparing the two modalities found that cryobiopsy was superior in diagnostic accuracy compared to transbronchial biopsy [17]. No studies were identified comparing TBLB vs TBLC for diagnosis specifically of T-cell lymphoma. Future data on diagnostic accuracy with these different techniques would be helpful for clinicians deciding on a diagnostic approach for pulmonary nodules concerning for lymphoma.

Because of the broad differential for pulmonary nodules and opacifications, lymphoma should remain an important diagnostic consideration in patients with persistent respiratory symptoms and progressive pulmonary opacities despite appropriate antimicrobial therapy. Several reports describe similar presentations in which delayed recognition contributed to clinical deterioration, and some patients died before receiving definitive treatment. Although this patient ultimately succumbed to lymphoma, our case illustrates that pulmonary involvement by T-cell lymphoma can demonstrate marked radiographic improvement and rapid resolution of respiratory failure with prompt initiation of lymphoma-directed chemotherapy. Early identification of suspected T-cell lymphoma and timely pursuit of biopsy are critical, as pulmonary T-cell lymphoma may respond favorably to treatment when diagnosed without delay.

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