Pulmonary involvement of peripheral T-cell lymphoma manifesting as crazy paving pattern

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Crazy paving pattern is a finding on computed tomography of the chest that is characterized by interlobular septal thickening and ground-glass opacities. Though classically associated with pulmonary alveolar proteinosis, the differential diagnosis for this pattern is broad, and initial workup includes bronchoscopy with bronchoalveolar lavage to evaluate for malignancy, diffuse alveolar hemorrhage, pulmonary alveolar proteinosis, infection, and eosinophilic pneumonia. Herein we present an unusual case of peripheral T-cell lymphoma not otherwise specified (PTCL NOS) with pulmonary involvement that demonstrated crazy paving pattern. The diagnosis was confirmed after cytology from bronchoalveolar lavage revealed atypical lymphocytes with an immunologic profile consistent with the patient's known PTCL NOS.

Crazy paving pattern is the appearance of ground-glass opacities with superimposed linear thickening on computed tomography (CT) of the chest that resembles irregularly shaped paving stones (1). Although classically associated with pulmonary alveolar proteinosis (PAP), the differential diagnosis for this finding is broad (1). Workup should include bronchoscopy with bronchoalveolar lavage (BAL).

CASE DESCRIPTION

A 77-year-old man with peripheral T-cell lymphoma not otherwise specified (PTCL NOS) presented with 5 months of dyspnea on exertion and cough productive of yellow sputum with occasional streaks of blood. He had been diagnosed with PTCL NOS 4 years prior when routine labs revealed a white-cell count of 28,000/mm³, with 77% lymphocytes. Peripheral smear revealed a predominance of lymphocytes with mature, clumped chromatin and frequent nuclear convolutions and lobulations. Peripheral flow cytometry demonstrated a predominant population of immunophenotypically aberrant T cells with a “double-negative” immunophenotype (CD3⁺, CD5⁺, CD7⁺, CD4⁻, CD8⁻, CD20⁻). Markers for human T-cell lymphotropic virus-1 were negative. Subsequent bone marrow biopsy was performed, with flow cytometry demonstrating abnormal T cells that were CD4⁻ and CD8⁻ by flow cytometry; immunohistochemistry revealed that the atypical T cells were negative for markers associated with angioimmunoblastic T-cell lymphoma and anaplastic large cell lymphoma. CT of the chest, abdomen,

and pelvis revealed enlarged axillary, mediastinal, and inguinal lymph nodes, all of which were <2 cm, and small pulmonary nodules in the right upper lobe with a tree-in-bud configuration. The patient was ultimately diagnosed with an atypical PTCL NOS. Given the absence of symptoms and a stable white blood cell count, the patient and his medical team elected to pursue expectant management without chemotherapy. His lymphocytosis was monitored serially over the 4 years prior to admission and remained stable. He did not have repeat chest imaging over that interval.

He was in his usual state of health until 5 months prior to admission when he developed cough, fever, and dyspnea on exertion. He was seen in an urgent care clinic and was treated with a course of levofloxacin, after which his symptoms improved. Three months later, his cough returned and was newly productive of blood-tinged sputum and several small blood clots. He received cefpodoxime and azithromycin for presumed community-acquired pneumonia. Despite this treatment, his symptoms persisted and the following month a CT of the chest was obtained, which revealed ground-glass opacities in the lower lobes. He was again treated with cefpodoxime and azithromycin, which temporarily improved his symptoms. One week prior to the current admission, he attempted a 4-mile hike, which he was previously able to complete without difficulty, and noted significant dyspnea throughout the hike. On the day prior to admission, he experienced shortness of breath with minimal exertion that limited his ability to ambulate, prompting his presentation to the emergency department.

In the emergency department, his temperature was 98.2°F; heart rate, 83 beats per minute; blood pressure, 137/79 mm Hg; and oxygen saturation, 88% on room air. His jugular venous pulse was 6 cm, fine crackles were heard in the bilateral lower lung fields, and lower extremities were not swollen. Laboratory results were notable for a white-cell count of 34,000/mm³, with 68% lymphocytes. Chest x-ray revealed bilateral patchy opacities in the lower lung zones, and CT of the chest showed intralobular septal thickening superimposed on ground-glass

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Figure 1. Chest CT with crazy paving pattern: (a) coronal view and (b) axial view.

opacities consistent with crazy paving pattern (*Figure 1*). A bronchoscopy with BAL revealed clear, frothy secretions in the airways. Gram stain and culture from the BAL did not reveal microorganisms. Cytology disclosed atypical lymphocytes with an immunoprofile consistent with the patient's prior T-cell lymphoma (*Figure 2*). Positron emission tomography-CT was remarkable for moderate uptake in the right upper lobe and mild diffuse bilateral low level uptake compatible with BAL findings of T-cell lymphoma. While his lymphoma had previously been managed expectantly, the severity of his pulmonary symptoms prompted initiation of chemotherapy. He was discharged with oxygen therapy and treated with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) as an out-patient. After his first round of chemotherapy, his cough and dyspnea improved.

Figure 2. Bronchoalveolar lavage fluid cytology revealing atypical lymphocytes with multilobed nuclei. The immunohistochemistry stains were consistent with a diagnosis of peripheral T-cell lymphoma.

DISCUSSION

Crazy paving refers to a pattern of linear thickening and ground-glass opacities on CT of the chest, resembling irregularly shaped paving stones (1). The linear thickening can manifest as thickening of interlobular septa with or without thickening of the intralobular interstitium or the linear deposition of material at the borders of the acini (1).

The differential diagnosis for crazy paving pattern is broad, and etiologies can be classified based on the duration of the patient's symptoms. For patients who present acutely, potential diagnoses include pulmonary edema, acute interstitial pneumonitis or adult respiratory distress syndrome, diffuse alveolar hemorrhage (DAH), infection, radiation pneumonitis, and eosinophilic pneumonia (1). For those with subacute or chronic presentations, one should consider interstitial lung disease with a usual interstitial pneumonia or nonspecific interstitial pneumonia pattern, PAP, organizing pneumonia, chronic eosinophilic pneumonia, and malignancy (1). In the absence of a clear diagnosis, patients with crazy paving pattern should be evaluated with bronchoscopy with BAL to distinguish between these etiologies. Some patients will need a surgical lung biopsy if the diagnosis remains unclear following BAL.

In our patient, DAH was initially considered given his hemoptysis. DAH is a clinicopathologic syndrome in which disruption of the alveolar and capillary basement membranes allows red blood cells to enter the alveolar space (2). DAH can present with hemoptysis, anemia, diffuse pulmonary infiltrates, and hypoxemic respiratory failure. The diagnosis is made when serial BALs reveal progressively more hemorrhagic fluid (2). Given the absence of bloody fluid seen on BAL, DAH was excluded in this patient.

BAL is also helpful in the diagnosis of pulmonary infection, eosinophilic pneumonia, PAP, and malignancy. The diagnosis of PAP, however, may require transbronchial or open surgical biopsy. The diagnosis is confirmed with a positive periodic

acid-Schiff (PAS) stain from BAL washings or lung biopsies (3). Because PAS staining may not be routinely performed on BAL washings, clinicians should specifically request PAS staining when suspecting the diagnosis of PAP.

PTCL is a subgroup within T-cell non-Hodgkin's lymphoma with an incidence of <1 per 100,000 people in the United States. The classification of the subtypes of PTCL is complex (4). PTCL NOS is the most common group of PTCL, accounting for 25.9% of cases (5). Eighty-seven percent of patients with PTCL NOS present with nodal disease, while extranodal disease involving the lungs and pleura occurs in 21% of cases (6, 7). The prognosis in PTCL NOS is generally poor, with a 10-year overall survival rate of approximately 10% (5). However, the prognostic index for PTCL (PIT) can further risk-stratify patients. The PIT includes age >60 years, normal or elevated lactate dehydrogenase levels, performance status, and bone marrow involvement; the 5-year overall survival is 62% for those with no adverse prognostic factors and 18% for those with 3 or 4 adverse prognostic factors (8).

First-line therapy of PTCL NOS is CHOP, which in a meta-analysis of 2912 patients had a 5-year overall survival of 37% (9). While more aggressive chemotherapy regimens including autologous stem cell transplantation have been attempted, they are typically reserved for more aggressive T-cell lymphomas, and further studies are needed to determine which subgroups of PTCL would benefit from these therapies (10).

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