Photo Quiz

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TANAFFOS

Pulmonary Nodules and Lymphadenopathy in a Patient with Advanced HIV Infection

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WHAT IS YOUR DIAGNOSIS?

A 28-year-old woman was admitted with a two-month history of dysphagia and a two-week history of non-massive hemoptysis. She had been diagnosed with human immunodeficiency virus (HIV) infection five years earlier and was receiving antiretroviral therapy, although adherence was poor.

On admission, she was afebrile and hemodynamically stable. Physical examination revealed multiple violaceous cutaneous plaques on the trunk and extremities. Lung examination was unremarkable. Multiple bilateral, non-tender, mobile cervical lymph nodes were palpable. On abdominal examination, the splenic edge was palpable below the left costal margin.

Laboratory studies demonstrated pancytopenia, with a white blood cell count of 2.46 × 10^9/L (absolute neutrophil count, 1.96 × 10^9/L), hemoglobin of 10.6 g/dL, and platelet count of 44 × 10^9/L. The erythrocyte sedimentation rate was 52 mm/h. Her HIV viral load was 1895 copies/mL, and the CD4+ T-lymphocyte count was 7 cells/µL.

Contrast-enhanced CT of the neck demonstrated multiple bilateral cervical and supraclavicular lymphadenopathies, the largest measuring approximately 125 × 90 mm, associated with contour deformity and luminal narrowing of the oropharynx. Endoscopic evaluation revealed an erythematous lesion on the mucosal surface of the left nasal cavity; however, further evaluation of the nasopharynx was not feasible because of significant upper airway obstruction.

Contrast-enhanced CT of the chest revealed multiple bilateral pulmonary nodules with mediastinal, hilar, and axillary lymphadenopathies (Figure 1). CT of the abdomen demonstrated mild hepatosplenomegaly.

Given the presence of pancytopenia and generalized lymphadenopathy, both infectious and hematologic etiologies were considered. Sputum smear examination for acid-fast bacilli and Mycobacterium tuberculosis GeneXpert testing were negative. Bone marrow examination and an excisional biopsy of a cervical lymph node were subsequently performed for diagnostic evaluation. Histopathologic findings from the lymph node biopsy are shown in Figure 2.

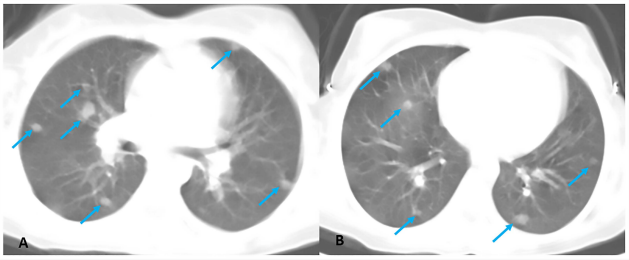

Figure 1. A & B: Contrast-enhanced chest CT (axial image) demonstrates multiple bilateral peribronchovascular and subpleural nodules, several with flame-like extensions (arrows)

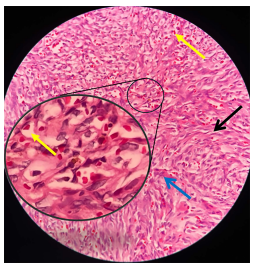

Figure 2. High-power photomicrograph showing intersecting fascicles of atypical spindle cells (black arrow) and erythrocytes within slit-like vascular spaces in longitudinal section (blue arrow) and sieve-like spaces in cross-section (yellow arrow)

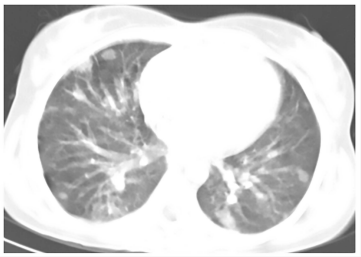

Figure 3. Follow-up contrast-enhanced chest CT demonstrates interval increase in the number and size of bilateral pulmonary nodules with more conspicuous peribronchovascular involvement

Answer

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Disseminated Kaposi Sarcoma

The final diagnosis was disseminated Kaposi sarcoma (KS) with cutaneous, lymph nodal, oropharyngeal, and pulmonary involvement in the setting of advanced HIV infection.

DISCUSSION

In this patient with advanced HIV infection, the combination of multiple pulmonary nodules, non-massive hemoptysis, pancytopenia, generalized lymphadenopathy, violaceous cutaneous plaques, and profound immunosuppression prompted a broad differential diagnosis, including tuberculosis, opportunistic infections, lymphoma, and Kaposi sarcoma. Given the negative results of the sputum smear for acid-fast bacilli and the Xpert MTB/RIF assay, and the concern for hematologic malignancy due to pancytopenia and diffuse lymphadenopathy, a bone marrow biopsy was performed; the findings showed no evidence of malignancy.

An excisional biopsy of a cervical lymph node was subsequently obtained for definitive diagnosis. Although the cutaneous lesions were clinically suggestive, the patient declined skin biopsy; histopathologic evaluation of the lymph node specimen established the diagnosis. Histopathologic evaluation of the cervical lymph node biopsy specimen demonstrated near-complete effacement of the native architecture by a vasoformative malignant neoplasm. The lesion was characterized by a dense proliferation of atypical spindle cells arranged in interlacing fascicles, forming characteristic irregular, slit-like vascular spaces containing red blood cells. Additionally, scattered hemosiderin-laden macrophages were present. Immunohistochemical analysis revealed that the neoplastic spindle cells were strongly positive for the vascular endothelial markers CD31 and CD34. These histomorphologic and immunophenotypic findings are consistent with Kaposi sarcoma (Figure 2). Plasma human herpesvirus 8 (HHV-8) PCR was also positive, supporting systemic HHV-8–associated disease. Taken together with the clinical and radiologic findings, these results established disseminated Kaposi sarcoma with pulmonary and oropharyngeal involvement.

HIV-associated malignancies remain a major cause of morbidity and mortality in patients with advanced HIV infection, with non-Hodgkin lymphoma and Kaposi sarcoma among the most common malignancies in this population (1, 2). Pulmonary nodules accompanied by mediastinal lymphadenopathy in HIV-infected patients should therefore raise suspicion for lymphoma, as this radiologic pattern is a well-recognized thoracic manifestation of the disease (2, 3). Accordingly, lymphoma was an important diagnostic consideration in this case.

At the same time, individuals with HIV are at markedly increased risk of developing Kaposi sarcoma compared with the general population, and the AIDS-related subtype typically occurs in younger patients than other immunosuppression-associated forms (4, 5). Pulmonary involvement is relatively common in AIDS-related KS, particularly in patients with cutaneous disease; approximately 45% of patients with cutaneous KS have concurrent pulmonary involvement (6). In addition to the skin, KS may affect the oropharyngeal mucosa, lymph nodes, liver, gastrointestinal tract, and spleen (4, 7). Therefore, in patients with advanced HIV infection who present with mucocutaneous lesions, diffuse lymphadenopathy, and pulmonary nodules, disseminated KS should be strongly considered alongside lymphoma and opportunistic infections.

Thoracic CT plays a central role in suggesting pulmonary KS. Although both lymphoma and KS may present with pulmonary nodules and mediastinal lymphadenopathy, pulmonary KS characteristically demonstrates peribronchovascular

nodules and ill-defined opacities with a flame-shaped configuration, reflecting tumor infiltration along the bronchovascular bundles (5, 8). These lesions are typically bilateral and may be associated with interlobular septal thickening, fissural nodularity, or pleural effusions. Recognition of this flame-shaped peribronchovascular pattern on CT (Figure 1), particularly in patients with advanced HIV infection and concomitant mucocutaneous lesions, may provide an important radiologic clue favoring pulmonary Kaposi sarcoma.

The patient's antiretroviral therapy was switched to a protease inhibitor–based second-line regimen, and systemic chemotherapy with intravenous doxorubicin hydrochloride (35 mg) was administered at 10-day intervals for two cycles**.** An initial partial response was observed, with reduction in the size of the cervical masses. She was discharged on the modified ART regimen with continuation of outpatient chemotherapy and prophylactic trimethoprim–sulfamethoxazole (one 400/80 mg tablet every 12 hours).

Approximately 50 days later, she was readmitted with progressive dyspnea, fever, and hypoxemia. Follow-up chest CT demonstrated interval progression of bilateral pulmonary nodules, with an increase in both number and size (Figure 3). Broad-spectrum antibiotics were initiated, and the trimethoprim–sulfamethoxazole dose was increased to sulfamethoxazole 4800 mg/day and trimethoprim 960 mg/day, administered in four divided doses**.** Despite treatment, her condition deteriorated, requiring endotracheal intubation, and she ultimately died following cardiac arrest. Unfortunately, disseminated Kaposi sarcoma is associated with substantially lower 3-year survival (53%) than localized disease (88%) (8, 9).

This case underscores several important teaching points. Pulmonary Kaposi sarcoma should remain in the differential diagnosis of pulmonary nodules and hemoptysis in patients with advanced HIV infection, particularly when accompanied by violaceous cutaneous lesions and generalized lymphadenopathy. Recognition of flame-shaped peribronchovascular nodules on chest CT—a characteristic pattern reflecting tumor infiltration along the bronchovascular bundles—may provide a key radiologic clue distinguishing pulmonary KS from other AIDS-related thoracic conditions. Finally, disseminated KS with visceral involvement may follow an aggressive clinical course and remains associated with substantial mortality despite antiretroviral therapy and chemotherapy.

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