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PHOTO QUIZ

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A Patient With Anemia, Lymphadenopathy, and Hepatosplenomegaly

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A 47-year-old man presented to the emergency department with 5 days of intermittent dizziness and fatigue. He described the sensation as if the room were spinning while he was standing. He reported that the sensation would last for approximately 2 minutes and was relieved on sitting. He reported increasing fatigue and feeling tired with routine activity in the previous 2 weeks. He did not have any history of vertigo, head trauma, loss of consciousness, seizures, fever, chills, cough, recent illness, or tinnitus.

History. The patient was originally from Ghana, where he had had an anemia workup a few years prior for an abnormally low hemoglobin level of 8 g/dL, for which he had received a 1-unit blood transfusion. However, he did not know the type or cause of the anemia. The patient's wife reported that she had noticed decreased body weight in the patient at that time. The patient then moved from Ghana to Italy, where he had had a pacemaker inserted after having become short of breath, with a heart rate of 45 beats/min.

The patient did not currently smoke. He had no history of alcoholism. He was sexually active with his wife. He did not report engaging in any high-risk behaviors. The patient had worked as

with his wife. He did not report engaging in any high-risk behaviors. The patient had worked as a stonecutter for several years.

Physical examination. At presentation, his vital signs were normal, with a heart rate of 73 beats/min, blood pressure of 143/77 mm Hg, temperature of 36.2°C, respiratory rate of 16 breaths/min, and oxygen saturation of 99% on room air. His height was 177 cm and his weight was 82.4 kg, resulting in a calculated body mass index of 26.3 kg/m2. He was anicteric, and the conjunctivas were pink. A chest-wall pacemaker was noted. The cardiac examination showed regular rate and rhythm, normal S1 and S2 only, and no murmurs. The lungs were clear to auscultation bilaterally. The abdomen was soft and nontender but with notable hepatosplenomegaly. No cervical, supraclavicular axillary, or inguinal adenopathy was present.

Diagnostic tests. The hemoglobin level was 9.1 g/dL (reference range, 13.0-17.0 g/dL) with a mean corpuscular volume of 62.9 μm3 (reference range, 80-100 μm3). Iron studies showed ferritin at 22.9 ng/mL (reference range, 18.0-464.0 ng/mL), iron at 24 μg/dL (reference range, 65-175 μg/dL), direct iron-binding capacity at 427 μg/dL (reference range, 261-462 μg/dL), and transferrin saturation at 6% (reference range, 20%-50%). The alkaline phosphatase level was 242 U/L (reference range, 53-128 U/L). The remainder of the findings of a complete blood cell count, a basic metabolic panel, and liver function tests were within normal limits. Lactate dehydrogenase was normal at 193 U/L. Hemoglobin electrophoresis showed hemoglobin A1 at 69.8%, hemoglobin A2 at 2.5%, hemoglobin F at 0%, and hemoglobin S at 27.7%, corresponding with an AS pattern of sickle-cell trait. Initial HIV test results were negative. A chest radiograph and a computed tomography (CT) scan of the abdomen were taken, the results of which are shown in **Figures 1-3**.

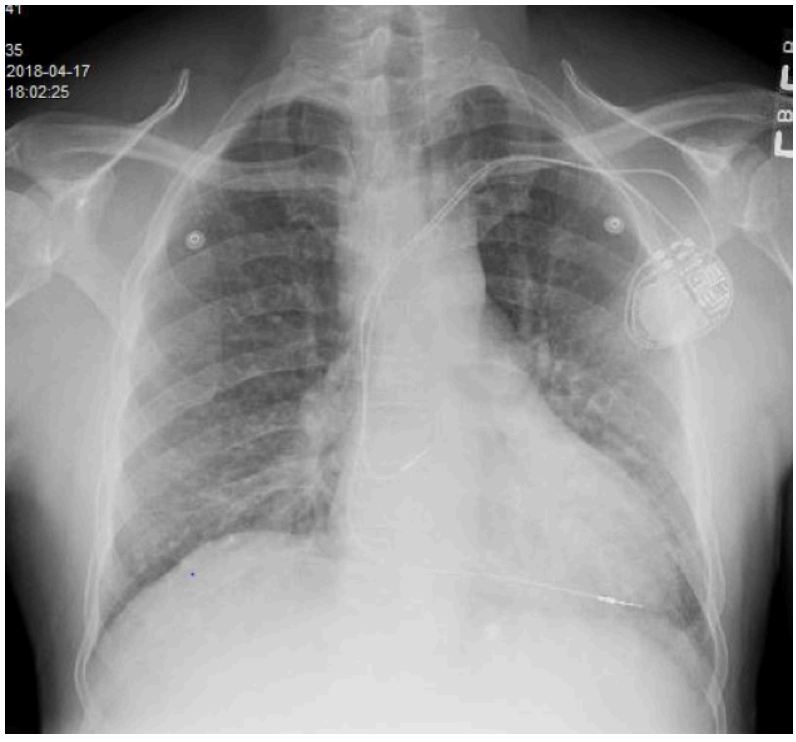

Figure 1.

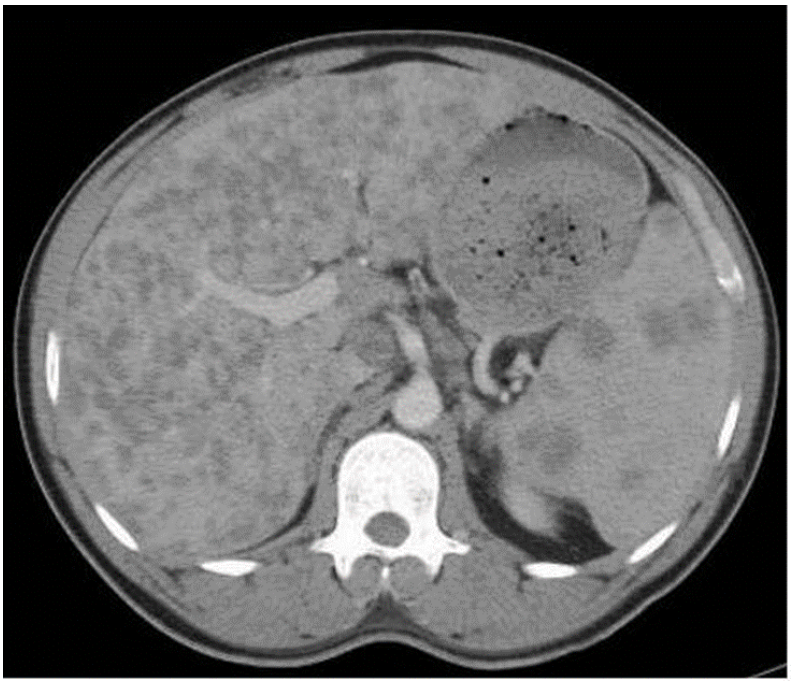

Figure 2

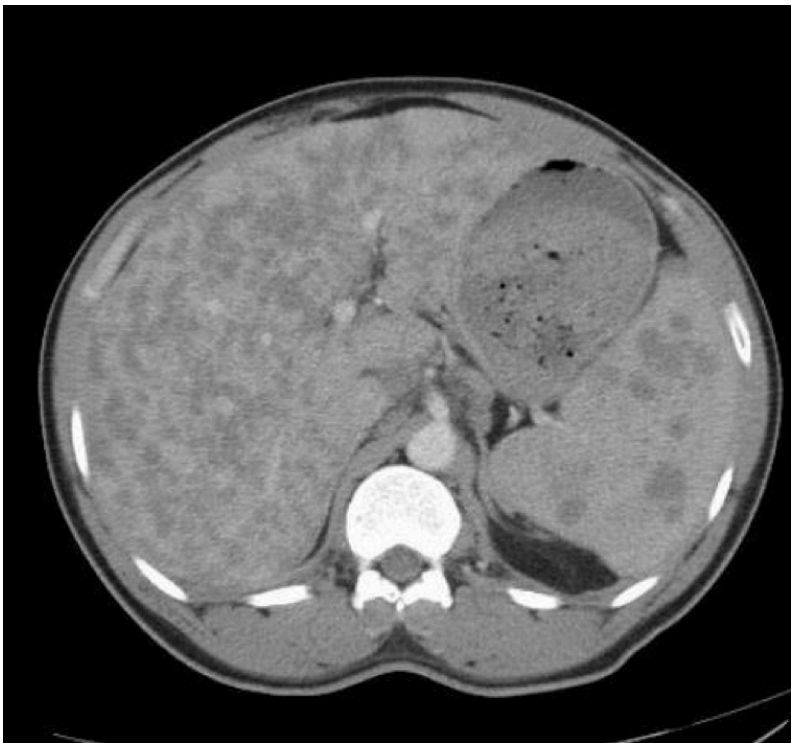

Figure 3

What's your diagnosis?

A. Berylliosis

B. Lymphoma

C. HIV

D. Sarcoidosis

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Answer: Sarcoidosis

The chest radiographs showed extensive mediastinal and bilateral lymphadenopathy (**Figure 1**).

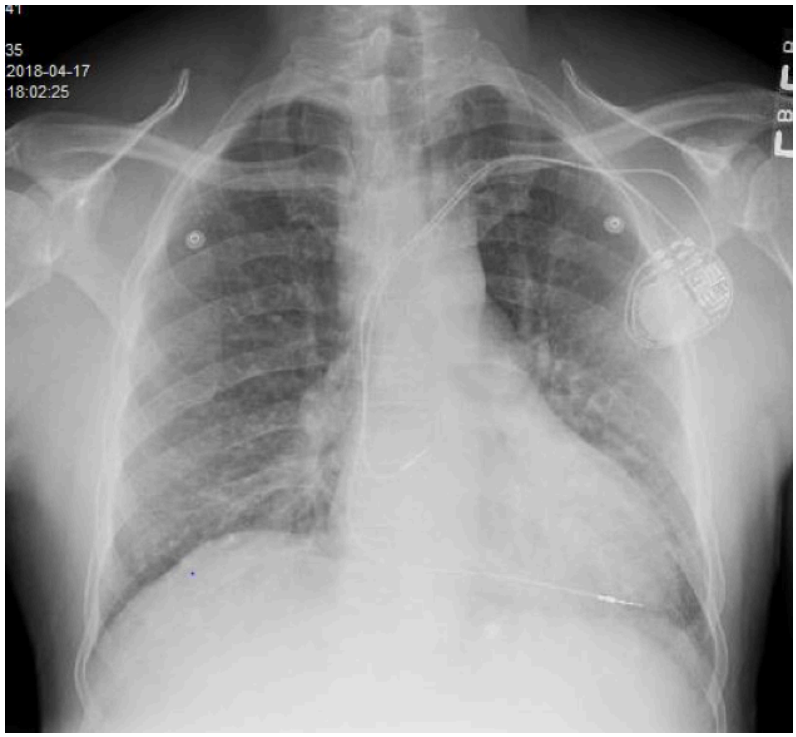

Figure 1.

The CT scan of the abdomen and pelvis (**Figures 2 and 3**) showed an enlarged liver almost completely replaced by multiple low-attenuation lesions, none larger than 20 to 30 mm. The spleen was also enlarged, with multiple lesions measuring up to 20 mm. Extensive enlarged upper abdominal, periportal, and retroperitoneal lymph nodes were noted. These radiographic findings were suggestive of sarcoidosis or lymphoma.

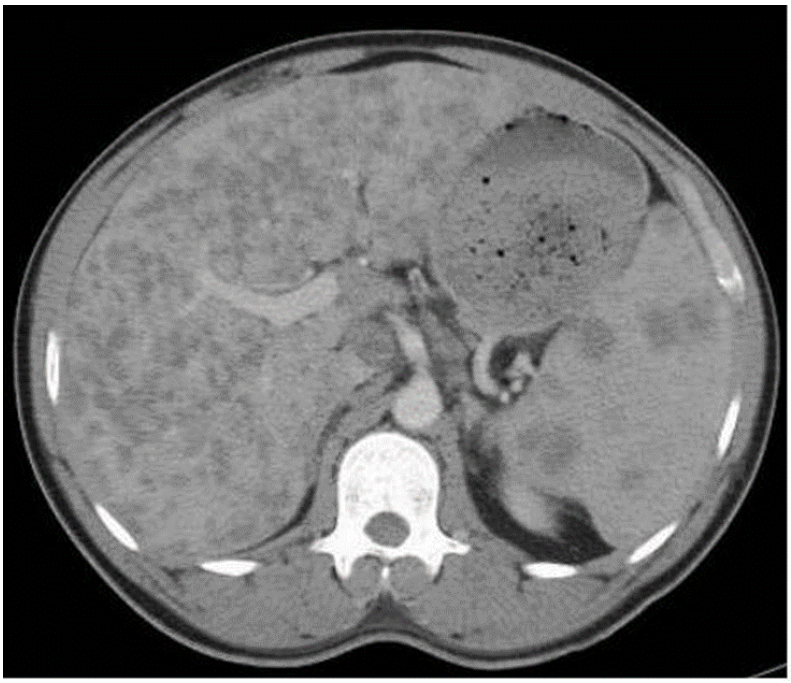

Figure 2

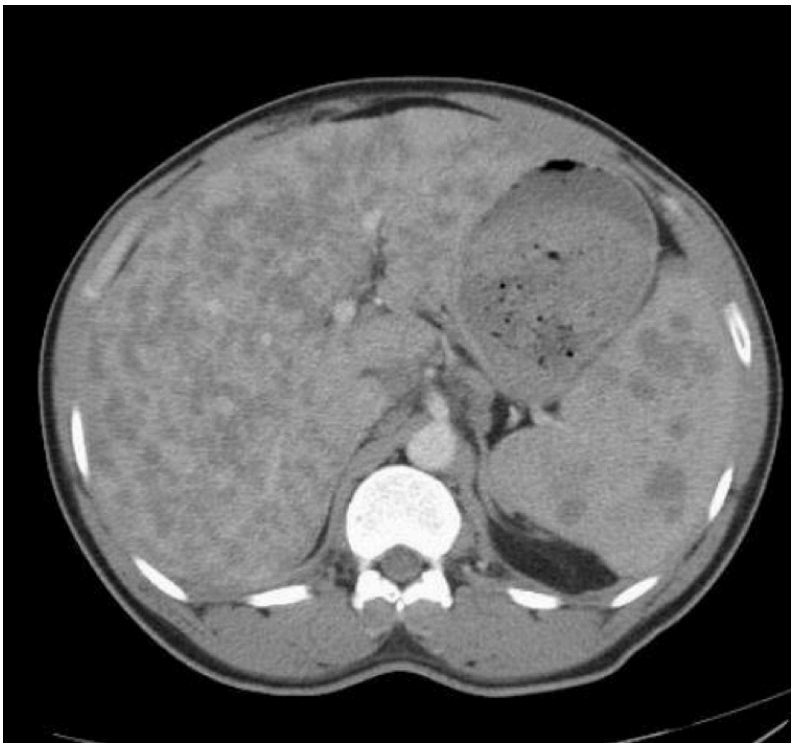

Figure 3

Further workup included tissue sampling, given the aggressive appearance of the lesions. The patient underwent a bronchoscopy with right paratracheal and subcarinal transbronchial needle aspiration, the results of which were negative for malignant cells. The acid-fast bacilli (AFB) smear was negative. The angiotensin-converting enzyme (ACE) levels were greater than 360 U/L (reference range, 9-67 U/L). In addition, records from a previous hospitalization in Italy showed a history of complete atrioventricular (AV) block. The imaging, tissue sample, and laboratory test results with clinical correlation were suggestive of sarcoidosis.

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Discussion. Sarcoidosis is a multisystemic granulomatous disorder of unknown etiology that is characterized by noncaseating granulomas on pathology results of involved organs. This disease process typically affects young adults. It often presents with bilateral adenopathy, pulmonary reticular opacities, and skin, joint, or eye lesions. Bilateral hilar adenopathy on chest radiographs is a classic finding in sarcoidosis, with hila symmetrically enlarged in approximately 50% of cases, or the right hila slightly more prominent. True unilateral adenopathy is seen in fewer than 5% of cases.[1]

There is no definitive test for sarcoidosis; the diagnosis is based on clinical and radiographic manifestations, exclusions of other diseases with similar presentation, and histopathology of noncaseating granulomas. A biopsy should be performed on a lesion that is accessible and appears affected, such as cutaneous lesions, palpable nodules, conjunctival lesions, enlarged parotid or lacrimal glands, or ocular lesions. If these sites are not involved, an alternative is a biopsy or fine-needle aspiration of a radiographically enlarged intrathoracic lymph node or lung parenchyma. Note that erythema nodosum lesions should not be biopsied, because histology tests will reveal panniculitis rather than granulomas.[2]

Of note, hepatic involvement occurs in most patients with sarcoidosis. Hepatic sarcoidosis is approximately twice as common in the African American population than in the white population.[3-5] Approximately 50% to 65% of patients with sarcoidosis will have granulomas on liver biopsy, but only 5% to 15% of patients have symptomatic hepatic sarcoidosis.[4,6,7] Most are asymptomatic and only have biochemical abnormalities such as elevated alkaline phosphatase and γ-glutamyltransferase levels. Hepatomegaly is noted in 5% to 15% of patients.[3,4] Typical CT findings are hepatosplenomegaly and numerous hypodense nodular lesions ranging in size from 1 mm to 3 cm.[8,9] Gastroenterological involvement is found in 1% of cases and mostly manifests as gastric ulceration or mural infiltration.[10] Liver biopsy is recommended when laboratory test results show moderate or severe liver abnormalities of more than 3 times the upper limit of normal.[11]

In addition, sarcoidosis can have cardiac involvement that can range from benign to life-threatening and can involve heart block, heart failure, valvular dysfunction, simulated infarction, or pericardial disease. Furthermore, sarcoidosis may have hematologic involvement. One study found that 11 of 30 patients with sarcoidosis had hematologic abnormalities, including anemia.[12] The pathogenesis of the anemia is not clear.

Differential diagnosis. Berylliosis is also a granulomatous disease that like sarcoidosis shows hilar adenopathy on chest radiographs. There is a remote possibility of berylliosis, given the patient's occupational history of stone and tile grinding and the potential for exposure to beryllium. An outpatient beryllium lymphocyte proliferation test is recommended to rule this out. Patients would typically present with dyspnea and cough, not anemia.

Lymphoma commonly presents with lymphadenopathy, hepatosplenomegaly, fever, weight loss, and night sweats. Although the patient had lymphadenopathy and hepatosplenomegaly, and his wife had noted weight loss, lymphoma is unlikely given that fine-needle aspiration of the paratracheal and subcarinal transbronchial lymph nodes did not show malignancy. It also would not explain the AV heart block requiring pacemaker insertion.

HIV involves nonspecific constitutional symptoms such as fever, fatigue, and myalgia. Frequently lymphadenopathy and sometimes mild hepatosplenomegaly are present. Our patient's chief concern was fatigue and weakness. However, HIV test results were negative.

The take-home message. Sarcoidosis is a granulomatous disorder of unknown etiology that can involve many organs. Although bilateral hilar adenopathy is the classic radiographic finding, it may manifest with heart block or hepatosplenomegaly and multiple lesions in the liver and spleen on CT imaging. Anemia is a rare manifestation of unknown pathogenesis. Sarcoidosis should be considered in the differential diagnosis among HIV, lymphoma, and berylliosis when presented with a similar CT image.

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