The Sarcoid-Lymphoma Syndrome

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Abstract

Whether a relationship exists between sarcoidosis and lymphoma is controversial. We present 4 patients diagnosed with sarcoidosis either during or after the treatment of lymphoma, review the data surrounding the entity known as "sarcoid-lymphoma syndrome" and discuss the diagnostic pitfalls it can present. As both entities are fluorine-18 fluorodeoxyglucose avid, histologic verification and clinical acumen are needed to avoid misdiagnosis before initiating therapy.

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Introduction

The association between lymphoma and sarcoidosis was first suggested by Bichel and Brincker in the 1960s.[1] Since then, additional descriptions of this possible connection have been published[2,3] but without providing a better understanding of this relationship. We report 4 additional cases of "sarcoidosis-lymphoma syndrome" (SLS), including its occurrence in 2 sisters, and review the published literature.

Case Reports

Patient 1 is a 48-year-old Native American woman with no significant past medical history who presented to her primary care physician in May 2003 with decreased appetite, postprandial abdominal pain, and a 5-pound weight loss. She also noted vaginal bleeding and irregular menses. Her gynecologist identified a 7.6-cm pelvic mass on the right and a 4.8-cm pelvic mass on the left by pelvic examination and sonography. A computed tomography (CT) scan demonstrated a poorly defined mass extending from the posterior margin of the stomach to the porta hepatis and central biliary system, with multiple enlarged retroperitoneal and periaortic lymph nodes. In addition, the CT showed bilateral adnexal masses measuring 6.5 cm × 7 cm on the right and 3 cm × 5 cm on the left.

The patient underwent an exploratory laparotomy and was found to have ascites and a tumor measuring 10 cm in its longest diameter, with extension to the gastroepiploic vessels and omentum. Although the frozen section was suspicious for lymphoma, the patient underwent a bilateral salpingo-oophorectomy and omentectomy. Flow cytometry and immunohistochemistry were positive for CD10, CD19, and CD20. The final diagnosis was diffuse large B-cell lymphoma (DLBCL) of follicular center origin involving the omentum, bilateral adnexal masses, and left ovary, with gastric implants. A repeat postoperative CT scan showed a 5.5 cm × 9 cm upper abdominal mass involving the medial gastric wall, gastrohepatic ligament, porta hepatis, and splenic hilum. There was also extensive adenopathy on both sides of the diaphragm, with lung nodules and hepatic lesions. A bone marrow biopsy and aspirate were negative for lymphoma. A positron emission tomography (PET) scan noted abnormal fluorine-18 fluorodeoxyglucose (FDG) uptake in the mediastinal, right hilar, and left supraclavicular nodal areas. The patient was classified as having stage IV disease and treated with 6 cycles of R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) beginning in November 2003. After 2 cycles, the PET and CT scans were negative. However, a PET scan 8 weeks after the completion of the sixth cycle of therapy revealed new foci of intense hypermetabolic uptake in the upper anterior mediastinum, right and left paratracheal areas, bilateral hila, and left posterior mediastinum, with standardized uptake values (SUVs) ranging from 6 to 12 (Figure 1). Mediastinoscopy and biopsy of the subcarinal lymph node revealed epithelioid histiocytes consistent with sarcoidosis. She is currently in remission for more than 6 years.

Patient 2, the sister of patient 1, is a 37-year-old Native American woman with a past medical history significant for sarcoidosis diagnosed in 1986. Hilar adenopathy was identified at the time of a routine chest radiograph before orthopedic surgery, and the diagnosis of sarcoid was confirmed by bronchoscopy. She was asymptomatic at the time. In October 1997, she presented with 2 enlarged supraclavicular lymph nodes. She did not undergo a biopsy but was initially treated at another institution with several courses of antibiotics, with no change in lymph node size. Physical examination revealed a left supraclavicular lymph node measuring 1.5 cm × 1.5 cm. A CT scan of her chest showed minimal indeterminate densities at the left lung base, with no evidence of nodules, masses, or lymphadenopathy. No additional lymphadenopathy was noted

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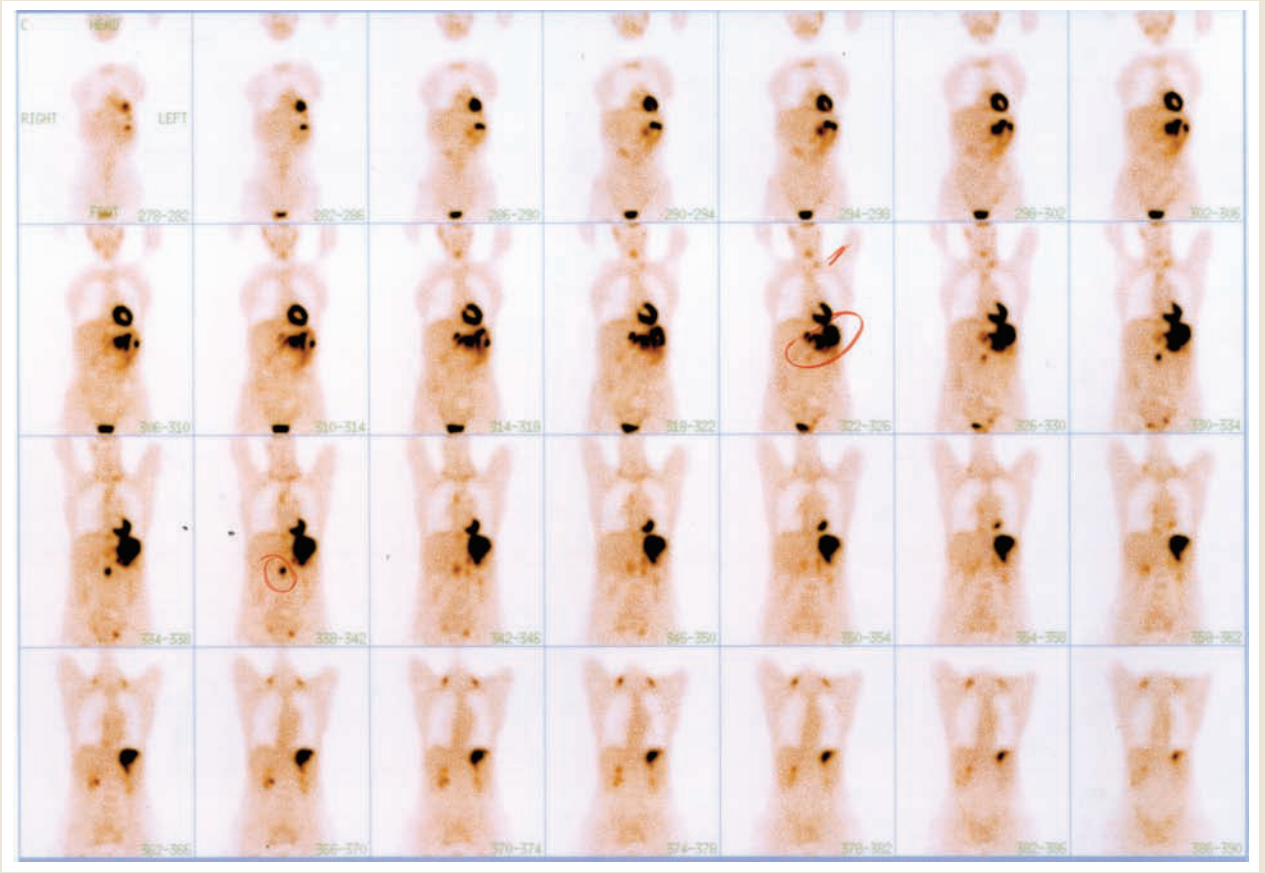
Figure 1A Positron Emission Tomography Images of Patient 1 Before Chemotherapy



in the abdomen or pelvis. Surgical excision of the lymph nodes revealed nodular architecture with malignant follicles composed of a mixture of small and large CD20-positive cells. She was diagnosed with grade 3 follicular lymphoma. Further staging included a hypocellular bone marrow with no evidence of lymphoma. She was managed with active surveillance.

A routine CT scan of the abdomen and pelvis in April 1998 revealed a 2.3 cm × 2.5 cm mass around the left common external iliac vessels. There were also multiple subcentimeter lymph nodes identified in the retrocaval region and a 3.5 cm × 2.5 cm periaortic lymph node. The CT scan of the chest and bone marrow aspirate and biopsy were negative. After a repeat lymph node biopsy again revealed a grade 3 follicular lymphoma, the patient was considered to have stage IIIA disease and treated at an outside hospital with cyclophosphamide and etoposide before planned stem cell collection in anticipation of a stem cell transplantation. A repeat CT scan showed a decrease in size of the periaortic lymph nodes to 0.8 cm × 1.8 cm and resolution of iliac adenopathy. Insurance clearance for the transplantation was denied, and she received 3 cycles of CHOP therapy. A subsequent CT scan in October 1998 noted subcentimeter left periaortic lymph nodes but no pulmonary lesions or thoracic adenopathy. Her most recent follow-up CT scan from 4 years ago was negative, and the patient is in complete remission after 12 years of follow-up.

Patient 3 is a 47-year-old woman with a medical history significant for cutaneous and ocular sarcoidosis initially diagnosed in 1985. She was noted to have left supraclavicular adenopathy in March 2004. She had experienced a 60-pound weight loss and complained of the recent onset of fevers and night sweats. Biopsy of the lymph node was consistent with nodular sclerosing Hodgkin lymphoma. A PET scan identified mediastinal adenopathy and pulmonary lesions. A bronchoscopy was not initially performed to distinguish underlying pulmonary sarcoidosis from lymphomatous involvement of the lungs. A bone marrow biopsy was negative. She was considered to have stage IIBE disease and was treated at an outside institution with 3 cycles of doxorubicin/bleomycin/vinblastine/dacarbazine along with radiation to her chest and achieved a complete response. In July 2007, her oncologist noted worsening nodal disease in her chest and assumed she had recurrence of her lymphoma. She was asymptomatic at that time. She was sent to Georgetown University Hospital for a second opinion. Bronchoscopy in September 2007 with a needle biopsy of a subcarinal node and transbronchial biopsy of the right upper lobe showed noncaseating granulomas. Therefore, she received no further treatment but remained under close observation with CT scans every 3-4 months. In April 2009, she had been having sarcoid flares of her eyes and was found to have increasing cervical, hilar, mediastinal, and mesenteric adenopathy. She is being followed by her pulmonologist for management of a presumed