CLINICAL VIGNETTE

Castleman's Disease: A Rare Cause of Lymphadenopathy

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Case Presentation

A 19-year-old male with a past medical history only significant for generalized anxiety disorder and attention deficit disorder presented to ambulatory care complaining of the sensation of a "ball" in the left axilla that had been present for the past 4-6 weeks. He denied any associated fever, chills, night sweats, pain, or expression of pus or oozing from the mass. The patient did report that the mass appeared to be progressively increasing in size over time. He also reported weight loss of 5 pounds over the past several weeks, which he attributed to increased physical activity.

There was family history of breast cancer in his mother, lymphoma in his brother, prostate cancer in his maternal grandfather, and colon cancer in his maternal grandmother. The patient's only prescription medication was amphetamine-dextroamphetamine. Vital signs revealed asymptomatic hypotension with a measured blood pressure of 92/64 mmHg. All other vital signs, including temperature, pulse, respiratory rate, and body mass index were within normal limits. On physical examination, the patient appeared pale with darkness noted under the eyes. Papulo-pustular acne was noted on the face, neck, anterior thorax, and posterior thorax. A large, firm, non-tender mass was noted deep in the left axillary fossa. Examination of the right axilla was normal. Lymph node examination of the head and neck was unremarkable.

Laboratory testing initially included normal complete blood count, differential and smear, sedimentation rate and C reactive protein. Additional evaluation included: comprehensive metabolic panel remarkable for minimally elevated glucose and albumin. Ultrasound confirmed a 11 X 22 mm lymph node-appearing mass in the left axilla and it was surgically excised. Pathology returned consistent with Castleman's disease, hyaline vascular (angiofollicular) variant, negative for lymphoma and malignancy. Flow cytometry showed no immunophenotypic evidence for non-Hodgkin's lymphoma. There were no significant plasma cells in the lymph node to suggest plasma cell variant. Subsequent testing for human herpes virus 8 (HHV-8) and human immunodeficiency virus (HIV) also returned negative.

The patient was evaluated by hematology/oncology for a presumed new diagnosis of unicentric Castleman's disease. The pathology sample was sent for a second opinion, which confirmed the original diagnosis. Additional testing to rule out underlying rheumatoid arthritis, lymphoma, or plasma cell dyscrasia returned negative. A CT of the chest, abdomen, and pelvis with contrast revealed an increased number of prominent lymph nodes seen within the left level 1 axillary nodal station, which was concordant with the patient's recently diagnosed Castleman's disease. Prominent, but not pathologically large lymph nodes, were seen in the right axilla, right hilum, and pelvis/groin, which were noted to have a slightly higher density. These findings were thought to represent additional areas of involvement of the Castleman's disease. Additionally, prominent soft tissue density was noted within the anterior mediastinum, which was thought to represent residual thymic tissue given the patient's age. Multiple tiny pulmonary nodules and pulmonary cysts were seen that were consistent with lymphocytic interstitial pneumonitis. Six months later, PET/CT from skull base to the mid-thigh showed stable to decreased lymph nodes within the left level 1 axillary nodal station, consistent with stable disease. Multiple pulmonary cysts were seen throughout the lungs which were not significantly changed from the prior study and most consistent with lymphocytic interstitial pneumonitis. The previously described prominent lymph nodes within the right axilla, right hilum, pelvis and groin were stable to decreased in size and most consistent with an improved reactive process, possibly superimposed on stable areas of disease. The patient was treated supportively without any further intervention. Follow-up imaging revealed no evidence of recurrent disease.

Discussion

Castleman's disease (CD) is an uncommon disorder characterized by a benign proliferation of the lymphoid tissue that may be localized or unicentric (UCD) or disseminated or multicentric (MCD). Approximately 6500 to 7700 new cases of CD are diagnosed each year in the United States, of which approximately 4900 to 5900 cases are estimated to be UCD.[1] While UCD can occur at any age, it is generally a disease of younger adults. The median age at presentation is approximately 35 years.[2,3] There is a slightly increased incidence of UCD in women than men.[4]

CD was first described in 1956 by Benjamin Castleman, who identified a group of patients with solitary hyperplasic mediastinal lymph nodes with small germinal center resembling Hassall's corpuscles of the thymus.[5] CD is described histologically as hyaline-vascular type, plasma cell type, or a mixed type[6] and is classified based on the number of enlarged lymph

node regions. UCD involves one or more lymph node(s) in a single region, while MCD involves multiple lymph node sites and is sub-classified into HHV-8-associated MCD and HHV-8-negative/idiopathic MCD.

As noted previously, UCD is the most common type and consists of an isolated benign lymphoproliferative disorder of young adults that is not associated with an HHV-8 infection and usually curable with surgical resection. The vast majority of patients are asymptomatic and their disease is identified incidentally on imaging studies as a soft tissue mass located in the neck or mediastinum. Preoperative diagnosis of hyaline-vascular Castleman's disease is difficult as the radiographical findings are not pathognomonic. The usual CT or MR appearance is a nonspecific homogeneous mass on non-contrast studies, with dense enhancement immediately after the infusion of iodinated or gadolinium material and slow washout with the degree of enhancement approaching that of large vessels.[7] The presence of central areas of fibrosis is a characteristic feature.[8] Once CD is diagnosed, MCD must be ruled out. In addition, UCD may be associated with an increased risk of B-cell lymphoma and Hodgkin lymphoma.[9]

The standard therapy for UCD hyaline-vascular form of CD is surgical excision. Surgery is curative with complete resection, with 5-year survival rates close to 100% with rare recurrences.[10] Patients whose lesions cannot be completely resected also have favorable outcomes. Partially resected masses may remain stable and asymptomatic for many years.[11] Radiation therapy may result in complete or partial remission rates of 40 and 10 percent. Successful use of rituximab has also been reported.[12]

After resection, patients should be followed for response to treatment and monitored for relapse or complications. Appropriate follow-up should be tailored to the specific CD variant and symptoms. Patients with unicentric disease without systemic involvement should have radiological assessment 6-12 months after initial therapy to verify no recurrence. Additional testing should only be performed in the event of recurrence or onset of new symptoms.

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