Case Report

Investigation of a Peculiar Case of Childhood Lymphadenopathy

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Abstract

Introduction
Lymphadenopathy is a common physical finding often associated with an infectious etiology. We present a case of a patient with generalized cervical and supraclavicular lymphadenopathy diagnosed with a rare malignancy. Health care providers should be aware of some uncommon historical or physical examination findings that warrant further investigation.

Clinical Findings
A 16-year-old female presented to the emergency department with 3 days of a fever, congestion and sore throat with swelling around the jaw. Her physical examination findings included bilateral mandibular swelling and generalized cervical lymphadenopathy with palpable supraclavicular lymph nodes.

Outcomes
Complete blood count showed pancytopenia with a white blood cell count of 4.4 x 10e3/uL, hemoglobin of 10.8 g/dL and platelets of 87 x 10e3/uL. CT scan of the neck with IV contrast revealed extensive cervical and mediastinal lymphadenopathy with suspicion of lymphoma. Biopsy results diagnosed a rare form of a hematologic malignancy called blastic plasmacytoid dendritic cell neoplasm.

Conclusions
The presence of supraclavicular lymphadenopathy should raise concern for non-infectious etiologies, such as malignant processes.

Keywords
lymphatic diseases; neoplasms; dendritic cells/pathology; hematologic neoplasms; leukemia; pediatrics

Case Presentation

A 16-year-old female presented to the emergency department (ED) with a 3 day history of fever of 100^{O}F, congestion, and mild sore throat. She had a decreased appetite but had been able to tolerate some oral fluids. She also had complaints of bilateral mandibular swelling, which had been increasing in size since the onset of symptoms. She denied any voice change, drooling or pain with neck movement. Her pertinent recent past medical history included a previous visit to the primary care provider for "bumps behind ears" 4 months prior to the ED visit. She also had a history of a breast mass with a negative biopsy 1 year prior to the ED visit. The review of systems was negative for weight loss, bruising, bleeding, shortness of breath, abdominal pain or headache.

Initial vital signs on arrival to the emergency department revealed a temperature of 99.6 F, heart rate of 131 beats/min, respiratory rate of 20 breaths/min, blood pressure of 131/85 mmHg and an oxygen saturation of 99%. Pertinent findings on physical examination revealed 1+ tonsils and erythema without exudate or petechiae. She had a large, left-sided, palpable, post-auricular mass and a smaller right-sided, palpable, post-auricular mass. She also had generalized lymphadenopathy of the cervical

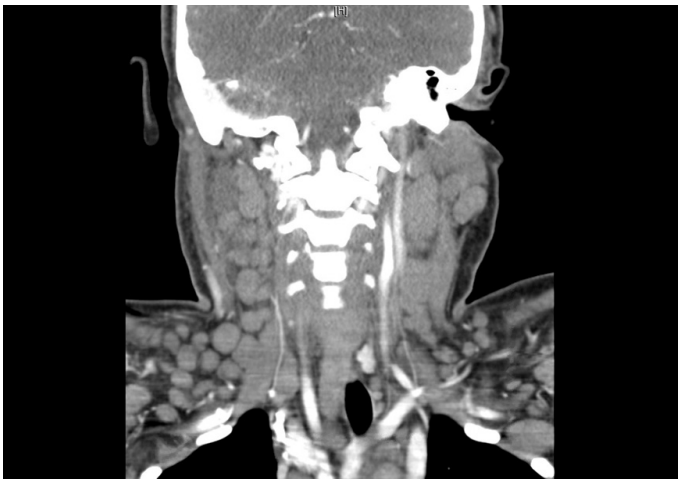

Figure 1. Coronal CT scan of the neck shows extensive generalized lymphadenopathy.

and supraclavicular lymph nodes as well as palpable, bilateral axillary lymph nodes. Examination of her right breast showed a small hyperpigmented macule and a well healed scar without any masses. Otherwise her examination was found to be unremarkable including no hepatosplenomegaly.

The patient was given a lactated ringers bolus for her tachycardia and dehydration. Her work up included a complete blood count (CBC), complete metabolic panel (CMP), as well as uric acid, phosphorus, lactate dehydrogenase (LDH) and a monospot test. A chest x-ray (CXR) was ordered to evaluate for mediastinal widening and a CT scan with IV contrast of the neck to evaluate the generalized lymphadenopathy.

Laboratory studies revealed a CBC showing pancytopenia with a white blood cell count of 4.4 x 10e3/uL, hemoglobin of 10.8 g/dL, platelets of 87 x 10e3/uL and a differential with segs 1%, bands 6%, lymph 78% and atypical lymph 12%. The metabolic panel was unremarkable except for a slightly elevated AST of 139 U/L and an ALT of 126 U/L. LDH was 392 U/L, uric acid 5.6 mg/dL, phosphate 2.8 mmol/L and the monospot test was negative. The CXR was normal with no mediastinal widening. Findings from the CT of the neck with IV contrast showed marked hypertrophy of the adenoids and palatine tonsils with extensive cervical lymphadenopathy (largest measuring 19.04 mm) and mediastinal lymphadenopathy (largest measuring 15.78 mm) with suspicion for lymphoma. (**Figures 1–4**) The patient was transferred to the regional tertiary pediatric center for pediatric oncology evaluation. At the pediatric center, a bone marrow biopsy was

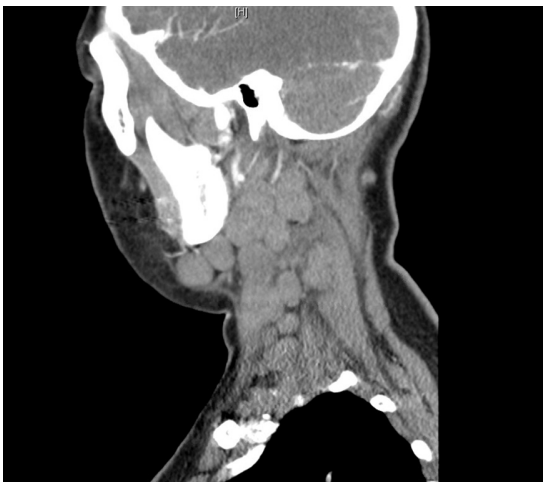

Figure 2. Sagittal CT scan of the neck shows extensive generalized lymphadenopathy.

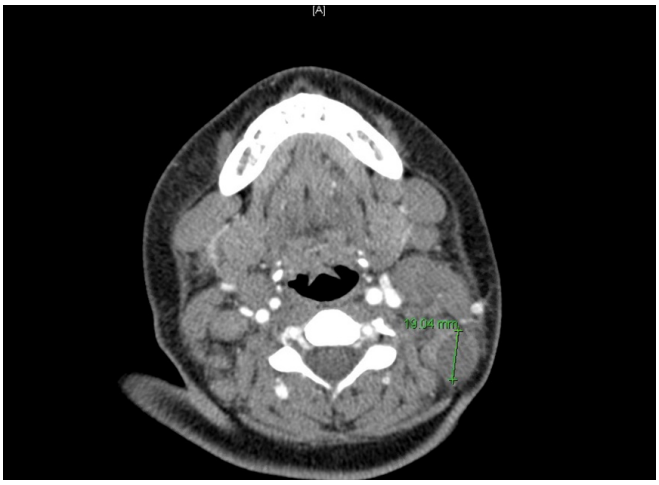

Figure 3. Axial CT scan of the neck shows a 19.04 mm cervical lymph node.

completed as well as a biopsy of the neck mass and the breast hyperpigmented macule. Results of the biopsy confirmed a rare form of a hematologic malignancy called blastic plasmacytoid dendritic cell neoplasm (BPDCN).

Discussion

Our patient exhibited generalized lymphadenopathy including swelling of the supraclavicular lymph nodes. Generalized lymphadenopathy refers to enlarged lymph nodes in more than two areas of the body, and it is usually evaluated based on size and location. Swelling of the supraclavicular lymph nodes in children is suspicious for malignancy and warrants further investigation. Since these lymph nodes drain the head, neck and mediastinum, our finding was especially suspicious for a malignant etiology, which led to further testing. A CBC revealed pancytopenia. A CT scan of the neck with IV contrast showed marked hypertrophy of the adenoids and palatine tonsils with extensive cervical and mediastinal lymphadenopathy. Normally, lymph nodes in the neck have a diameter of 12 mm and 12.6 mm in the mediastinum which compares to the size of a pea. Our patient had cervical lymph nodes that measure 19.04 mm and mediastinal nodes measuring 15.78 mm. Due to the lymph node enlargement and its diffuse pattern coupled with the finding of pancytopenia, a malignancy was suspected and led to the diagnosis of BPDCN.

BPDCN is an aggressive hematologic malignancy which presents with cutaneous lesions and frequently involves the bone marrow as well as the lymph nodes. Before being categorized by the World Health Organization in 2008, BPDCN was thought to be a natural killer cell leukemia/lymphoma.[1] With further investigation, the ma-

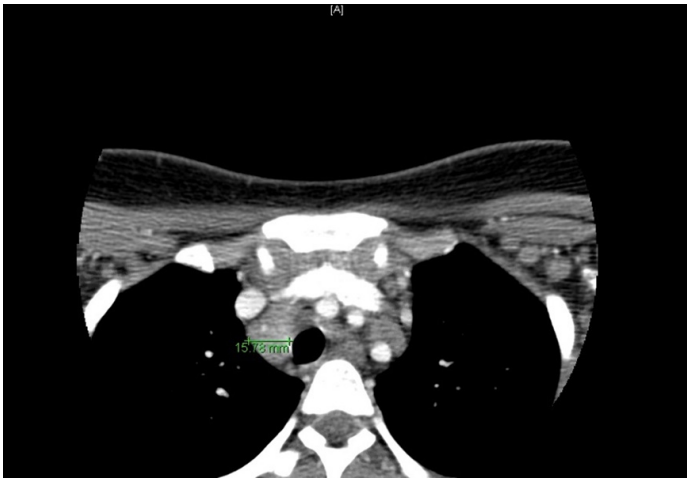

Figure 4. Axial CT scan of the upper mediastinum shows a 15.78 mm lymph node.

lignant cells have been recognized as a subtype of dendritic cells called plasmacytoid dendritic cells. Plasmacytoid dendritic cells reside in lymph tissues such as lymph nodes and tonsils. These cells secrete large amount of interferons and other cytokines in the setting of autoimmune diseases or viral infections.[2] The main surface antigens that contribute to a diagnosis of BPDCN include CD4, CD56, and CD123.[3] In 2016, BPDCN was established as its own entity by the World Health Organization.[4]

BPDCN is a very rare hematologic neoplasm. Due to prior poor classification and many changes to its nomenclature, the exact incidence of BPDCN is unknown. According to recent literature, BPDCN accounts for 0.7 percent of all cutaneous lymphomas.[5] Skin lesions seem to take an indolent course before rapid spread to the bone marrow.[1] Skin lesions can present with macules, nodules and plaques that are hyperpigmented, erythematous or ulcerative. The skin lesions can vary between one or two isolated lesions to disseminated skin lesions of varying sizes. Skin pathology is typically accompanied by cytopenia, lymphadenopathy and sometimes splenomegaly. Liver involvement is not usually seen, though if present, it usually occurs with bone marrow involvement.[5] In addition to lymphatic spread, systemic dissemination can involve the soft tissues, the lungs and the central nervous system.[5,6] As described in this case report, the patient presented with extensive lymphadenopathy, elevated liver enzymes and pancytopenia. She is a prime example of how the diagnosis of BPDCN can be difficult, as many cases are mistaken for acute myeloid leukemia and/or cutaneous T-cell lymphoma.[5]

In addition to CT imaging for further investigation of lymphadenopathy, imaging can be used to evaluate the extent of skin lesion involvement. In the majority of cases, CT and PET/CT images can reveal the depth of cutaneous lesions and necrosis, highlighting the specific target for biopsy.[6] Although our patient did not have multiple skin lesions that were evaluated by the CT imaging, the CT did demonstrate extensive lymphadenopathy with a high suspicion for malignancy which led to the ultimate decision to transfer the patient to a pediatric tertiary care center for pediatric oncology evaluation.
The most current management for BPDCN includes treatment with tagraxofusp and, in some eligible cases, hematopoietic stem cell transplants. Tagraxofusp, the first FDA approved treatment for BPDCN, specifically targets the BPDCN marker CD123 with promising results.[3] Though acute lymphoblastic leukemia/lymphoblastic lymphomas (ALL/LBL) treatment regimens have had positive outcomes for BPDCN, tagraxofusp is a much more targeted option. The most serious side effect from treatment with tagraxofusp is capillary leak syndrome, which can be fatal.[3] Tazgraxofusp is recommended for children greater than 2 years of age, and, in most cases, can be followed with allogeneic hematopoietic stem cell transplantation. In children less than 2 years of age, treatment with ALL/LBL treatment regimens are recommended.[5]

Conclusion

The diagnosis of BPDCN, a rare hematologic neoplasm, was based on physical examination findings of generalized lymphadenopathy but, more specifically, abnormal supraclavicular lymphadenopathy. A high index of suspicion for a malignant process should be considered for patients with palpable supraclavicular lymph nodes.

Conflicts of Interest

The authors declare they have no conflicts of interest.

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