An Unusual Reason for Neck Masses: A Case Report

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Kikuchi-Fujimoto disease (KFD), also known as histiocytic necrotizing lymphadenitis, is a benign and self-limited disease. Enlargement of lymph nodes with pain is a common manifestation of KFD especially within the cervical region. However, the etiology and management of this disease are still relatively uncertain. Therefore, KFD is easily misdiagnosed or missed. I present a case of an 8-year-old boy who presented to our pediatric emergency department with a 2-week history of prolonged fever and painful neck mass previously had been treated with antibiotics at clinic. KFD was diagnosed after lymph node biopsy and he recovered under supportive treatment.

Key words: Kikuchi-Fujimoto disease, histiocytic necrotizing lymphadenitis, lymphadenopathy, rare diseases, child

Introduction

In the pediatric emergency department, physicians often encounter patients with enlarged cervical lymph nodes. Up to 90% of children between the ages of 4 to 8 have experienced palpable cervical lymph nodes. Mostly, lymphadenopathy represents a transient response to a benign local inflammatory process. Around 15% of biopsied cervical lymph nodes in children result in malignancy1,2. Kikuchi-Fujimoto disease (KFD), or histiocytic necrotizing lymphadenitis, is a benign, self-limiting and rare differential diagnosis of cervical lymphadenopathy. There is no definite etiology. The most common manifestations are persisted fever and localized enlarged lymph nodes. Neither specific diagnostic laboratory tests nor imaging studies are available despite of pathological confirmation3-6. Therefore, KFD is easily misdiagnosed as other diseases initially such as tuberculous lymphadenitis, cat scratch disease or lymphoma7,8.

Case Report

An 8-year-old Asia boy was brought to our pediatric emergent department in November 2013 after presenting with fever and a painful lesion over right cervical region for 12 days without other symptoms. He had been in good health in the past. Furthermore, he had already been treated with oral amoxicillin prescribed from local clinics for a week without improvement.

On physical exam, he had right neck mass measured around 4×5cm in size and daily fever up to 40°C. His complete blood count revealed 5200 cells/uL of white blood cells with 38% of neutrophil. C-reactive protein (CRP) was 0.87 mg/dL. Viral capsid antigen (VCA) IgG for Eptstein-Barr Virus (EBV) showed positive while IgM was negative.
Tuberculin (TB) skin test and TB polymerase chain reaction (TB-PCR) were all negative. Computed tomography (CT) imaging of his neck was performed and multiple homogeneous enlarged lymph nodes with nodal necrosis and perinodal infiltration were found (Fig. 1, 2). Despite empiric antibiotics treatment with Amoxicillin/clavulanate (Augmentin), his fever persisted. He underwent a cervical lymph node biopsy on the fifth day of hospitalization. Microscopic examination showed lymph nodes with neutrophil-poor necrosis and karyorrhectic nuclear debris surrounded by foamy histiocytes without malignant cell. No microorganism was found either by acid-fast stain or by immunohistochemistry with anti-Bartonella henselae antibody. The histology was consistent with histiocytic necrotizing lymphadenitis, or KFD. His symptoms subsided spontaneously after 10 days of supportive treatment and he was discharged.

**Discussion**

Cervical lymphadenopathy is a common finding on physical examination that physicians encounter in the emergency department. It could be divided into inflammatory/reactive and neoplastic etiologies. Inflammatory/reactive lymphadenopathy can be the result of infectious lymphadenitis, Kawasaki disease, or KFD. Viral, staphylococcal, mycobacterial, and Bartonella
henselae infection are common etiologies of infectious lymphadenitis\textsuperscript{(1,2)}. Although it is rare in children, malignancies such as lymphoma or leukemia are also contributed to lymphadenopathy. Constitutional type B symptoms such as fever, malaise, weight loss, and night sweats suggest a possible malignancy\textsuperscript{(2)}. Due to wide varieties of differential diagnosis and associated treatment, cervical lymphadenopathy is definitely a diagnostic challenge for physicians.

KFD, or histiocytic necrotizing lymphadenitis, is a benign and self-limited disorder, characterized by regional cervical lymphadenopathy with tenderness and fever. KFD was first described in 1972 independently by two Japanese pathologists, Dr. Masahiro Kikuchi\textsuperscript{(9)} and Dr. Fujimoto\textsuperscript{(10)} and affects predominantly young adult Asian females\textsuperscript{(3,5,11)}. However, male predilection was reported in some pediatric studies with a 1.4 to 3:1 male to female ratio\textsuperscript{(4,6,11,12)}. Although KFD is primarily considered as a rare disease, the true incidence may be higher while KFD is increasingly recognized around the world\textsuperscript{(6)}. The pathogenesis is unconfirmed currently. However viral etiology, inclusive of EBV, cytomegalovirus, parvovirus B19, human herpesvirus 6, human herpesvirus 7 and human herpesvirus 8, was suggested by previous studies\textsuperscript{(13,14)}.

Imaging studies such as sonography, CT and positron emission tomography (PET) may contribute to differentiation between KFD and other etiologies of cervical lymphadenopathy. Sonography may find elongated or oval hypoechoic lymph nodes with increased perinodal echogenicity and possess a smaller size, less round, less micronodular reticular echotexture and more signs of matting and cortical widening than those with lymphoma\textsuperscript{(15,16)}. On CT of KFD, mild-to-moderate multiple necrotic foci with indistinct margins and higher necrosis attenuation indices without calcification within the nodes are the characteristic patterns from tuberculous lymphadenitis\textsuperscript{(12,17)}. Tsujikawa et al reported that the affected nodes of KFD show high 2-[\textit{F}-18]fluoro-2-deoxy-D-glucose (FDG) uptake for their relative smaller size than lymphoma on PET and noncervical lesions of KFD.
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An unusual reason for neck masses can also be detected by PET\(^{18}\).

The definite diagnosis of KFD relies on histological examination of a lymph node excision biopsy. The affected lymph nodes reveal focal necrosis with perinodal lymphocytes and histiocytes infiltration along with abundant karyorrhectic debris in the paracortical region\(^{11,20,21}\). KFD can be classified into three histological subtypes from proliferative type (>50%) to necrotizing type (~30%) and end up into xanthomatous type (<20%)\(^{19,21}\). Moreover, the extent of the infiltration is highlighted by the expression of CD68 antigen. CD68 is used as a marker of histiocyte. Therefore, KFD may be a hyperimmune reaction of the histiocyte lineage to viral infections\(^{11,20}\).

However, several previous reports suggest that KFD may associate with autoimmune diseases such as systemic lupus erythematosus (SLE), hemophagocytic lymphohistiocytosis (HLH) and thyroiditis especially among patients with positive anti-nuclear antibody (ANA)\(^{3-6,12,20,22-25}\).

In conclusion, cervical lymphadenopathy though is a common finding that frequently be found in emergency department. Physicians should keep in mind that KFD may be the possible differential diagnosis for cervical lymphadenopathy after excluding other relative prevalent diagnosis such as bacterial or viral infection, Kawasaki disease and malignancy. Imaging exams and biopsy should be considered when empiric antibiotics are unresponsive and the diagnosis is uncertain. Most cases of KFD take very benign and self-limiting courses without special management, however, long-term follow-up is necessary at least every 6 months to monitor for the possible later recurrence and development of autoimmune disease.

References


菊地氏病，又稱組織球壞死性淋巴腺炎，是一個良性且自限性的疾病。常以頸部淋巴結腫大作為臨床病徵。然而，此病的致病原因及處置目前尚未被確立，所以菊地氏病很容易被誤診或是被忽略掉。我要提出一個8歲男孩的病例報告，起初在診所以抗生素治療2周，但由於持續高燒及頸部腫大疼痛被送至本院兒科急診處理。經過淋巴結病理切片後，診斷為菊地氏病，在支持療法下順利恢復健康。

關鍵詞：菊地氏病，組織球壞死性淋巴腺炎，淋巴腺炎，罕見疾病，兒童