

CLINICAL VIGNETTE

Kikuchi-Fujimoto Disease as a Cause of Recurrent Cervical Lymphadenopathy

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Introduction

Kikuchi-Fujimoto disease is an uncommon benign syndrome of necrotizing lymphadenopathy with a distinctive histologic appearance first described in 1972. Initially thought to be localized to patients of Asian descent, it has since been diagnosed across all demographics. Because of its broad constellation of clinical presentations, the difficulty in confirming diagnosis, and the serious rheumatologic and neoplastic illnesses with which it can be confused, it is important to consider it in the differential diagnosis of neck lymphadenopathy. Here is a 41-year-old woman with recurrent cervical and supraclavicular lymphadenopathy concerning for Kikuchi-Fujimoto disease.

Case Report

A 41-year-old female with past medical history of hypothyroidism and alopecia areata presented to a primary care clinic with a one month history of painless lymph node enlargement in the neck with no associated symptoms such as fevers, weight loss, night sweats, or recent illnesses. She had experienced similar lymph node enlargements in 1997 and 2010, with reportedly inconclusive biopsy results. Physical examination revealed temperature 36.9°C, blood pressure 106/70 mm Hg, pulse 79, and oxygen saturation 99% on room air. She was in no apparent distress; exam was notable for a one-centimeter hard, mobile, non-tender, left-sided supraclavicular lymph node without any overlying skin changes. The throat appeared normal, and there was no axillary or inguinal lymphadenopathy. The abdomen was soft without organomegaly or masses. Laboratory evaluation included normal CBC, CMP, ESR, CRP, ANA and HIV, and a depressed TSH of 0.04 mcIU/mL. An ultrasound-guided FNA was performed; results were benign but nondiagnostic: "Polymorphous lymphoid population present, consisting of predominantly small lymphocytes with occasional admixed histiocytes; flow cytometry negative for monotypic B cell population and T cell abnormalities." Records from the patient's 1997 cervical lymph node biopsy were obtained and were read as "histiocytic necrotizing lymphadenitis consistent with Kikuchi-Fujimoto disease." The patient did not return for her subsequent office visits and was lost to follow-up.

Discussion

Lymphadenopathy can be subdivided into localized or generalized presentations, both with broad differential diagnoses. Lymphadenopathy localized to the cervical and supraclavicular region is generally related to pathologies of the head and neck, whether infectious (EBV, CMV, toxoplasmosis, tuberculosis, and *Bartonella*) or inflammatory (lymphoma, head and neck cancer, SLE, and Kikuchi-Fujimoto). Generally, the majority of cases of cervical lymphadenopathy are benign.¹

Kikuchi-Fujimoto disease is a syndrome of necrotizing lymphadenitis that most commonly presents as modest (1-2 cm) cervical lymphadenopathy in an otherwise-healthy young woman; low-grade, self-limiting fever is the most common additional symptom. A myriad of other complaints are often found as well and may include night sweats, fatigue, nausea, vomiting, arthralgias, and weight loss. A nonspecific rash may occur and on biopsy is typically consistent with leukocytoclastic vasculitis.² Laboratory findings are generally normal but less often include leukopenia, atypical lymphocytes, anemia, and elevated inflammatory markers.¹ Many infectious causes such as HIV, CMV, EBV, toxoplasmosis, and *Yersinia enterocolitica* are often checked as well but typically have low diagnostic yield.

Although the disease is benign, biopsy is recommended given the serious range of illnesses in the differential diagnoses, particularly with increasing age. The substantial false-negative rate and low diagnostic accuracy of fine needle aspiration (approaching 50%) make excision biopsy the preferred method.¹ Although excisional biopsy remains the gold standard, the histologic findings are not pathognomonic and in fact are very similar to and may even be confused with other illnesses such as SLE, tuberculous lymphadenitis, and lymphoma.³ Pathologic results show necrosis and a typical histiocytic infiltrate either in the early "proliferative phase" in which blast cells may be confused with lymphoma or the later "necrotizing phase," showing necrosis with histiocyte predominance.

Treatment of Kikuchi-Fujimoto disease is symptomatic; rare severe cases have been treated with intravenous

immunoglobulin and glucocorticoids, although evidence is lacking regarding efficacy. Prognosis is excellent with all symptoms typically resolving spontaneously over the course of several months. A minority of patients experience a relapsing course; predictive factors for recurrence include fever, systemic symptoms, and long duration of illness.⁴

The exact cause of Kikuchi-Fujimoto disease is unknown but is thought to be a hyperimmune T-cell immune response to an infectious trigger such as EBV, HIV, CMV, or other illnesses, subsequently leading to cellular apoptosis. Supporting evidence of infectious trigger (the most common association appears to be EBV) are the common findings of peripheral blood abnormalities as well as a distinct progression of benign histiologic results: an initial lymphoproliferative phase followed by necrotizing changes.⁵ There is also evidence of an association with autoimmune disorders with some recommending the monitoring of conditions such as lupus after the resolution of the acute illness.⁶

Conclusion

In the aforementioned patient with recurring cervical/supraclavicular lymphadenopathy, the exact cause remains unclear. Although the most recent biopsy was nondiagnostic, this may be due to the low diagnostic yield of fine needle aspiration or the fact that the pathology of Kikuchi-Fujimoto disease evolves over time and mimics other disorders. Furthermore, the patient's history of hypothyroidism and alopecia areata suggest a possible autoimmune link to her recurring lymphadenopathy. In young patients with such presentations, it is important to maintain a low threshold for early excisional biopsy in order to better direct treatment and to include Kikuchi-Fujimoto disease as a possible cause of recurrent lymphadenopathy.

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Submitted February 11, 2015