Kikuchi-Fujimoto disease: A report of 3 cases

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Abstract
Cervical lymphadenopathy has many underlying etiologies. One of its rare causes is Kikuchi-Fujimoto disease (Kikuchi’s disease, histiocytic necrotizing lymphadenitis). We discovered such a cause in a 37-year-old woman who had presented with malaise, night sweats, and weight loss in addition to cervical lymphadenopathy. We based our diagnosis on excisional lymph node biopsy. We also review 2 other cases of Kikuchi’s disease that were diagnosed by others at our institution. Clinically and histologically, Kikuchi’s disease is very similar to lymphoma, and distinguishing the two is difficult. However, despite the fact that Kikuchi’s disease is benign, an accurate diagnosis is important because misdiagnosis might lead to unnecessary surgery and/or chemotherapy.

Introduction
Kikuchi-Fujimoto disease (Kikuchi’s disease, histiocytic necrotizing lymphadenitis) is a rare cause of cervical lymphadenopathy. It was first described by Kikuchi of Japan in 1972 and later the same year by Fujimoto et al. It is most common among young Asian women. Only a few isolated cases have been reported in Europe (it was first reported in the United Kingdom in 1985). Kikuchi’s disease is likewise uncommon in the United States. However, there is speculation that the disease is under-recognized and underdiagnosed in the Western world.

The cause of Kikuchi’s disease is unknown. A number of viruses have been implicated—including cytomegalovirus, Epstein-Barr virus, human herpesvirus, varicella zoster virus, and parainfluenza virus—but studies have failed to identify a specific pathogen.

The most common presenting symptom of Kikuchi’s disease is cervical lymphadenopathy (~80% of cases), usually in the posterior triangle; associated fever and weight loss are often present. Affected patients may also exhibit skin manifestations and central nervous system involvement. Systemic lupus erythematosus (SLE) can follow or coexist with Kikuchi’s disease in patients previously undiagnosed with SLE. As it is a benign disease, most symptoms resolve within 6 months without treatment. Approximately 3% of patients develop a recurrence, usually in 6 to 12 years.

Clinically and histologically, Kikuchi’s disease can be mistaken for SLE or, more important, for malignant lymphoma. Turner et al described 25 patients with Kikuchi’s disease who had been initially misdiagnosed with lymphoma; 11 of these patients had been subjected to unnecessary invasive procedures. Likewise, Dorfman and Berry reported that 40% of patients with Kikuchi’s disease in their series had been initially misdiagnosed pathologically and that some had been unnecessarily treated with chemotherapy.

A diagnosis of Kikuchi’s disease can be established only by excisional lymph node biopsy. Fine-needle aspiration cytology may suggest Kikuchi’s disease, but Tong et al found that it was accurate in only 56.7% of cases. No radiologic findings are specific to Kikuchi’s disease; both computed tomography (CT) and magnetic resonance imaging (MRI) demonstrate multiple enlarged lymph nodes, which may mimic malignant lymphoma and various other nodal diseases such as metastasis, tuberculosis, and lupus lymphadenitis.

Serologic investigations are unhelpful; at most, they may reveal that the complete blood count (CBC) is normal or slightly elevated, or they may demonstrate leukopenia. Most patients will have a mildly elevated erythrocyte sedimentation rate (ESR) or C-reactive protein level.

We report a case of Kikuchi’s disease that we treated at Galway University Hospital (patient 1), and we review 2 other cases that were encountered by others at our institution.

Case reports
Patient 1. In 1995, a 37-year-old woman presented with a 3-week history of left-sided cervical lymphadenopathy affecting the posterior triangle. She was otherwise asympto-
tomatic. The previous year, she had presented with a left axillary mass, which was excised and sent for histologic analysis. The analysis had been inconclusive. Toxoplasmosis and SLE had been proposed as possible etiologies, but no further investigations had been undertaken.

On this occasion, two nodes from the posterior triangle were excised and sent for histologic analysis. Kikuchi’s disease had been suspected, and it was confirmed by a pathologist at another hospital. This prompted a histopathologist at our institution to review the patient’s histology slides from the previous year, and this reanalysis also showed Kikuchi’s disease. The patient recovered uneventfully, and 11 years later she had not exhibited any evidence of recurrence.

**Patient 2.** In 2000, a 47-year-old woman presented with a 4-week history of cervical lymphadenopathy in the posterior triangle and associated fever, lethargy, and a maculopapular rash on her upper limbs. Initially, an infectious cause was considered, and a number of investigations were undertaken. However, the CBC, ESR, liver function test results, blood cultures, and bone marrow biopsy findings were normal. Likewise, serologic investigations for brucellosis, toxoplasmosis, Lyme disease, and hepatitis B and C virus infections were negative. Finally, autoimmunity screening for anti-nuclear factor (ANF), rheumatoid factor, and antineutrophil cytoplasmic antibody also yielded negative results.

Next, an excisional lymph node biopsy was performed. Findings on histologic examination suggested cat-scratch disease, but the patient had no history of contact with cats. A serum sample was sent to a laboratory in the U.K. for evaluation of IgM and IgG levels for *Bartonella henselae*. When the results were negative for current or recent infection, the lymph node histology was reviewed. It was upon reexamination that Kikuchi’s disease was diagnosed.

Six months later, the patient presented to her general practitioner with a facial rash, and she was referred for a dermatology opinion. Discoid lupus erythematosus was diagnosed on the basis of a positive skin biopsy and a serum ANF of 1:20.

At 6 years of follow-up, the patient exhibited no evidence of recurrence of either Kikuchi’s disease or SLE.

**Patient 3.** In 2004, a 33-year-old woman presented with a 4-week history of cervical lymphadenopathy in the posterior triangle. She had no other symptoms. Serology for brucellosis and toxoplasmosis was negative, but histologic examination of an excisional lymph node biopsy specimens identified Kikuchi’s disease. No other investigation or treatment was necessary, and the patient’s condition resolved. She remained well 2 years later.

**Discussion**

It has been postulated that Kikuchi’s disease may be a form of early SLE because of the high frequency of SLE flare-ups seen in patients with Kikuchi’s disease. In our patient 2, serologic markers for SLE were initially negative, but she presented 6 months later with discoid lupus erythematosus and a positive ANF result. As of early 2007, patients 1 and 3 had not developed SLE. Cat-scratch disease was initially considered for patient 2, but it was ruled out after an indirect fluorescent antibody test for *B. henselae* was negative. In patient 1, the Kikuchi disease actually represented a recurrence of disease that had been undiagnosed a year earlier. None of these 3 patients had been initially misdiagnosed with lymphoma, and none required any treatment for their symptoms.

Jang et al. suggested using an oral glucocorticoid for patients with severe and/or persistent symptoms and for those who experience a recurrence. The use of other oral immunosuppressants has also been suggested in the literature. However, of our 3 patients, only patient 1 experienced lethargy and fever, and these symptoms were not severe enough to warrant oral glucocorticoid therapy. Patients 2 and 3 complained only of cervical lymphadenopathy, and it resolved spontaneously in both cases. All 3 patients continue to undergo follow-up to look for recurrence of Kikuchi’s disease and SLE.

**References**