Kikuchi-Fujimoto Disease Masquerading as Metastatic Papillary Carcinoma of the Thyroid

S. Garg  
Northwell Health

M. Villa  
Northwell Health

J. R. Asirvatham  
Northwell Health

T. Mathew  
Northwell Health

L. J. Auguste  
Hofstra Northwell School of Medicine

Follow this and additional works at: https://academicworks.medicine.hofstra.edu/articles

Part of the Pathology Commons, and the Surgery Commons

Recommended Citation

This Article is brought to you for free and open access by Donald and Barbara Zucker School of Medicine Academic Works. It has been accepted for inclusion in Journal Articles by an authorized administrator of Donald and Barbara Zucker School of Medicine Academic Works. For more information, please contact academicworks@hofstra.edu.
Kikuchi-Fujimoto Disease Masquerading as Metastatic Papillary Carcinoma of the Thyroid

Shailesh Garg, MD1 Manuel Villa, MD1 Jaya Ruth Asirvatham, MD2 Thomas Mathew, MD3 Louis-Joseph Auguste, MD1

1 Department of Surgery, North Shore-LIJ Health System, Manhasset, New York
2 Department of Laboratories, North Shore-LIJ Health System, Manhasset, New York
3 Department of Medicine, North Shore-LIJ Health System, Manhasset, New York


Abstract

Kikuchi-Fujimoto disease also known as histiocytic necrotizing lymphadenitis is a rare cervical inflammatory lymphadenitis that is most commonly seen in young Asian women. It is mainly characterized by lymphadenopathy, hepatosplenomegaly, fever, nocturnal sweats, myalgia, weight loss, and arthralgia, and commonly follows a self-limited course. The differential diagnosis is challenging as many other conditions such as malignant lymphoma, metastatic disease, tuberculosis and infectious lymphadenopathies can present in a similar way. We present an unusual case of Kikuchi-Fujimoto disease masquerading as metastatic papillary carcinoma of the thyroid.

A 30-year-old young female presented, 2 months post-partum, with complaints of neck pain and fever. A computed tomography scan showed enlarged right-sided lymph nodes and a thyroid nodule. Subsequent biopsy of a thyroid nodule revealed papillary thyroid carcinoma and reactive inflammation in one of the lymph nodes. She underwent an elective total thyroidectomy, central node dissection and a right modified lymph node dissection for enlarged lymph nodes. Her recovery was uneventful and the pathology report was consistent with a papillary carcinoma of the thyroid with one lymph node positive for metastatic disease and several other lymph nodes showing histiocytic necrotizing lymphadenitis.

This coexistence of Kikuchi-Fujimoto disease with localized metastatic papillary thyroid cancer is unusual and presents an interesting, challenging, and complex management dilemma.

Keywords
► Kikuchi disease
► cervical lymphadenopathy
► Kikuchi-Fujimoto disease
► histiocytic necrotizing lymphadenitis

Initially described in Japan in 1972, Kikuchi-Fujimoto disease is a rare clinical condition most commonly affecting young women in the third and fourth decades. The disease is more frequently found in Asia though it has also been described in Caucasians too. The incidence is higher in females than males with a ratio of 3 to 4:1.

It presents typically as cervical lymphadenitis with low-grade fever, malaise, and fatigue although generalized disease has been reported. Given the nonspecific presentation, the differential diagnosis is broad and the disease can mimic as lymphoma, tuberculosis, metastatic disease, systemic lupus erythematosus (SLE), cat scratch disease and infectious mononucleosis. The pathogenesis of this disease is still not clear and is believed to be an immune response of T cells and histiocytes to an inciting agent.

Definitive diagnosis is made by lymph node biopsy showing patchy, irregular areas of eosinophilic necrosis with karyorrhectic debris surrounded by large aggregates of histiocytes. The course of the illness is usually benign and self-limited, and the symptoms resolve within 1 to 6 months with

published online
January 14, 2015

Copyright © 2015 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA.
Tel: +1(212) 584-4662.

ISSN 1061-1711.
no real effective treatment. In this case report, we describe a very unusual presentation of Kikuchi-Fujimoto disease in a young female masquerading as metastatic papillary carcinoma of thyroid.

**Case Presentation**

Our patient is a 30-year-old female of Indian origin who initially presented to her primary care physician for neck pain, swelling, fever, chills and fatigue for approximately 2 weeks. She gave no history of recent travel, sick contacts or recent exposure to people with tuberculosis. She denied any cough, shortness of breath, chest pain, diarrhea, night sweats or any recent weight loss. On physical examination, she had enlarged and tender lymph nodes in the neck that prompted a neck ultrasound showing multiple enlarged lymph nodes bilaterally in the neck. The largest one on the right side measured $1.9 \times 0.8 \times 1.2$ cm and the largest one on the left measured $2.7 \times 0.4 \times 1.1$ cm. The ultrasound also revealed a normal-sized thyroid gland with a $6 \times 8 \times 6$ mm solid nodule in the upper pole of the right thyroid lobe.

Given her clinical presentation and symptomatology, she was initially thought to have upper respiratory infection and was treated with antibiotics and analgesics for 2 weeks with some symptomatic improvement. However, upon discontinuing the antibiotics, her symptoms recurred with increased neck swelling and more palpable lymph nodes especially on the right side of her neck. Her blood work at that time was within normal limits except for a low percentage of polymorphonuclear white cells of 33.9%, an elevated percentage of monocytes of 13.4% and an elevated thyroid stimulating hormone of 13.36 mIU/mL.

On physical examination, the patient was in apparent good health. The examination of the oral cavity showed no abnormality. She had no exophthalmia and no lid lag. The thyroid gland was not enlarged. Multiple lymph nodes were palpated bilaterally, particularly at levels II and V on the right side and at level V on the left side. No axillary lymphadenopathy was appreciated. The liver and spleen were not palpable.

With no symptom resolution, a computed tomography scan of her neck was done revealing extensive lymphadenopathy on the right side of her neck as well as a 6-mm nodule in the right thyroid lobe (Figs. 1 and 2). There was no lymphadenopathy noted in the mediastinum and all other head and neck structures were considered normal with no other obvious pathology.

The patient’s significant past medical history consisted of a recent uneventful cesarean section delivering a healthy baby and two previous benign breast biopsies. She did not smoke cigarettes, abuse alcohol or use recreational drugs. She denied any dysphagia, dyspnea or hoarseness.

There was no personal or family history of SLE, tuberculosis, lymphoma, cancer or autoimmune disorder, and based on available findings her differential diagnoses were Hashimoto thyroiditis, thyroid cancer with possible metastasis and/or viral lymphadenopathy.

In the process of reaching a diagnosis and obvious concern for thyroid cancer, she underwent a fine needle aspiration (FNA) biopsy of the thyroid nodule and of the larger right sided lymph node. It revealed a papillary cancer in the thyroid nodule and reactive inflammatory changes in the lymph node.

Given this pathologic finding and after a thorough discussion of the nature of her disease, the patient was scheduled for surgery. It is worth mentioning that her surgery had to be rescheduled as she was febrile with some upper respiratory symptoms on the day of her presurgical testing. A week later, she underwent a total thyroidectomy with central node dissection and a right radical modified lymph node dissection that proceeded uneventfully.

During her surgery, she had extensive lymphadenopathy at all levels, which is unusual in case of thyroid carcinoma that resulted in a type III comprehensive neck dissection encompassing submandibular gland and lymph nodes level I to VI.
Pathology assessment showed papillary carcinoma of thyroid with one positive lymph node (►Figs. 3 and 4) and remaining lymph nodes showing necrotizing histiocytic lymphadenitis (►Fig. 5). Patient recovered well from her surgery and later on underwent radioactive iodine I-131 ablation postoperatively with post therapy whole body I-131 scan demonstrating no iodine avid tissue in the thyroid bed.

One month later, she presented to our office with resolution of fevers and resolution of neck pain.

**Discussion**

Kikuchi disease, also known as Kikuchi-Fujimoto disease is a histiocytic necrotizing lymphadenitis that was first described in 1972 independently by Kikuchi\(^1\) and Fujimoto et al.\(^2\)

It is an unusual, rare and benign condition that has been mainly described in women younger than 40 years of age. It has been described in men too and practically all ethnic groups, though more commonly in Asian people.\(^3\)

The most common presentation is painful cervical lymphadenitis, although it can present sometimes as generalized lymphadenopathy. Other common complaints include low-grade fever, fatigue, weight loss and arthritis. In a retrospective literature review that described 244 patients with Kikuchi disease, the most common symptoms were fever (35%), fatigue (7%), and joint pain (7%). The most common clinical and laboratory findings were lymphadenopathy (100%), rash (10%), arthritis (7%), hepatosplenomegaly (3%), leukopenia (43%), elevated sedimentation rate (40%), and anemia (23%).\(^4\) The lymphadenopathy is usually cervical but may involve axillary, mediastinal, and iliac nodes. Cervical lymphadenopathy is most commonly seen in the posterior cervical triangle and jugular chain.\(^5\)

The presentation is so vague that it easily mimics other diseases such as lymphoma, tuberculous adenitis, metastatic disease, SLE, cat scratch disease and infectious mononucleosis thereby making diagnosis and treatment all the more difficult.\(^6\)

The pathogenesis of Kikuchi disease is unclear but is believed to be an immune response of T cells and histiocytes to an unknown inciting agent. Pathogens implicated in triggering this response include Epstein-Barr virus,\(^7,8\) Human Herpes virus 6 and 8,\(^9\) Human Immunodeficiency virus, parvovirus B19,\(^10\) Toxoplasma, Yersinia and Paromyxoma viruses.\(^5\) A constant finding consistent with a viral etiology is increased levels of interferon-\(\alpha\) and of other proteins in the cytoplasm of stimulated lymphocytes, histiocytes, and vascular endothelium.\(^11\) The cellular destruction seen in this disease is hypothesized to be due to apoptotic cell death mediated by CD8 T lymphocytes with some role of interferon-\(\gamma\) and interleukin-6.\(^12,13\)

Anemia, leukopenia, and elevated erythrocyte sedimentation rate can be seen on laboratory studies.\(^14\) Leukopenia is fairly common among these patients as seen in our patient.

**Fig. 3** Papillary thyroid carcinoma with clear overlapping nuclei (H & E, ×200).

**Fig. 4** Lymph node with metastatic papillary thyroid carcinoma (H & E, ×100).

**Fig. 5** Histiocytic necrotizing lymphadenitis (H & E, ×400).
too and is consistent with Kikuchi disease as described in some reports.\textsuperscript{15,16}

Currently, there are no definitive laboratory tests available for diagnosis of Kikuchi disease and lymph node biopsy is the only way to diagnose this disease. This disease being rare and unusual, it is very important to exclude other life-threatening disorders. Patients often have been misdiagnosed as having lymphoma and treated with chemotherapy.\textsuperscript{17}

The histology in Kikuchi disease is unique and at most times can be differentiated from other infectious causes of lymphadenopathy but not from that seen in some patients with SLE. The lymph node usually shows patchy irregular brightly eosinophilic areas of necrosis\textsuperscript{5,18} that contain fibrinoid deposits and apoptotic nuclear debris, surrounded by large aggregates of pale staining histiocytes, small lymphocytes and plasma cells. Characteristically, neutrophils and eosinophils are absent in this entity. Nests of plasmacytoid monocytes and immunoblasts can be seen at the periphery.\textsuperscript{19}

Kikuchi disease usually runs a benign course and cervical lymphadenopathy usually resolves within 1 to 6 months.\textsuperscript{16,18} There is no special treatment recommended for this disease and in general therapy is targeted toward symptom relief. However, in complicated cases, high dose glucocorticoids with intravenous immunoglobulin have been shown to have some benefit.\textsuperscript{20}

Although uncommon, a recurrence rate of 3 to 4\% has been reported.\textsuperscript{19} Also interestingly, the diagnosis of Kikuchi disease can precede, postdate or coincide with diagnosis of SLE. Kikuchi disease not only shares sex and age predisposition but also shares some histologic features with SLE. Tubuloreticular structures in the lymphocytes and endothelial cells in patients with SLE have been observed to be similar to those seen in this disease.\textsuperscript{21} Though self-limited, patient should be followed for a few years since recurrence is quite common and some patients can develop SLE.\textsuperscript{15,22}

The coexistence of Kikuchi disease and papillary thyroid carcinoma in our patient is rare and so far has rarely been reported in the extensively searched literature. The management of thyroid nodule with FNA biopsy showing cancer is total thyroidectomy for all tumors larger than 1 cm while lymph node dissection is sufficient for tumors smaller than 1 cm with clinically uninvolved nodes.\textsuperscript{23}

The American Thyroid Association consensus statement also recommends therapeutic central neck dissection in patients with clinically involved nodes and prophylactic central neck dissection in advanced primary tumors (T3 or T4) without evidence of nodal involvement.\textsuperscript{23} Our patient had enlarged lymph nodes both on physical examination and radiological imaging necessitating total thyroidectomy with comprehensive central node dissection.

**Conclusion**

Although a rare disease, Kikuchi disease should be in the differential diagnosis when a young woman presents with cervical lymphadenopathy. At the same time, it is important to rule out other diseases that can cause significant physical and emotional disturbance such as in our patient. Also, the coexistence of Kikuchi disease and papillary thyroid carcinoma in our patient is unique and presents a very complex and challenging clinical scenario. First, the decision to perform a neck dissection for clinically positive nodes despite FNA showing reactive changes and second, the intraoperative decision regarding how extensive should the node dissection be were challenging decisions to be made. In summary, although Kikuchi disease is a rare entity, we should consider it in the differential diagnosis when a young woman presents with fever and cervical lymphadenopathy.

**References**