Case Report

Two Cases of Lymphadenopathy

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Abstract: Lymphadenopathy is a common presentation in many diseases including connective tissue diseases, infection and malignancies. A detailed history, full physical examination, baseline and specific investigations are essential to make a definite diagnosis. We present two cases of lymphadenopathy with unusual diagnoses: Kikuchi’s lymphadenitis and Kimura’s disease. Both diseases are more commonly found in Asia and the Far East.

Keywords: Kikuchi’s lymphadenitis, Kimura’s disease, Lymphadenopathy

Case 1 History

A 29-year-old lady was referred to our medical clinic in December 2000 for suspected systemic lupus erythematosus (SLE). She presented to the surgeon two months prior to the current clinic visit because of right cervical lymphadenopathy. Fine needle aspiration of lymph node did not reveal any malignancy or tuberculosis. Excisional biopsy of lymph node was also performed which showed histological evidence of Kikuchi’s lymphadenitis (Figure 1).

She was well and asymptomatic. She did not have any symptoms suggestive of SLE. Physical examination confirmed a small, non-tender and firm lymph node at the right cervical region. Baseline blood tests were performed and the results were as follows: hemoglobin 12.6 gm/L, white cell count 4.9x10^9/L with normal differential count, ESR 9 mm/hr, normal albumin to globulin ratio, normal C3 and C4 level, and ANA was 1:40.

The diagnosis is Kikuchi’s lymphadenopathy without evidence of SLE. She would continue to be followed up in the medical clinic to monitor her progress.

Discussion

Kikuchi’s histiocytic necrotizing lymphadenitis (Kikuchi-Fujimoto disease) is an uncommon, benign condition of unknown cause. It is a self-limiting, SLE-like autoimmune condition caused by virus infected transformed lymphocytes. This disease was first detected in Japan in 1972 as a well-defined clinicopathologic entity. The exact pathogenesis was not certain but mostly believed to be a viral cause or post-viral hyperimmune reaction. Causative infectious agents suggested include Epstein-Barr virus (EBV), human herpes virus 5, human immunodeficiency virus, parovirus B19, paramyxo and parainfluenza viruses, Yersinia and toxoplasmosis.

This disease is usually found in healthy young women under 40 years of age. They usually present with fever, localized cervical and posterior auricular lymphadenopathy, systemic symptoms such as night sweats, gastrointestinal upset, weight loss, myalgia and arthralgia. Up to 40% of patients will
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present with transient skin rash such as facial erythema, erythematous papules, plaques, nodules and ulcers.³

Other causes of lymphadenopathy have to be ruled out before the diagnosis of Kikuchi’s lymphadenitis is made. TB lymphadenitis, lymphoma, lupus lymphadenopathy and other infectious disease such as EBV infection are other common causes.⁴,⁵ Baseline blood tests and histological diagnosis are essential to confirm the diagnosis of Kikuchi’s lymphadenitis and exclude other causes. Patients with Kikuchi’s lymphadenitis generally have normal CBP, ESR and negative ANA serology.

The diagnosis is usually based on histological findings. There are characteristic histological features found on lymph node biopsy. These include abundant karyorrhectic nuclear debris and histiocytic cellular infiltrate without neutrophilic infiltration, presence of eosinophilic granular debris and immunoblasts and absence of hematoxylin body which is an amorphic aggregate of basophilic material, a pathognomonic of lupus.

The disease runs a benign course and is usually self-limiting. The symptoms usually resolve within one to four months spontaneously. No treatment is effective so far. The disease does recur although it is uncommon. Infrequently, patients may develop SLE later.⁶,⁷ Kikuchi's lymphadenitis may occur simultaneously with SLE or presents as a flare up in known SLE patient.⁸,¹² Therefore, all patients should be followed up to look for features of SLE or recurrence of the disease. If the symptoms persist or deteriorate, we should repeat lymph node biopsy to rule out other differential diagnoses. According to several case reports, systemic steroids could be tried in severe and persistent cases.¹³

In summary, Kikuchi’s lymphadenitis is a benign condition and most of the patients' symptoms will disappear spontaneously. However, patients should be monitored regularly to look for SLE and the diagnosis should be reviewed if symptoms persist.

Case 2 History

A 52-year-old lady presented with on & off chest discomfort for several months and was followed up in the medical clinic. She had been admitted to the hospital with constitutional symptoms and chest discomfort. Physical examination at that
time found generalized lymphadenopathy involving bilateral cervical, axillary and groin regions. Cardiac examination revealed an ejection systolic murmur.

Investigations showed abnormal blood results. She had normochromic normocytic anaemia, hemoglobin 10.5 gm/L, normal white cell count but eosinophilia (1.5x10^9/L), serum globulin 64 gm/L, and ESR>130 mm/hr. Myeloma screening including bone marrow examination was negative. ANA was 1:160 and anti-dsDNA was <10 IU/ml. Echocardiogram was performed and it was essentially normal. CT abdomen was also normal. Excisional biopsy of lymph node was performed and it showed reactive changes only.

She continued to have persistent generalized lymphadenopathy, eosinophilia and hyperglobulinemia. She was referred to the rheumatologist for suspected underlying connective tissue or systemic lupus erythematosus (SLE). In view of uncertain diagnosis and high suspicion of tuberculous adenopathy or lymphoma, a second excisional biopsy of lymph node was performed at right groin region. This time, the biopsy report confirmed Kimura's disease (Figure 2).

She was started on prednisolone 30 mg daily. A few weeks later, lymphadenopathy was getting smaller, eosinophil count was normalized, anaemia was corrected, and globulin level returned back to normal. Azathioprine 50 mg daily was started and prednisolone was gradually tapered. She remained well on follow up.

**Discussion**

Kimura's disease is a rare, benign angiolymphoid proliferative disorder of unknown etiology. It occurs endemically in the Far East. This disease was first described in China by Kim and Szeto in 1937 as eosinophilic hyperplastic lymphogranuloma. Then it was described by Kimura in Japan in 1984 as a distinct clinicopathological entity which affects predominantly young to middle-aged oriental males. This disease is usually confused with another disease called angiolymphoid hyperplasia with eosinophilia (ALHE). Both diseases share similar clinical and histopathological features. In western literature, both terms represented the same disease. It was thought that Kimura's disease was a variant of ALHE. However, many cases of Kimura's disease were reported in Far East and it was believed to be a separate entity from ALHE. Kimura's disease is likely an allergic reaction to some infectious agents because it is associated with eosinophilia and elevation of IgE level.
This disease is usually found in young Asian males. They present with subcutaneous nodules or masses predominantly around head and neck region, localized or generalized lymphadenopathy and enlargement of salivary gland.\textsuperscript{15} The diagnosis is based on clinical features, hypereosinophilia, hyperglobulinemia with elevation of IgE level and characteristic biopsy findings.

The characteristic histological features of Kimura's disease are proliferation of dense lymphoid follicles with formation of reactive germinal centers, massive infiltration of eosinophils in the sinus and interfollicular areas, proliferation of post-capillary venules and intense deposition of IgE within the germinal centers in a reticular pattern on immunohistochemical staining.\textsuperscript{16}

A recent study showed that the clinicopathological features of Kimura's disease in Chinese patients were similar to that found in other Asian patients.\textsuperscript{17}

Kimura's disease is associated with other organ involvement. There is a high prevalence of renal involvement among patients with Kimura's disease. They usually present with proteinuria or nephrotic syndrome.\textsuperscript{18} It is believed that immuno-allergic immune complexes play an important part in pathogenesis. Different renal pathologies are identified and they are minimal change, membranous nephropathy, minimally proliferative GN or mesangial proliferative GN.\textsuperscript{19} All kinds of renal pathologies respond to steroid very well in particular minimal change nephropathy.\textsuperscript{20} Kimura's disease is also associated with atopic bronchial asthma and eosinophilic myocarditis. Both conditions improve with systemic steroids.

The presentation of Kimura's disease and its association are similar to Churg-Strauss syndrome. Accordingly, careful history taking and specific investigations are required to distinguish these two conditions.

Treatment of Kimura's disease can be local or systemic. Local treatment includes topical steroids for superficial skin lesions and surgical excision or radiotherapy for localized lesion.\textsuperscript{21} Systemic treatment such as systemic steroids is good for generalized lymphadenopathy, renal or cardiac involvement. Immunosuppressants such as azathioprine or cyclosporin can be used in those who do not respond to steroids or as a steroid sparing agent.\textsuperscript{22,23}

Prognosis is generally good in Kimura's disease. They usually respond to treatment very well. However, this disease has a high recurrence rate when steroid is tapered down or is stopped. Careful and close monitoring is required.

In summary, Kimura's disease is a rare disease with distinct clinicopathological features and it responds to steroids well. However, we should distinguish this disease from other differential diagnosis such as Churg-Strauss syndrome. All patients should have disease monitoring regularly to look for any associated systemic organ involvement.

References

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