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Case Report

Kikuchi disease: An unusual cause of cervical lymphadenopathy in a young female

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ABSTRACT

Kikuchi-Fujimoto disease (KD), also known as histiocytic necrotizing lymphadenitis, is a rare cause of unilateral cervical lymphadenopathy usually described in adolescents and young adults with female preponderance. Clinically patients present with palpable lymphadenopathy, fever, and loss of weight. Hence, it should be differentiated from other causes of lymphadenopathy such as tuberculosis, lymphoma, or malignancy. Although the majority resolve spontaneously without treatment some may require non-steroidal anti-inflammatory drug or steroids. It may also be associated with systemic lupus erythematosus. Hence early detection, prompt diagnosis, and follow-up of the patient are essential in all cases of unilateral cervical lymphadenopathy in young adults. Here, we describe a 22-year old female who presented with unilateral neck swelling and was clinically diagnosed initially as a case of tuberculous lymphadenitis which on biopsy turned out to be KD.

Keywords: Kikuchi disease, Necrotizing lymphadenopathy, Systemic lupus erythematosus, Rash

INTRODUCTION

Kikuchi disease (KD) is a benign self-limiting disease first described in Japan. It is a rare disease of unknown etiology although it has been reported in association with a number of autoimmune and infectious diseases and is seen frequently in coexistence with systemic lupus erythematosus (SLE). It is highly prevalent in Asian countries, most commonly in Japan. KD mainly affects young females and is characterized clinically by painful cervical lymphadenopathy, fever, night sweats, myalgia, and anorexia. Differential diagnoses include tuberculosis, infectious mononucleosis, and lymphoma. Due to increased FDG uptake on ^{18}F-FDG PET scan, it may be mistaken for metastatic lymphadenopathy in patients with known primary.

CASE REPORT

A 22-year-old female with no previous significant medical history presented with unilateral painful cervical lymphadenopathy, pharyngitis, fever, dry cough, malaise, and anorexia for 3 weeks. Fever was high grade in nature with evening rise of temperature and was associated with drenching night sweats and fainting episodes. She had been well and healthy until the onset of current illness. There was no history of headache, skin rashes, recent significant weight loss, or any infectious illness. Personal and family history were unremarkable. On examination, she was febrile - 101°C, Blood pressure: 90/60 mmHg over the right upper arm. There were multiple tender lymph nodes over the cervical region and axilla of the right side. Few right supraclavicular nodes were also palpable. There were no palpable lymph nodes on the left. No hepatosplenomegaly or skin manifestations were found.

Laboratory workup revealed a haemoglobin level of 12.1 g, Total count of 5500 cells/cu mm, neutrophils: 42%, lymphocytes:52%, eosinophils: 0%, monocytes: 06%, basophils: 0, Acute phase reactants were elevated with erythrocyte sedimentation rate (ESR): 54 mm/h and C-reactive protein (CRP) 8.68 mg. Liver function tests were normal. Serology for hepatitis B and C and HIV were negative. There were no clinical manifestations of any rheumatological disease, SLE, or vasculitis. Anti-dsDNA, anti-RO, anti-LA, p-ANCA, and c-ANCA were negative. Peripheral smear showed reactive lymphocytosis with few reactive lymphocytes (10%).

Ultrasound scan of the neck showed multiple cervical nodes on the right side of the neck including level Ia, b, c level II, III, IV, and V with supraclavicular nodes. The largest lymph node was level II node of size 18 mm × 12 mm. Most of the

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lymph nodes were hypoechoic rounded with loss of fatty hilum. Some nodes showed central necrosis [Figure 1]. Color doppler showed increased peripheral vascularity. On the left side, few hypoechoic nodes were present, the largest one measuring 5 mm × 7 mm. Based on the ultrasound appearances a provisional diagnosis of tuberculous lymphadenitis versus lymphoma was given.

Plain computed tomography (CT) scan neck showed multiple isodense lymph nodes of varying sizes in the right side of the neck [Figure 2]. There were no left cervical nodes. Few right supraclavicular nodes were also present. CT Chest did not reveal any mediastinal nodes or lung lesions.

Ultrasound-guided fine-needle aspiration cytology of right cervical lymph node was done which showed mature and transformed lymphocytes, histiocytes, and a few atypical cells with irregular nuclear membrane and clumped chromatin. Since it was inconclusive, excision biopsy of the right level II cervical node was done which was consistent with KD. Biopsy showed congested blood vessels on the surface. Cut section was grey white with faint lobulation and specs of hemorrhage. Microscopy revealed effacement of architecture, showing paracortical necrosis composed of apoptotic debris, fibrin deposits surrounded by lymphocytes, and few monocytoid cells and histiocytes [Figure 3]. The diagnosis was necrotizing lymphadenitis suggestive of KD.

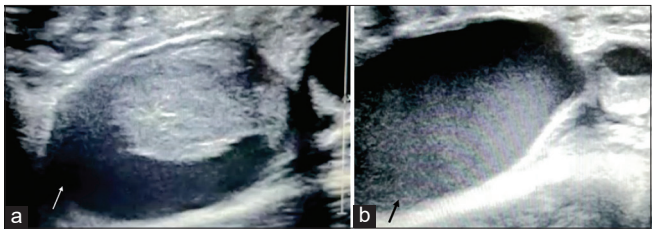

Figure 1: Ultrasound scan of neck: multiple cervical lymph nodes of varying sizes with some showing necrosis (arrow in a and b).

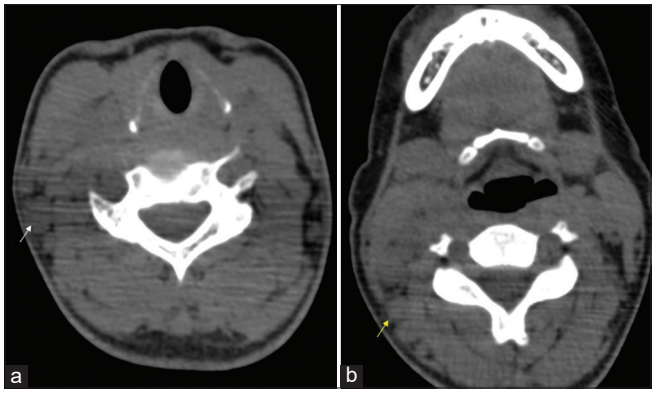

Figure 2: Computed tomography scan of neck and upper chest; marked asymmetrical cervical and supraclavicular lymphadenopathy more on the right side (arrow in a and b).

Three weeks after the diagnosis was made, the patient developed multiple erythematous macules and petechiae over the right leg and dorsum of the foot [Figure 4]. It was tender and associated with pitting pedal edema. She also complained of arthralgia over the right knee joint. Based on the diagnosis of KD and arthralgia, she was started on a short course of acetaminophen after which the symptoms subsided.

DISCUSSION

KD or histiocytic necrotizing lymphadenitis is an uncommon cause of cervical lymphadenopathy first described by Kikuchi and Fujimoto in 1972.[1,2] It is highly prevalent in Asians and is a rare benign self-limiting disease commonly affecting adolescents and young adults with a female-male incidence in the ratio of 2:1.[3,4] Its etiology is unrecognized. The accepted hypothesis is that of viral-autoimmune etiology.

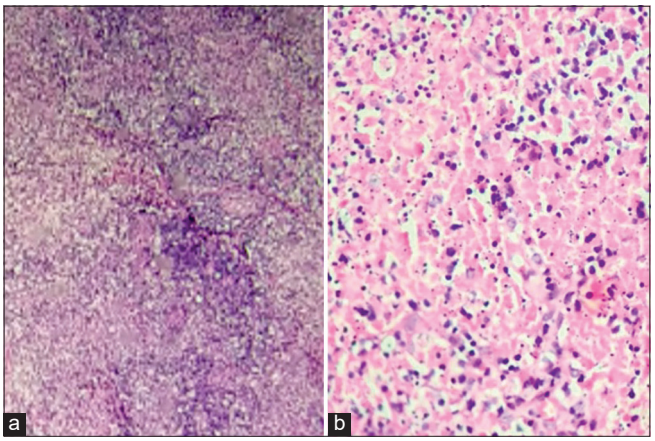

Figure 3: Excisional lymph node biopsy. (a) paracortical necrotic lesion with karyorrhexis and sheets of lymphocytes. (b) Phagocytes and foamy histiocyte with lymphocytes.

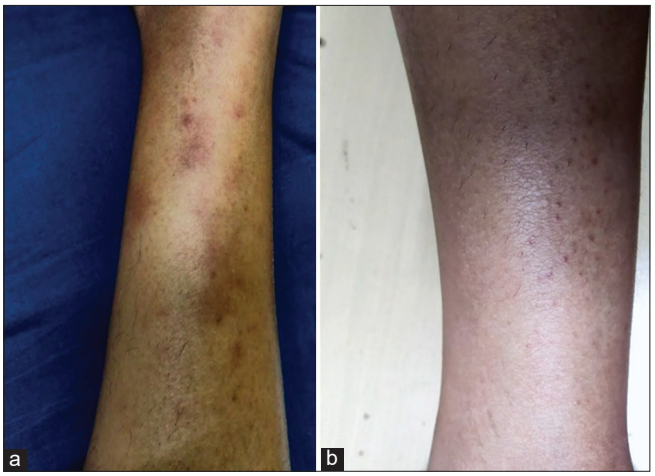

Figure 4: (a) Multiple erythematous macules and rashes over the right shin. (b) Petechial rashes over the right leg.

The pathogenesis of KD is unknown, although various studies have proved that it is a T cell-mediated inflammatory response against viral infections particularly the Ebstein-Barr virus or human herpes virus, but a specific viral agent is not yet identified.[5]

The clinical manifestations of KD include cervical lymphadenopathy and fever which occur in 80% of patients. The lymph nodes are usually 2–3 cm in size, most commonly involving the posterior cervical lymph nodes followed by axillary and rarely supraclavicular lymph nodes. Fever usually ranges from 1 to 7 weeks and may be associated with chills, evening rise of temperature, night sweats, cough, pharyngitis, malaise, anorexia, headache, arthralgia, and skin manifestations.[6]

Extranodal manifestations of the disease are uncommon. They can involve various organs including skin, bone marrow, myocardium, or central nervous system. Studies show that up to 30% of cases are associated with skin manifestations such as acneiform eruptions, papules, plaques, petechiae, or nodules. When skin manifestations are present, it indicates severe disease. Association between Kikuchi disease and SLE have been reported. KD can precede (30%), coincide (47%), or follow (23%) the diagnosis of SLE. Hence, ANA testing must be done in patients diagnosed with KD and these patients must be under constant follow-up evaluation for SLE. Hepatosplenomegaly has also been reported in some patients.[7]

Neurological manifestations though rare have been documented which include cerebellar ataxia and aseptic meningitis. The kinetic tremor and gait ataxia preceded cervical lymphadenopathy. The diagnosis of KD was made based on pathology. Lymphocyte-dominant pleocytosis was observed in cerebrospinal fluid.[8]

There are no specific laboratory findings for the diagnosis of KD. Lab studies show leukocytosis in approximately 2–5% cases and leukopenia in 25–58% cases, elevated ESR and CRP with or without elevated transaminases. Radiological imaging via CT typically shows enlarged enhancing lymph nodes with necrosis.[9] Diagnosis is confirmed by excisional biopsy and histopathological examination of lymph nodes which characteristically shows paracortical foci with necrosis and histiocytic cellular infiltrate. Antinuclear antibody may be positive in about 7% of patients.

KD is a self-limiting illnesss which usually resolves spontaneously. Rate of recurrence is low. Treatment is supportive, mainly with analgesics like non-steroidal anti-inflammatory drugs (NSAIDs) to resolve lymph node pain and fever. Extranodal KD responds well to corticosteroids. In steroid-resistant cases, good response to Hydroxychloroquine and intravenous immunoglobulins have been reported.[10] In our case, patient responded well to short course of NSAIDs and there was no evidence of SLE after 1 year follow-up.

CONCLUSION

Kikuchi disease should be considered in the differential diagnosis of any patient who comes with cervical lymphadenopathy. It is a relatively benign disease and carries a good prognosis though association with connective tissue disease like SLE has to be excluded.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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