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Kikuchi's Disease

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Fifteen year old male presented with high grade intermittent fever and cervical lymphadenopathy. He had multiple enlarged bilateral cervical lymph nodes. The examination of other systems was normal. Work up for sepsis, malignancy and autoimmune disease were negative. Viral serology was negative. Histopathology of lymph node was consistent with kikuchi's disease.

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Kikuchi's disease is a rare, benign clinicopathological condition of unknown etiology. Patients usually presented with fever and lymphadenopathy. Its association with Systemic Lupus Erythematosus (SLE) makes it necessary to be aware of this condition and follow up these cases. Histopathology of the involved lymph node differentiate Kikuchi's disease from several more serious conditions particularly lymphomas, which it may mimic[1].

Kikuchi's disease was recognized for the first time as a separate syndrome or disease in Japan by Kikuchi's and Fujimoto independently in two separate cases among young woman in 1972.The initial description was referred as Kikuchi's and Fujimoto disease or Kikuchi's histiocytic necrotizing lymphadenitis[2].

Kikuchi's disease is primarily a disease of young women (M:F ratio 1:4), the mean age at presentation is 30 years old. It is most commonly seen in Japan and other Asian countries but also has been reported in USA, Western Europe and other part of the world[3].

The aim of publishing this case is to be aware of this rare disease, and to consider it as one of the differential diagnosis of young patients with cervical lymphadenopathy and fever of unknown origin.

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THE CASE

Fifteen year old Asian boy with no previous medical illness, presented to emergency department with history of fever and cervical swellings for 20 days. Fever was intermittent, high grade, accompanied by non-productive cough. He was anorexic and had a weight loss of 1kg over the same period. He had noticed swellings on both sides of his neck, which were painful and had gradually increased in size over the last 3 weeks. He gave also history of skin rash after he took a single dose of augmentin; the rash was maculopapular localized only to the upper chest, which fade by itself within two days without any medication. There was no history of nausea, vomiting, jaundice or loose motion. No history of arthralgia, mouth ulceration or headache. No history of respiratory or genitourinary symptoms. There was no history of proceeding URTI. No history of contact with TB patient or sick patient with similar illness, and no history of contact with animals or ingestion of raw milk. No history of recent travel abroad.

Physical examination on the day of admission: He was conscious, oriented, febrile with temperature of 39.3c, tachycardic with pulse of 111 beats/min. He had 7-8 tender, firm, enlarged bilateral cervical lymph nodes (distributed mainly over both posterior cervical chain) the largest was 3x4 cm; there was no cellulitic changes of the overlying skin and no discharging sinuses. No other palpable lymph node and no skin rash. Abdominal examination did not reveal palpable liver or spleen. Other physical examinations were normal.

Investigations on the day of admission revealed WBC 2,500 cells/mm3, with normal differential, ESR 30 mm/hr. Blood and urine cultures were sterile. Toxoplasma serology, Widal test, EBV & CMV serology (both IgM and IgG) were negative. VDRL test was negative. RA latex and ANA were negative. Other parameters were all normal.

Chest x-ray and ultrasonography of the abdomen were normal. PPD test was negative (indurations of 5x5mm).

During the hospital stay, the patient's fever continued to spike. WBC count continued to be low (as shown in graph 1). On the fourth day of hospitalization the patient developed maculopapular rash which started on the face then spread to involve the whole body sparing the palms and soles; the rash initially was discrete, but on the next day became confluent. There was no history of taking antibiotics or NSAID during his hospitalization prior to the development of rash. The rash continued within the same intensity for 7 days, then started to fade gradually over 3-4 days.

Graph 1: WBC Counts

Fine needle aspiration cytology on one of the cervical lymph nodes was done and showed reactive hyperplasia suggestive of a viral etiology. This was followed by an excisional biopsy of one of the enlarged left cervical node. Histopathology revealed lymph node with essentially preserved architecture with multiple areas of paracortical necrosis and karyorrhexis with fibrin deposits on these necrotic zones. The tissue bordering these necrotic areas showed histiocytic response with histiocytes engulfing necrotic nuclear debris as well as large areas of proliferating monocytoid cells which was positive for CD3. The histiocytes were CD 68 positive. Conspicuous absence of neutrophils was noted (Figure 1 and 2).

No granulomas were seen. Gram stain and stain for acid fast bacillus were negative. Culture of the aspirated material was negative and Flow cytometry of the excisional biopsy showed a reactive pattern. The findings were consistent with a necrotizing histiocytic lymphadenitis i.e., Kikuchi's disease.

The patient was discharged in a relatively good condition, but his fever continued to spike at home, his WBC count started to improve by the end of fourth week from the onset of his illness. The lymphadenopathy persistent and was of the same size.

In view of persistent fever, the patient was started on steroid therapy (prednisilone 1 mg/kg.daily).

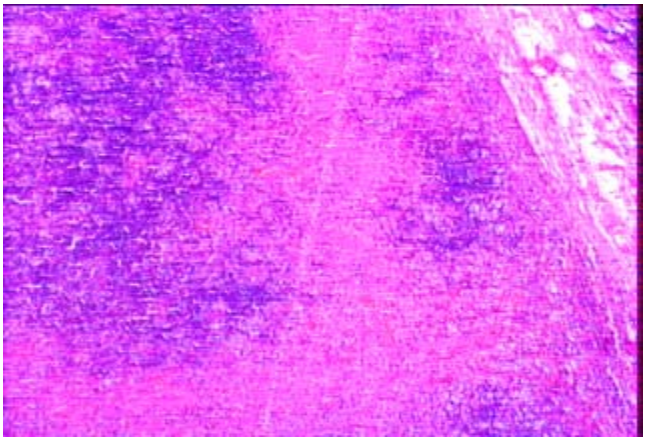

Fig 1: Low power view of the lymph node with peripheral capsule, shows large areas of paracortical necrosis and surrounding (blue) areas of proliferating lymphoid cells. Haematoxylin and Eosin x 100

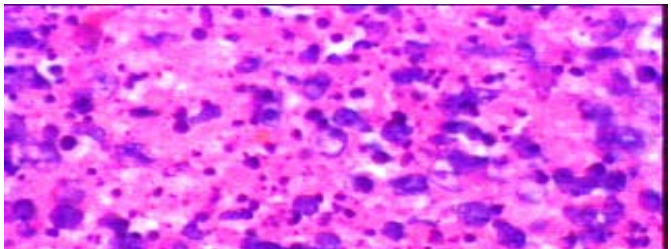

Fig 2: High power view to show karyorrhectic debris (blue dots), fibrin like pink necrotic material and proliferating monocytoid T-cells.
Haematoxylin and Eosin x 400

DISCUSSION

This patient presented with fever, cervical lymphadenopathy and rash, his initial clinical evaluation and laboratory workup did not reveal the diagnosis, biopsy of one of the cervical lymph nodes showed the characteristic histological finding of Kikuchi's disease. To my knowledge, it is the first case of Kikuchi's disease to be reported in Bahrain.

The exact etiology and the pathogenesis of Kikuchi's disease is unknown, but the clinical presentation, course and histological changes of the involved lymph nodes suggest an immunological response of T lymphocyte and histiocytes to an infectious process such as viral agents like Epstein Barr virus (EBV) , human immunodeficiency virus (HIV), Herpes simplex virus and others. Toxoplasma and other bacterial agent like Yersinia enterocolitica have also been implemented[4,5].

A possible role for gamma interferon and Interleukin-6 in the pathogenesis of Kikuchis disease was suggested by Kubota et al[6].

Some previous studies have suggested that a disorder in cellular immunity is responsible for Kikuchi's disease; with Apoptotic cell death being the principle finding in the pathogenesis of this disease[7].

The most common clinical presentation of Kikuchi's disease is fever and cervical lymphadenopathy.

Fever is a primary symptom in 30 to 50 percent of patients. It is typically low grade and persists for about one week; though rarely for up to one month[2].

Lymph node involvement is usually cervical and localized. Kuo et al. reported 79 Chinese patients with Kikuchi's disease; all of them had cervical node involvement[8].

The nodal enlargement is often associated with dull or acute pain. The nodes are usually only moderately enlarged (1 to 2 cm in diameter) but occasionally are much larger though usually does not exceed 7 cm, typically they are firm, smooth, discrete, and mobile. Occasionally patients may present with generalized lymphadenopathy such as axillary, inguinal, mediastinal and celiac lymph nodes.

Systemic symptoms may accompany fever and lymphadenopathy, this may include: Night sweats, nausea, vomiting, weight loss. A variety of other symptoms may occur in patients with Kikuchi's disease, which may include myalgia, arthralgia, chest and abdominal pain; splenomegaly and/or hepatomegaly may be encountered[9].

The Cutaneous manifestation associated with kikuchi's disease is relatively common. Kuo et al. reported cutaneous manifestation in 40% of patients with kikuchi's disease; they may be manifested either simultaneously or after the illness. Those Cutaneous manifestation are variable, may include transient skin rashes, similar to rubella or drug-induced eruptions, facial or malar "butterfly rash", other less common manifestation would be facial erythema, erythematous papules, plaques, nodules, scattered indurate lesions, ulcers, polymorphous light eruptions, leukocytoclastic vasculitis and oral ulceration[10]. Cutaneous involvement tends to occur in patients who had more severe and protracted course[8].

Kikuchi's disease causes some diagnostic difficulties due to lack of specific clinical finding, as well as blood investigation. The definitive diagnosis is based on histological findings of the affected lymph node with paracortical necrosis and intervening areas of T lymphoblast like cell proliferation. Skin biopsy of cutaneous lesions from few patients with Kikuchis disease and skin eruption in one series shows specific constellation of histologic features that parallel the histological finding of lymph node[11].

Full blood count usually normal, but leucopenia may predominate in 20-30%; atypical lymphocytes have been reported in 25% of cases. Other nonspecific finding that may encounter; though uncommon; include: thrombocytopenia, pancytopenia, elevated ESR, abnormal LFT, and elevated LDH[2]. ANA, Anti-DNA, RA latex usually negative.

The most frequent finding in Bone Marrow examination is increase in macrophages without atypical cells [2].

No effective treatment has been established for patients with Kikuchi's disease. The natural history of the disease is that signs and symptoms usually resolve within one to four months from the onset of illness. However, patients with severe or persisting symptoms could be treated with corticosteroids[12].

Affected patients should be followed for few years because of the possibility of recurrences of Kikuchi's disease which has been reported in 3% of cases, recurrence may continue for more than ten years.

The disease is usually self limited; with good outcome. In one series 59 of 64 patients (92 percent), for whom data were available, were alive and well at a median of 32 months of follow-up[8].

CONCLUSION

We are reporting a rare case of Kikuchi's disease; which might be the first case to be reported in Bahrain.

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