Kikuchi's disease: a Singapore case series

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ABSTRACT

Introduction: Kikuchi's disease is a benign form of cervical lymphadenopathy that commonly affects young adults. We report a case series from our hospital.

Methods: The clinical features of 23 cases of Kikuchi's disease diagnosed at Changi General Hospital over a seven year period are presented. The cases were identified from pathology records using the search term histiocytic necrotising lymphadenitis.

Results: Most of our patients (78 percent) were young women who presented with cervical lymphadenopathy. The median age was 31 years. In the 18 cases who completed follow-up at the hospital, there was spontaneous resolution of symptoms within a six-month period. One patient demonstrated seropositivity for systemic lupus erythematosus(SLE) and was initially started on steroids. However, the treatment was discontinued shortly afterwards since she did not meet the diagnostic criteria for SLE. Excision biopsy of the affected lymph node was the diagnostic method of choice.

Conclusion: Kikuchi's disease is not uncommon in the Singaporean population. Establishing an early diagnosis is crucial since the clinical presentation can mimic tuberculous lymphadenitis or malignant lymphoma. The diagnostic method of choice is excision biopsy.

Keywords: histiocytic necrotising lymphadenitis, Kikuchi's disease, lymph node, lymphadenopathy

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INTRODUCTION

Histiocytic necrotising lymphadenitis was first described independently in 1972 by Kikuchi[1] (276 cases) and Fujimoto et al[2], both from Japan. Hence, the entity is also known as Kikuchi-Fujimoto's disease or simply Kikuchi's disease (KD). It classically presents as a painful cervical lymphadenopathy in young adults, usually females. Unilateral involvement of the posterior cervical group is the commonest picture. Although most of the cases have been reported in the Oriental races, the entity has also been described in the Caucasian, Hispanic, Middle Eastern and Indian populations. In a study of 108 patients in California[3], 68 patients were white and 8 were black.

Less common manifestations include fever, axillary and mesenteric lymphadenopathy, splenomegaly, parotid gland enlargement, cutaneous rash, arthralgias, myalgias, aseptic meningitis[4], bone marrow haemophagocytosis[5,6] and interstitial lung disease[7]. The cutaneous lesions include erythematous macules, papules, plaques and nodules[8]. The aetiology is unknown, although a viral or autoimmune pathogenesis has been suggested. Several articles have described an association of KD with autoimmune disorders, notably systemic lupus erythematosus (SLE), mixed connective tissue disease and Still's disease. The strongest link is with SLE, although the exact nature of this association has yet not been established[3,9-13].

SLE patients can develop a lymphadenopathy that is clinically and histologically similar to KD. This may manifest in different ways: prior to the development of clinically-evident SLE, concurrent with the onset of lupus, or later during the course of the disease. Chua et al reported a SLE patient with erythema multiforme-like lesions and KD in 1996[14]. The most important differential diagnoses to consider in patients presenting with typical features of KD are tuberculous lymphadenitis and malignant lymphoma. Yoshino et al reported two cases of KD occurring in the course of remission of diffuse large B-cell lymphoma[15]. Immunohistochemistry can be used to differentiate KD from malignant lymphoma.

The disease is usually self-limiting with symptoms resolving within a period of 6 months. However, two fatalities have been reported in the literature[16,17]. One was a 38-year-old patient who

Table I. Clinical characteristics of patients (n=23).

Lymph node involved	Fever	Raised ESR*	WBC* count (X 10^9/ L)	Positive Mantoux test	Sputum or laryngeal AFB* stain	Diagnostic features of KD on FNAC*
Cervical 23/23	9/23	8/13	Range 0.8 - 7.9	1/9	0/7	0/13
Mesenteric 1/23			Mean 4.2			
			Median 4.2			

* ESR: erythrocyte sedimentation rate, FNAC: fine needle aspiration cytology, WBC: white blood cell, AFB: acid fast bacilli

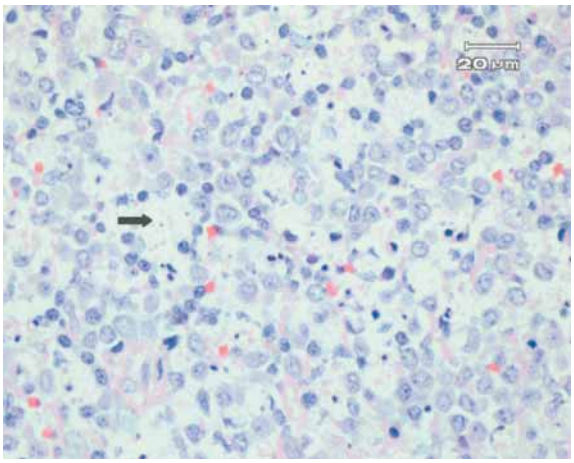

Fig. 1 Photomicrograph of a lymph node biopsy shows abundant histiocytes with focal areas of karyorrhexis (arrow). [Haematoxylin & eosin, x 600]

died of abrupt heart failure and the second was a case of fatal pulmonary haemorrhage. The risk of recurrence is low, with two large studies reporting a range of 3.3% to 4%[1,18]. Blood investigations are non-specific, but may reveal a leucopenia, atypical lymphocytosis or elevated erythrocyte sedimentation rate (ESR).

The diagnostic test of choice is an excision biopsy of the involved lymph node which shows patchy areas of necrosis with karyorrhexis, especially in the cortical and paracortical areas (Fig. 1). Karyorrhexis refers to the breakdown of nuclear chromatin which is dispersed as fine granules in the cytoplasm. These areas are surrounded by an inflammatory infiltrate consisting of histiocytes, lymphoid cells and immunoblasts. Granulocytes are strikingly absent. The cell death is primarily from an apoptotic process and hence the term "necrosis" is not strictly correct. Fine-needle aspiration cytology (FNAC) may show the characteristic features, but is frequently non-diagnostic[19,20]. As previously mentioned, Kikuchi's disease is a self-limited disease with spontaneous resolution of symptoms in almost all cases within a six-month period. Systemic steroids have been found to be of symptomatic benefit in a few cases[21,22].

METHODS

We did a manual search through the pathology department records for cases diagnosed with "histiocytic necrotising lymphadenitis" over the period 1996-2002. The pathologist reviewed all the slides to reconfirm the diagnoses. We reviewed the case notes and collected the relevant data. We describe an illustrative case in detail and present the collective data from all 23 cases in Table I.

Illustrative case

A 13-year-old Malay girl was referred by a general practitioner for "neck lumps". She gave a history of developing a neck swelling about two weeks prior to admission that was associated with nocturnal fevers. She was prescribed a course of amoxycyllin, but her symptoms remained unabated. She had no significant past medical history, no history of contact with tuberculosis (TB) and no recent travel. Examination revealed a 4 cm enlargement of the posterior cervical lymph nodes on the left neck and smaller lymph nodes on the right side. The lymph nodes were firm, mildly tender and mobile. No other lymph nodes were enlarged.

The initial blood tests showed a leucopenia of 2000/uL with 46% lymphocytes, haemoglobin 10.9 g/dL, platelets 278,000/uL and ESR 46mm/hr. Other baseline blood tests and the chest radiograph were normal. Toxoplasma and Ebstein Barr virus (EBV) titres, antinuclear antibody (ANA) and Mantoux tests were all negative. FNAC of the left neck mass showed reactive lymphoid hyperplasia.

Computed tomography (CT) of the neck confirmed multiple, enlarged lymph modes in the posterior cervical chain. CT of the abdomen showed mesenteric lymphadenopathy. CT of the thorax was normal. Excision biopsy of the left nodal mass showed KD. She was discharged and seen two weeks later in the clinic where she reported mild improvement in symptoms. She subsequently defaulted her follow-up appointment.

RESULTS

In our series, there was a distinct female preponderance (18 of 23 cases). Thirteen patients were Chinese, nine

were Malay, and one was a Bangladeshi. Most patients were young, with a median age of 31 (range 13-52) years. All of them had a presenting complaint of cervical lymphadeopathy. CT of the abdomen revealed mesenteric lymph node enlargement in one patient. Fever was the second commonest symptom and was seen in nine patients. One patient had a maculopapular rash. The average duration of symptoms was three weeks (range 1 week to 2 months). None of the patients gave a history of significant weight loss or night sweats.

FNAC of the affected lymph node was performed in 13 cases, and was inconclusive in all of them. Six of the specimens were reported as lymphoid hyperplasia , five as reactive or atypical lymphocytes, one as chronic inflammation, and one as normal. The diagnoses were established by excision biopsy in all the 23 cases. There was no characteristic picture in the blood investigations, although there was a trend towards low white blood cell counts.

One patient, a 39-year-old Chinese woman who presented with fever and cervical lymphadenopathy, tested positive both for ANA and anti-double stranded deoxyribonucleic acid antibody (anti-dsDNA) and was started on steroids for a presumptive diagnosis of SLE. However, the steroids were discontinued a few days later when it was ascertained that she did not meet the diagnostic criteria for SLE (American Rheumatology Association criteria). Her symptoms had completely resolved when she was seen in the outpatient clinic six weeks later.

Twelve patients had an extensive TB workup done, including sputum and laryngeal smears for acid-fast bacilli, TB cultures and Mantoux testing. Once the diagnosis of KD was established, only symptomatic treatment with acetaminophen was given. Of the 23 cases, five were lost to follow-up before documented resolution of symptoms. The remaining 18 had an average symptom duration of two months (range 2 weeks to 6 months).

DISCUSSION

Our patient characteristics were quite similar to what has previously been described in the literature; mostly young women presenting with cervical lymphadenopathy. An extensive TB workup was ordered in 12 of the 23 cases, before the diagnosis was established. FNAC of the lymph nodes was non-revealing in all of the 13 cases where it was performed. Excision biopsy was the diagnostic test of choice. The decision for an initial FNAC was usually made by the surgical team, although on most occasions, the referring team had requested an excision biopsy as the initial procedure.

While FNAC is highly reliable in the identification of metastatic carcinoma and melanoma in lymph nodes obviating the need for excision biopsy, the case is not the same with malignant lymphomas[23]. High rates of false-negatives and the prognostic importance of architectural assessment in some lymphoid tumours limit the role of a simple FNAC. However, recent studies have indicated that complementing FNAC with immunocytochemical evaluation of the aspirate can increase the diagnostic accuracy to around 85-90%[23-25].

In the case of TB lymphadenitis, older studies have mentioned high sensitivity and specificity for FNAC aspirates (comparable to excision biopsy) sent for histological and microbiological analysis[26,27]. A study published in 2004, however, demonstrated the advantage of combining FNAC with polymerase chain reaction (100% sensitivity) over FNAC alone (68% sensitivity)[28]. These facts emphasise the need for a high index of suspicion and performing a definitive test (such as excision biopsy) of the node to arrive at an early diagnosis in patients with KD. In a search of the medical literature, we did not come across any case series hitherto reported from Singapore.

In conclusion, Kikuchi's disease is a benign lymphadenopathy that commonly occurs in young adults. Early diagnosis is essential since the clinical features can resemble TB lymphadenitis or malignant lymphoma. Referral to the surgeons and proceeding directly for an excision biopsy of the involved node is a prudent course of action.

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