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Short communication

# Recurrent Kikuchi–Fujimoto disease: Case report

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**Abstract**

Kikuchi–Fujimoto disease, also known as histiocytic necrotising lymphadenitis, is a self-limiting condition of uncertain aetiology characterised by lymphadenopathy, pyrexia, and neutropenia. Some reported cases have been associated with systemic lupus erythematosus and there have been suggestions that Kikuchi's disease could represent a mild form of lupus but without definite evidence. We describe an unusual case of histiocytic necrotising lymphadenitis in an Asian woman who had recurrent episodes for five years before a diagnosis was made.


*Keywords:* Kikuchi–Fujimoto disease; Lymphadenopathy; Neutropenia; Systemic-lupus-erythematosus; Apoptotic necrosis; Histiocytes

## Introduction

Kikuchi's disease is a benign, self-limiting condition characterised by lymphadenitis, fever, neutropenia, and occasional skin rashes. The female to male ratio is 4:1 and the disease is particularly prevalent in young women of Asian descent in their third decade.[1] Cases have been recorded throughout the world, since the disease was first reported by Kikuchi and Fujimoto in 1972 in Japan[2,3] but the diagnosis remains difficult. The disease was first reported in the UK in 1985 and a large series was reviewed in 1998.[4]

## Case report

A 24-year-old Bangladeshi woman who arrived in the UK in June 2003 reported to the accident and emergency department of Bart's and The London NHS Trust, Whitechapel in September 2003, complaining of feeling generally unwell, fever, and swollen glands in the neck for the previous three weeks. She gave a history of eczematous rashes on the upper and lower extremities over the past five years, during which she also experienced recurrent bouts of fever, and cervical and occasionally axillary lymphadenopathy. Investigations in Bangladesh included examination of a fine needle aspiration cytology specimen of the cervical lymph nodes, which was reported as chronic nonspecific lymphadenitis. A Heaf test, carried out at the same time, was reported as nonreactive. Multiple examinations of the blood failed to show malaria parasites and her erythrocyte sedimentation rate ranged between 20 and 30 mm/h, with a maximum of 95 mm/h recorded in September 2002. Her haemoglobin was 9.6 g/dl and a white cell count was $6 \times 10^9\,l^{-1}$. Two separate radiographs of the chest were also reported as normal. In November 2002, she started antituberculous treatment but later it was discontinued, as her diagnosis was changed to rickettsial fever, subsequently treated empirically with doxycycline. For her eczematous rash she occasionally applied topical hydrocortisone ointment.

On examination in the accident and emergency department she was pyrexial with a temperature of 38 °C and looked

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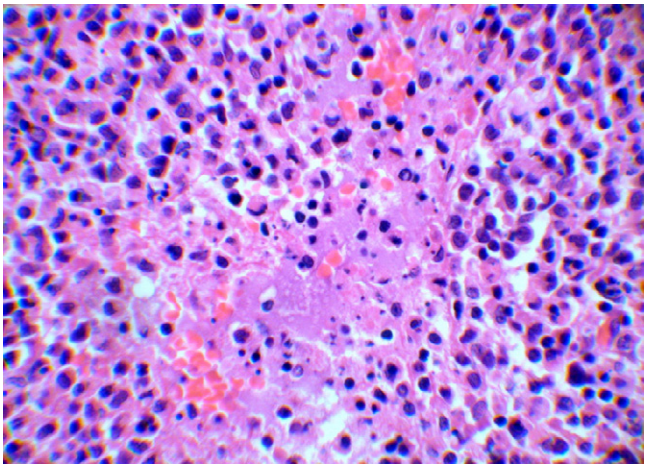

Fig. 1. Lymph node showing zones of necrosis containing abundant karyorrhectic cellular debris surrounded by zones of histiocytes and immunoblasts.

pale. There were matted rubbery lymph nodes in the anterior cervical chain and a single pea-sized submental lymph node. No axillary or inguinal lymph nodes were palpable. She had erythematous, scaly, itchy, maculopapular lesions on both upper and lower limbs. She had no splinter haemorrhages.

Investigations showed haemoglobin of 12.3 g/dl, mean corpuscular volume of 87.5 fl, and total white cell count of $2.7 \times 10^9\,l^{-1}$ with neutrophils $1.5 \times 10^9\,l^{-1}$ and lymphocytes $1.0 \times 10^9\,l^{-1}$. Liver function tests, blood urea, and electrolytes were within reference ranges. Her erythrocyte sedimentation rate was raised to 41 mm/h and C-reactive protein was 10 mg/l. The radiograph of her chest was unremarkable with no focus of infection, and an autoantibody screen was normal. She was referred to an oral and maxillofacial surgeon who did an excisional biopsy of the submental lymph node under general anaesthesia. She made a good postoperative recovery.

Macroscopically the specimen measured 8 mm × 5 mm × 6 mm, was partly encapsulated, was irregular and nodular, and the cut surface was pale and fleshy with peripheral greyish zones. Microscopically there were zones of apoptotic necrosis surrounded by pale staining histiocytes and scattered lymphocytes without any evidence of a granuloma (Figs. 1 and 2). A pathologist confirmed the diagnosis of necrotising lymphadenitis consistent with Kikuchi's disease. A detailed explanation of the benign self-limiting nature of the disease was given to the patient and a long-term follow-up is planned.

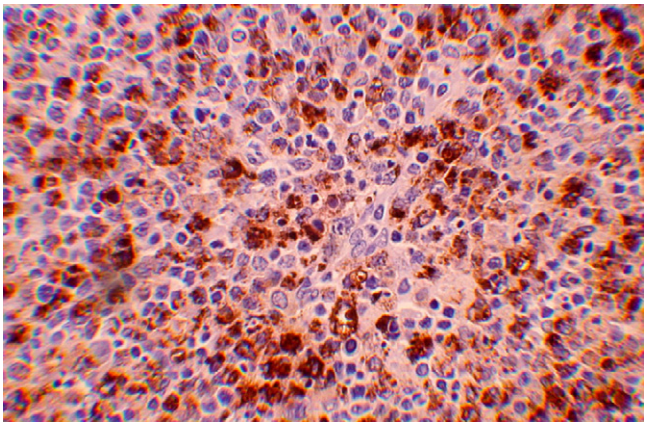

Fig. 2. Positive myeloperioxidase activity within the population of histiocytes.

## Discussion

The presenting features of fever, night sweats, cervical lymphadenopathy, and neutropenia, particularly in Asian women, may suggest a clinical diagnosis of tuberculosis and the condition can be confused with lymphoma or even malaria.[1] Tuberculosis should be excluded by histopathological examination of the involved lymph nodes. The presence of zones of caseation necrosis along with acid-fast bacilli will confirm the diagnosis. Alternatively, a culture may be required. Lymphoma can be ruled out by examination of bone marrow, and biopsy specimens from skin and lymph nodes by the lack of large Reed Sternberg cells with twisted nuclei. Malaria has to be differentiated by history, clinical examination, and repeated microscopy of the blood particularly at peaks of fever.

Though classically described as affecting women more than men, in a ratio of 4:1, some reports from eastern countries indicate that the ratio is closer to 1:1.[5] The aetiology of the disease remains unknown although associations with toxoplasmosis, *Yersinia enterocolitica*, cytomegalovirus, human herpes virus, varicella zoster virus, para-influenza virus and Epstein–Barr virus have all been implicated without any convincing corroborating evidence. An association with systemic lupus erythematosis and other connective tissue disorders has given credence to an autoimmune aetiology.[6] It has been suggested that long-standing Kikuchi's disease may lead to lupus, but this association remains to be substantiated.[7] Report of an association with intestinal giardiasis also indicates a possible chronic infective cause.[8] Histological examination of lymph nodes that shows apoptotic necrosis with histiocytic and lymphocytic infiltration confirms the diagnosis.[4] Three histological subtypes of the disease have been labelled proliferative, necrotising, and xanthomatous.[9] However, no study has shown progression of the disease from a proliferative to a necrotising to a xanthomatous stage.[9]

Our case was unusual, as the patient had endured recurring episodes of the disease for the previous five years, without a definitive diagnosis being made. She had various treatments with no success. There are few documented reports of recurrent disease.[10] A definite diagnosis alleviated her cancer phobia and her condition has improved without treatment and without any further recurrences. Management of the condition remains symptomatic. It is important to diagnose the disease early so that the patients can be spared medication and psychological stress. With the possibility that systemic lupus erythematosis can develop in such patients, long-term follow-up is appropriate. It is hoped that more maxillofacial

surgeons will become aware of this condition as more such cases are reported.

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