

Kikuchi's Disease With Pulmonary And Central Lymph Node Involvement: Rapid Response To Ciprofloxacin And Ceftazidime

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Citation

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Abstract

Kikuchi's disease is a rare, self-limiting illness usually presenting with fever and cervical lymphadenopathy. We report a case of Kikuchi's disease presenting with hilar and mediastinal lymphadenopathy in association with lung infiltration that rapidly responded to ciprofloxacin and ceftazidime treatment. Lung involvement in Kikuchi's disease is extremely rare. Also mediastinal and hilar lymphadenopathy has only been rarely described. Despite our best efforts we could only find one such recent report with central lymphadenopathy associated with this illness. Rapid response to antibiotics in this case raises the possibility of a bacterial aetiology.

CASE HISTORY

A 37-year-old, Caucasian schoolteacher was admitted to hospital with a two-week history of fever, productive cough, mild shortness of breath and myalgia. She had received a course of amoxicillin, six days prior to admission for suspected sinusitis. This was however discontinued three days later when she developed a generalized urticarial rash. She was a non-smoker and consumed alcohol occasionally. She did not keep any pets at home. She did not have any history of foreign travel or high-risk behaviour for HIV disease. Background medical history included asthma for which she took regular salmeterol and fluticasone inhalers.

On examination she was pyrexial with a temperature of 39.3°C. Her throat appeared inflamed with slightly enlarged tonsils. She had a generalized urticarial rash. She also had tender cervical and axillary lymphadenopathy. Her respiratory rate was 14 per minute. Oxygen saturation was 94% on air. Blood pressure was 120/72 mmHg. She was tachycardic with a pulse rate of 110 bpm. Her heart sounds were normal. Chest was clear with good air entry. Abdomen was soft, non-tender. There was no evidence of organomegaly. Neurological examination was completely normal.

Admission bloods showed normal renal function, liver enzymes and liver function tests. White cell count was $6.5 \times$

$10^9/l$ with a lymphopenia of $0.26 \times 10^9/l$. Haemoglobin was 13.5 g/dl. Platelet count was $116 \times 10^9/l$. Monospot test was negative. C-reactive protein was 246 mg/l. Chest X-ray revealed bilateral hilar lymphadenopathy.

Three days after admission the patient's condition deteriorated. She became more breathless. Oxygen saturation on air was 91%. She remained pyrexial and chest auscultation revealed bilateral basal crepitations. There was no clinical evidence of deep venous thrombosis. Repeat chest X-ray at this stage revealed hilar and mediastinal lymphadenopathy with lung infiltration (figure I).

Figure 1

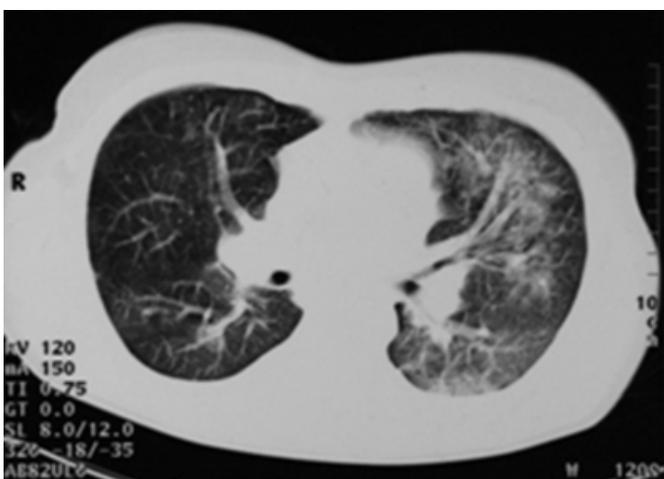
Figure 1: Chest x-ray showing hilar and mediastinal lymphadenopathy with lung infiltration.



She was commenced on intravenous ceftazidime and ciprofloxacin. CT scan of her cervical region and chest revealed enlarged deep cervical, axillary, bilateral hilar and mediastinal lymph nodes. Also there was small bilateral pleural effusions and ground glass appearance of both lung fields more pronounced on the left side (figure II). An abdominal CT scan showed mild splenomegaly.

Figure 2

Figure 2: CT chest showing, mediastinal lymph nodes and ground glass appearance of both lung fields.

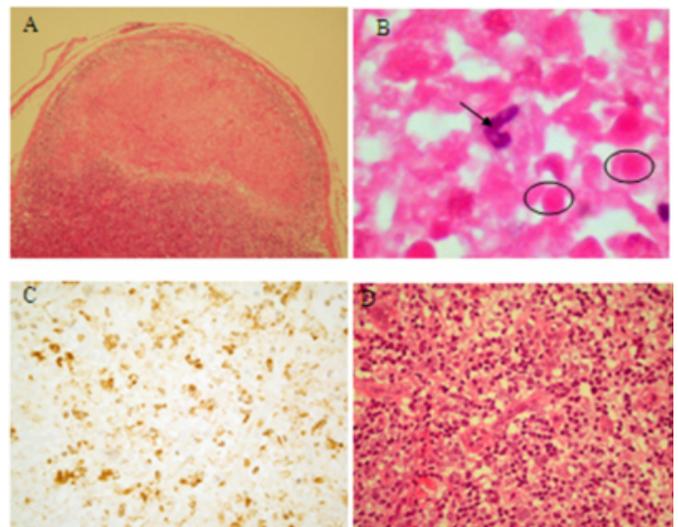


Differential diagnosis at this stage included an infective cause, sarcoidosis, connective tissue disease or lymphoma. Multiple investigations were carried out and the results were as follows. Repeated blood cultures were negative. Sputum samples did not reveal acid and alcohol fast bacilli and the culture results were negative. Mycoplasma IgM, legionella serology and urinary legionella antigen tests were also negative. EBV IgM, CMV IgM, Toxoplasma agglutination test, serology for parvovirus, measles, rubella, chlamydia pneumoniae, influenza A, influenza B, adenovirus, herpes simplex virus, human herpes virus 6 and 8 were negative. Serum calcium and ACE levels were normal. ANF, ANCA, ds DNA and complement screen were also normal.

Finally a cervical lymph node biopsy was carried out and samples were sent for culture and histological tests. Lymph node culture results were negative. However histology showed necrotising histiocytic lymphadenitis with no polymorph neutrophils, accompanied by angioimmunoblastic lymphadenopathy-like reactive changes (figure III), supportive of Kikuchi's disease or histiocytic necrotising lymphadenitis.

Figure 3

Figure 3: Histology specimen- Pale necrotic zone (A and C) consisting of necrotic KP1 positive histiocytes, histiocytes having crescentic nuclei (B), And Angio-immunoblastic lymphadenopathy-like reactive changes (D).



The patient's clinical condition improved rapidly after commencing antibiotics and the chest X-ray appearances showed a marked improvement with resolution of hilar and mediastinal lymphadenopathy 7 days later. The patient was discharged home and followed up as an out patient for about 12 months and she remained well.

DISCUSSION

Kikuchi's disease [Kikuchi-Fujimoto disease] or histiocytic necrotising lymphadenitis is a rare, benign self-limiting cervical lymphadenitis of unknown origin. Kikuchi and Fujimoto first described it independently in 1972. Although it has been reported worldwide it remains a poorly recognised clinicopathological entity. There is a female predominance with a male to female ratio of 1:4 and it usually affects young women with a mean age of 30 years ¹.

Aetiology of Kikuchi's disease is unknown. However various agents have been proposed. These include Adenovirus, Parvovirus B19, Cytomegalovirus, Epstein Barr virus, Varicella Zoster virus, Herpes Simplex virus, Human Herpes virus 6 and 8, ¹ Dengue virus ² and Human Immunodeficiency virus. ³ Bacteria such as Mycobacterium szulgai, Yersinia enterocolitica, Toxoplasma, ⁴ Protozoa and certain neoplastic conditions ⁵ and autoimmune disorders have also been postulated. These agents are thought to stimulate a particular immune response leading to this condition. Kikuchi's disease has been reported in association with systemic lupus erythematosus [SLE] and mixed connective tissue disease [MCTD] where biopsy of enlarged lymph nodes in these conditions showed characteristic features of Kikuchi's disease. ⁶ There are also reports on Kikuchi's disease progressing to SLE. ⁷ Some authors therefore believe that Kikuchi's disease and autoimmune rheumatic disorders may share a common aetiology and stress the importance of following these patients for several years to diagnose autoimmune disorders early as prognosis and management differ. Familial occurrence has been reported and genetic predisposition has been proposed. ⁸

Kikuchi's disease usually presents with a brief illness, unexplained fever and cervical lymphadenopathy. Axillary and rarely inguinal nodes could also be involved. Other features include sore throat, myalgia, weight loss, arthralgia and arthritis. ¹⁰ Cutaneous involvement is well described. Facial rash, exudative erythema, erythematous papules, vasculitis, plaques and nodules can occur in 30-40% of cases. ^{10,9} Hepatosplenomegaly, deranged liver function tests, leucopenia and haemophagocytic syndrome has been described. ¹¹ There are also reports on Kikuchi's disease being associated with anterior uveitis ¹² and brainstem encephalitis. ¹³

Diagnosis is based on histopathological findings of a lymph node biopsy. Lymphoma, autoimmune disease and

infections are important differential diagnoses which need to be excluded. Histological features are characteristic in typical cases where a patchy or confluent area of histiocytic necrosis, with no polymorph neutrophils, and presence of the so called macrophages with crescentic nuclei are seen. ¹⁸

Usually it is a self-limiting disease but recurrences could occur. Systemic steroids have been successfully used in patients with severe and persisting symptoms with recurrence. ¹⁴ Successful use of intravenous immunoglobulin in severe Kikuchi's disease has also been described. ¹⁹

This case of Kikuchi's disease is interesting due to three reasons. Peripheral lymphadenopathy is well described in this illness, but in addition to cervical and axillary lymph nodes she also had central hilar and mediastinal lymphadenopathy. To our knowledge this has been described only once, recently by Aydogan et al. ¹⁶ Lung involvement in Kikuchi's disease is also extremely rare ¹⁷. Our patient may therefore be one of the very few cases of Kikuchi's disease associated with extensive lung infiltration. Finally, a previous report from India suggested Kikuchi's disease responding rapidly to ciprofloxacin. ¹⁵ This is interesting because our case also showed a rapid response to ciprofloxacin and ceftazidime with clinical and radiological improvement in five days. The rapid response to antibiotics raises the possibility of a bacterial aetiology and we therefore recommend a trial of antibiotic therapy to be considered in Kikuchi's disease.

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