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

M Hakeem, V Jadhav, I Nawroz, D Bhattacharyya

Citation

M Hakeem, V Jadhav, I Nawroz, D Bhattacharyya. *Kikuchi's Disease With Pulmonary And Central Lymph Node Involvement: Rapid Response To Ciprofloxacin And Ceftazidime*. The Internet Journal of Pulmonary Medicine. 2006 Volume 7 Number 1.

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 ciproxin 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 amoxycillin, 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.

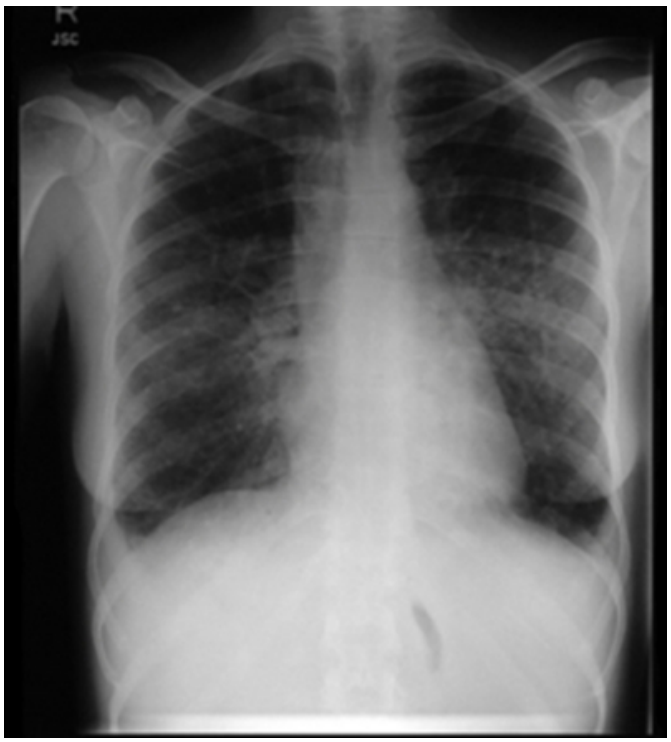
On examination she was pyrexial with a temperature of 39.3°C. Her throat appeared inflamed with slightly enlarged tonsils. She had a generalized urticarial rash. She also had tender cervical and axillary lymphadenopathy. Her respiratory rate was 14 per minute. Oxygen saturation was 94% on air. Blood pressure was 120/72 mmHg. She was tachycardic with a pulse rate of 110 bpm. Her hearts 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 x 10^9 /l with a lymphopenia of 0.26 x 10^9 /l. Haemoglobin was 13.5 g/dl. Platelet count was 116 x 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

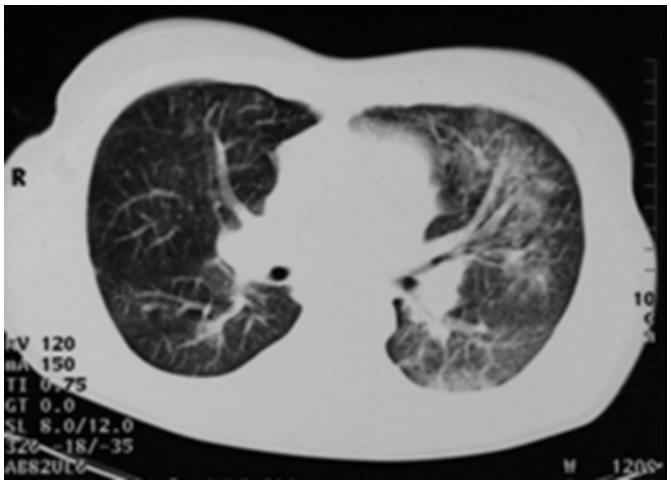
Figure 1: Chest x-ray showing hilar and mediastinal lymphadenopathy with lung infiltration.



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.

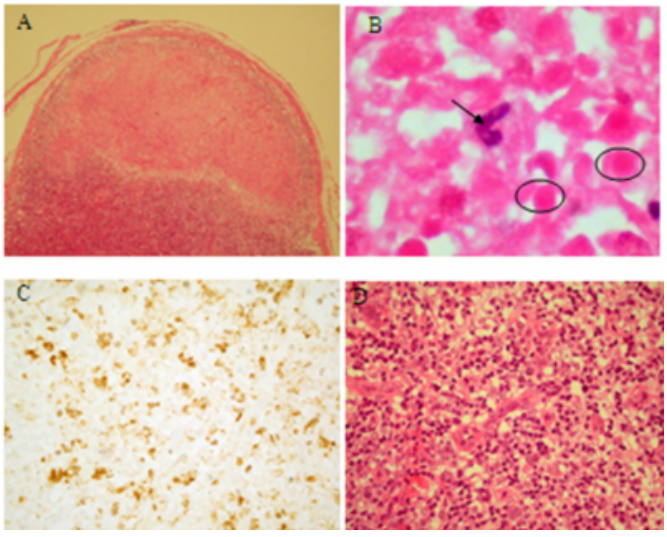


Differential diagnosis at this stage included an infective cause, sarcoidosis, connective tissue disease or lymphoma. Multiple investigations were carried out and the results were as follows. Repeated blood cultures were negative. Sputum samples did not reveal acid and alcohol fast bacilli and the culture 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. [1,9] 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 histopathalogical 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 cresentic 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 Kikuch'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 Aydogen 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.

ACKNOWLEDGEMENT

We thank Nancy Steele for her excellent secretarial help.

CORRESPONDENCE TO

Dr M J M L Hakeem Staff Grade in Infectious Diseases Infectious Diseases Unit Fife Acute Hospitals Victoria Hospital Hayfield Road KIRKCALDY Fife Scotland UK KY2 5AH E-mail: lukman.hakeem@faht.scot.nhs.uk Tel No: +44 1592 643355 Fax No: +44 1592 648037

References

1. Sathiyasekaran M, Varadharajan R, Shivbalan S. Kikuchi's disease. Indian Paediatrics 2004; 41:192-194.
2. Harris VK, Danda D, Murali NS et al. Unusual association of Kikuchi's disease and dengue virus in evolving in to systemic lupus erythematosis. J Indian Med Assoc.2000 Jul; 98[7]: 391-393.
3. Kucukardali Y, Cankir Z, Top C et al. Kikuchi's disease: Report of one case and overview. The Int J of Emergency and Intensive care med.2002; 6[2]
4. Kikuchi M, Yoshizumi T, Nakamura H. Necrotising lymphadenitis: possible acute toxoplasmic infection.

Virchows Arch 1977; 376: 247-253.
5. Radhi JM, Skinnider L, McFadden A. Kikuchi's lymphadenitis and carcinoma of the stomach. J Clin Pathol. 1997 Jun; 50[6]: 530-531.
6. Gourley I, Bell AL, Biggart D. Kikuchi's disease as a presenting feature of mixed connective tissue disease. Clin Rheumatol. 1995 Jan; 14(1): 104-107.
7. Litwin MD, Kirkham B, Henderson DR et al. Histiocytic necrotising lymphadenitis in systemic lupus erythematosis. 1992 Jun; 51(6): 805-807.
8. Amir AR, Amr SS, Sheikh SS. Kikuchi-Fujimoto disease: report of familial occurrence in two human leucocyte antigen- identical non twin sisters. J Intern Med 2002; 252:79-83.
9. Yen HR, Lin PY, Chuang WY et al. Skin manifestations of Kikuchi-Fufimoto disease: case report review. Eur J Pediatr 2004 Apr;163(4-5):210-213.
10. Douglas M, Bradbury R, Kannangara S et al. Arthritis as an unusual manifestation of Kikuchi-Fujimoto disease. Rheumatology (Oxford) 2003 Aug; 42(8): 1010-1012.
11. Mahadeva U, Allport T, Bain B et al. Haemophagocytic syndrome and histiocytic necrotising lymphadenitis (Kikuchi's disease). J Clin Pathol 2000 Aug; 53(8): 636-638.
12. Kim SH, Kim SJ, Chung H et al. Bilateral anterior uveitis as an unusual manifestation of Kikuchi-Fujimoto disease. Rheumatology (Oxford) 2004 Aug; 43(8): 1056-1057.
13. Shafqat S, Memon SB, Hyder S et al. Brainstem encephalitis with Kikuchi-Fujimoto disease. J Coll Physicians Surg Pak 2003 Nov; 13(11): 663-664.
14. Jang YJ, Park KH, Seok HJ. Management of Kikuchi's disease using glucocorticoid. J Laryngol Otol 2000 Sep; 114(9): 709-711.
15. Mahajan VK, Sharma NL. Kikuchi-Fujimoto disease: immediate
remission with ciprofloxacin. Int J Dermatol 2004 May; 43(5): 370-372.
16. Aydogan T, Kanbay M,Uraldi C et al. Kikuchi Fujimoto disease secondary to
Entamoeba histolytica:case report. J. Infect. 2006 Oct; 53(4): e171-3
17. Sharma OP. Unusual systemic disorders associated with interstitial lung disease.
Curr Opin Pulm Med 2001; 7:291-294.
18. Boone JL, Kuzma C. Kikuchi disease. e- Medicine. May 2006.
http://www.emedicine.com/med/topic3663.htm
19. Noursadeghi M, Aqel N, Gibson P, et al. Successful treatment of Kikuch's disease
with intravenous immunoglobulin. Rheumatology (oxford) 2006 Feb; 45(2):235-7.

Author Information

Mohamed J. M. L. Hakeem, MRCP UK
Staff Grade in Infectious Diseases

Vittal Jadhav, MRCP UK
SHO in Infectious Diseases

Ibrahim Nawroz, MBChB, FRCPath, DipFM
Consultant Pathologist

Diptendu N. Bhattacharyya, FRCP (Edin), MSc, DTM&H London
Consultant I.D. Physician