CASE REPORT

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A Rare Cause of PUO with Aplastic Crisis: The Great Masquerader

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Abstract

Kikuchi Disease is also known as Kikuchi Fujimoto Disease or Histiocytic Necrotising Lymphadenitis. Few studies suggest infectious and others suggest autoimmune aetiology. Multi-organ involvement is seen like bone marrow and liver. Lymph node biopsy is an important investigation for diagnosis. Here, we report the case of a 24-year-old female who presented with the complaints of high-grade fever, erythematous pruritic rash and cervical lymphadenopathy associated with aplastic anaemia, who was diagnosed as Kikuchi Disease. She was treated with hydroxychloroquine and followed up for recurrence and progression.

Key words: Kikuchi, histiocytic necrotizing lymphadenitis, aplastic anaemia.

Introduction

Kikuchi Disease is a rare and benign condition of lymphohistiocytic cells of uncertain aetiology[1]. It is characterised by fever, lymphadenopathy, erythematous rash, and leucopenia. The exact aetiology is not known, but based on its clinical presentation, course and histologic changes, it suggests an immune response of T-cells and histiocytes to some inciting agents like EBV, HHV, HIV, Parvovirus B19, Paramyxovirus, Parainfluenza Virus, Yersinia Enterocolitica and Toxoplasma. Of the autoimmune illnesses, Systemic Lupus Erythematosus (SLE) is the most common illness known to develop in connection with Kikuchi Disease. Hydroxychloroquine, steroids and IVIg are used in the treatment of Kikuchi Disease[2]. However, it is a self-limiting illness seen in predominantly young females less than 40 years.

Case

A 24-year-old female, resident of Delhi and native of Nepal with no co-morbidities presented with complaints of fever for 20 days, high grade, continuous associated with chills, rigors and erythematous pruritic rash which appeared on day 3 of illness, resolved spontaneously after 2 days. These complaints were associated with sore throat, generalised bodyache and nausea. Fever was documented as 102° F. On examination, there were pallor and bilateral cervical lymphadenopathy with largest of size 2 x 2 cm. On ENT examination, there was posterior pharyngeal wall congestion with normal tonsils. Rest of the systemic examination was within normal limits. Haemogram showed a haemoglobin of 8.3 g/dl, total leukocyte count 1,200 cells/cumm with DLC of 40/55/2/3, platelet count 0.8 lakh/cumm. Liver Function Tests were deranged with AST/ALT 206/79 U/L with normal total bilirubin. There was progressive fall in haemoglobin, total leucocyte count and platelet count during the hospital stay. Patient was managed as a case of febrile neutropenia with pancytopenia and appropriate antibiotics were administered and aetiological work-up was done. IgM dengue and chikungunya were negative, EBV serology was equivocal. HbsAg, anti HCV, HIV ELISA and CMV DNA PCR were negative. Serology for IgM parvovirus B19 was positive. ANA by immunofluorescence was positive in titres of 1:640 (homogenous pattern). ESR was 74 mm/hr, quantitative CRP 56.8 mg/dl, LDH 940 U/L, C3 and C4 levels were normal. Extended Nuclear Antigen (ENA) and Vasculitis Profile were negative. Radiological investigations did not reveal any abnormality.

Patient continued to run fever; however, cultures remained sterile and antibiotics were upgraded and antifungals were started. Patient underwent bone marrow studies and cervical lymph node biopsy on day 4 of illness. Simultaneously, patient was started on filgrastim 300 microgram daily for 7 days until day 10 of admission following which, cell lines improved to Hb of 9.6, TLC - 10,600 and platelet count - 1.8 lac/cc. Bone marrow biopsy was suggestive of hypocellular marrow with few lymphocytes, plasma cells, and mast cells. There was no atypical cell, parasite or granuloma with an overall impression of aplastic anaemia. Lymph node biopsy suggested diffuse sheet of foamy histiocytes, karyorrhectic debris with dense fibrin deposition, lymphoid collection along with scattered plasma cells and tingible body macrophages. Overall, the features were suggestive of Kikuchi Necrotising Lymphadenitis. Gram's stain, ZN stain and PAS stain were negative.

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Patient was managed as a case of Kikuchi necrotising lymphadenitis with aplastic crisis. Patient was started on tablet Hydroxychloroquine 200 mg BD along with haematinics on day 10 and all other drugs were withdrawn. Patient became afebrile on day 15, lymph nodes decreased in size and haematological parameters improved. Patient was discharged with stable vitals on day 16. 2 weeks after discharge, the lymph node completely regressed and patient continued to remain afebrile. Complete blood count showed a haemoglobin of 11.8 g/dl, TLC - 6,000 cells/cumm and platelet count - 3.2 lakh/mm, and liver function tests normalised. After 6 months, hydroxychloroquine was stopped and patient is being followed up for recurrence and progression.

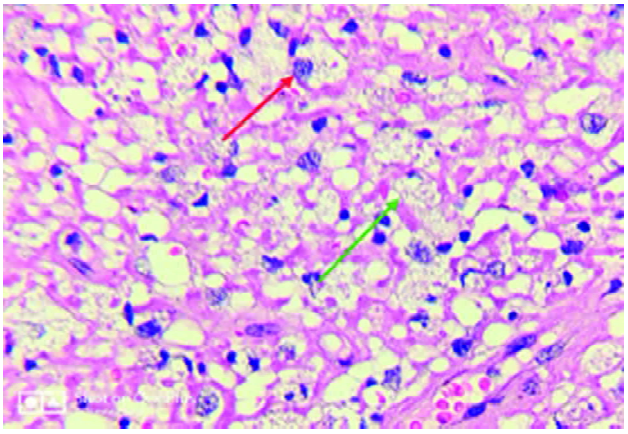

Fig. 1: *40x view: Red and green arrow-large cells with central to eccentric round nucleus with abundant vacuolated cytoplasm – foamy histiocytes.*

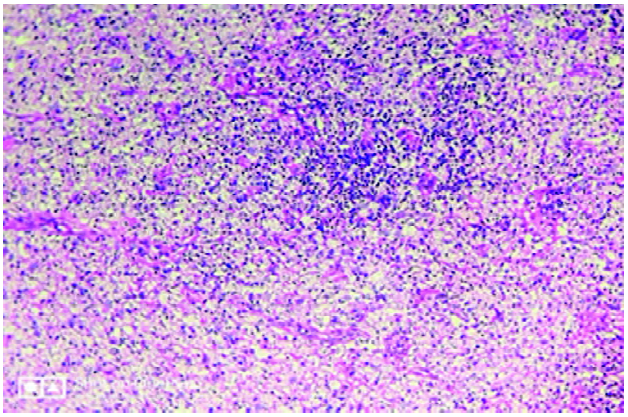

Fig. 2: *10x view: Large round to oval cells with abundant clear cytoplasm – foamy histiocytes.*

Discussion

The exact aetiology of Kikuchi disease is not known yet. However, there are a few case reports of various viral agents like HIV, EBV, HTLV-1, Parvovirus B19 being possible aetiological agents, but none have been proven so far[3]. In many scenarios, Kikuchi disease has been seen in association with SLE and a possible autoimmune mechanism has also been proposed[1].

Kikuchi disease is characterised by tender cervical lymphadenopathy in 60 - 90% cases with fever as a common symptom associated with other B symptoms like weight loss, night sweats, fatigue, sore throat, and skin involvement as erythematous, maculopapular, nodular and other cutaneous lupus-like rashes occurs in 40% of cases. There are no strict diagnostic criteria defined till now for this disease. Initial laboratory work-up reveals elevated inflammatory markers, deranged liver function tests in the form of transaminitis. Leukopenia occurs in around 22 - 58% of cases with atypical peripheral lymphocytes. Autoimmune work-up specifically evaluating for SLE and associated antibodies should be done[4].

Histological characteristics of lymph node biopsy in Kikuchi disease remain unique and ultimately clinches the diagnosis[5]. At present there are no guidelines for the treatment of Kikuchi disease. Few studies suggest usage of hydroxychloroquine, steroids, and IVIg alone or in combination[6]. Our case had positive ANA titres and positive Parvovirus B19 serology. However, further work-up for SLE was not fulfilling EULAR/ACR criteria.

Conclusion

Kikuchi disease can be mistaken for tuberculosis, lymphoma, or SLE as it may have varied presentations. Therefore, tissue biopsy must be performed to establish the diagnosis. A proper follow-up should be done as it may be an initial manifestation of SLE.

References

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