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Case report

CASE OF KIKUCHI' S DISEASE AND SYSTEMIC LUPUS ERYTHEMATOSUS ASSOCIATED WITH ANTIPHOSPHOLIPID ANTIBODY SYNDROME AND COMPLICATED BY HEMOPHAGOCYTIC SYNDROME (HPS)

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ABSTRACT

Kikuchi disease is a rare benign self limited lymphadenopathy. It is often associated with Systemic Lupus Erythematosus which can be diagnosed before; at the same time or after a diagnosis of Kikuchi disease is made. Again SLE is usually associated with APLA syndrome. Furthermore both SLE and Kikuchi disease can be complicated by HPS. We present a unique case in which Kikuchi disease and SLE were diagnosed together and disease course was complicated by Hemophagocytic syndrome (HPS). SLE was also associated with Anti Phospholipid Antibody Syndrome (APS) in this patient.

Keywords: Kikuchi, SLE, APLA, Hemophagocytic syndrome

INTRODUCTION

Kikuchi disease or histiocytic necrotizing lymphadenitis a rare, benign, self limiting cervical lymphadenitis of unknown etiology[1] mainly affecting young adults with females outnumbering males.[2] Sometimes association with SLE has led to the probability of autoimmune etiology being one of factors leading to Kikuchi disease. SLE is probably the most common underlying diseases of APLA syndrome.[3] Hemophagocytic syndrome is a rare but potentially fatal disease of normal but overactive histiocytes and lymphocytes often complicating connective tissue disorder & haematological malignancies. Kikuchi disease can independently lead to hemophagocytic syndrome in rare instances. Kikuchi disease and SLE with APLA syndrome can coexist rarely & may be complicated by hemophagocytic syndrome.

CASE REPORT

A 16 year Hindu Male from rural Bengal, student by profession, presented with fever, joint pain and glandular swelling in neck and axilla for last 1 month. Fever was high grade reaching upto 104˚F; continuous; chill and rigor; intense constitutional symptoms, no localising symptoms; relieved partly on medications. Joint pain involved mainly small joints of both upper limb and lower limbs [metacarpophalangeal joint (MCP), Proximal interphalangeal joint (PIP), distal interphalangeal joint(DIP), metatarsophalangeal joint (MTP), Interphalangeal joints (IP)] ; simultaneous onset;

additive; pain, Restriction of movement present but no swelling or redness. Painless glandular swelling in the neck and axilla started for last 15 days; gradually increasing in size but no discharge. No history of bleeding manifestations, purpuric rash, bone pain. No history of morning stiffness, pain in large joints or spine, oral or genital ulcers, facial rash, erythematous, evanescent rash over the trunk during spikes of fever. No history of prior tuberculosis, malaria, kalaazar. No history of chronic intake of any drug or any family history of arthritis. A significant history of spontaneous development of painful swelling in Right thigh 1 year ago which was documented as deep vein thrombosis involving iliofemoral veins. On clinical examination, patient had significant pallor, mild icterus. Lymph nodes palpable in right supraclavicular middle group, bilateral axillary central group and posterior triangle; all were soft, mobile, nontender with no fixity; mediastinal percussion resonant. No sternal tenderness. Chest -Bilateral Vesicular breath sounds heard normally with normal S1, S2. Abdomen was soft, nontender; spleen palpable 2cm below Left costal margin, nontender, no rub; liver not palpable; no free fluid. Musculoskeletal exam reveals pain, slight swelling, range of movement restricted in bilateral MCP, PIP, DIP joints in upper limb; MTP, IP joints in lower limb; tenderness at bilateral Achilles tendon insertion; Axial system uninvolved. Routine blood tests show Hb-7.2 gm/dl, PCV-22.3%, TLC-2300/cmm; N-69%; L-25%; M-5% ; E-1% , Platelet-41000/cmm , Reticulocyte-2%, MCV-72.4fl; MCH-23.3pg; MCHC-32.2%, RDW-16%; Peripheral blood smear shows hypochromic, microcytic RBCs; anisocytosis, elliptocytes, tear drop cells but no abnormal cells, ESR- 84mm/1st hr, Ur-19mg/dl; Cr-1mg/dl; LDH-1890U/L, Bil-0.7mg/dl; SGOT-39U/L; SGPT-56U/L; Alkaline phosphatase-112; Albumin-3.2gm/dl; Gloulinb-2.8gm/dl; A:G ratio:1.1, Na^{+}-137.3meq/l; K^{+}-3.89meq/l; Ca^{++}-8.9mg/dl; TG-360mg/dl, PT-13s; INR-1.03; APTT-70s

HBsAg, Anti HCV, ICTC were all negative; Chest X Ray-within normal limit; USG Whole abdomen showed mild splenomegaly; ECHO Cardiography: Normal; Malaria parasite Dual Antigen-Negative; Malaria Parasite on slide-not found. Dengue serology was Negative. Blood and urine Cultures were sent on day of admission; Sputum AFB-Not found; Mantoux-negative; urine routine & microscopic examination -normal. Patient was started on empirical IV antibiotics after sending blood and urine cultures; Bone marrow aspiration and Lymph node excision biopsy done. In the background of history of spontaneous DVT and isolated APTT rise, testing for Antiphospholipid antibody syndrome was done. PTT-A(test)-161.3s(N--35-42s)

- PTT-A(control)-39s(N—35-42s)
- PTT-A1:1 Mixing test-108.9s
- Interpretation- NOT CORRECTED
- DRVV(diluted russel viper venom)(test)-155.2s (N—35-42s)
- DRVV(control)-38.3s (N—35-42s)

DRVV ratio: 4.05 (N-0.85-1.12), Cardiolipin Ab-IgG-Positive 57.53 GPL U/ml (N<10 U/ml) antiphospholipid Ab IgG-POSITIVE 35.11 GPL U/ml (N<10 U/ml); lupus anticoagulant was positive. A diagnosis of possible APLA syndrome was made based on the presence of 1 episode of venous thrombosis; anticardiolipin Ab >40 GPL U/ml and lupus anticoagulant positivity. Patient was started on inj.LMWH (given for 5 days with target INR 2-3) with oral Warfarin to be given lifelong.Blood culture & sensitivity, Urine culture & sensitivity reports reached our hands which revealed no growth; Bone marrow aspiration showed reactive hyperplasia; no leukemic cells; Hemophagocytosis noted; Ferritin -1480mcg/l ; serum Fe-28mg/dl; Transferrinsaturation36%.

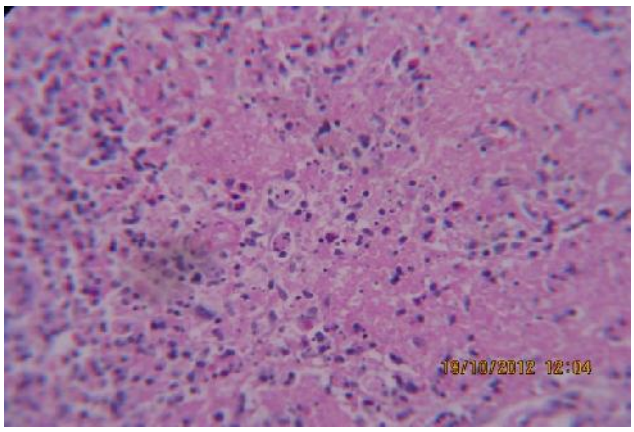

Fig 1: Bone marrow showing hemophagocytosis (40 x)

X ray both hands- No erosive features. A diagnosis of HPS was made due to presence of fever, pancytopenia, splenomegaly, raised ferritin (>500ng/ml), raised Triglyceride (>250mg/dl) and evidence of hemophagocytosis on BMAspiration. Patient continued to have high fever and on 11th day of admission became disoriented with irrelevant words. CT brain was normal; CSF Study revealed no features of acute CNS infection. Psychiatry referral done; a diagnosis of psychosis was made. Now workup for collagen vascular diseases was done- ANA-2+ homogeneously at 1:200 dil; C3—50.9mg/dl(N—90-180mg/dl) C4—7.3mg/dl (N-10-40mg/dl). Anti ds-DNA-negative; A diagnosis of SLE was made based on the presence of clinical features (non erosive arthritis involving more than 2 peripheral joints with tenderness,swelling; psychosis without other causes)and lab features (an abnormal titre of ANA in the absence of drugs known to induce ANAs and leucopenia (<4000/cmm), lymphopenia(<1500/cmm), thrombocytopenia(<100000/cmm)in the absence of offending drugs). Patient was treated accordingly. Fever gradually abated and patient became conscious and responsive. He was put on oral steroids 1mg/kg/day with gradual tapering. LN HPE report reached our hands which revealed Necrotizing Histiocytic Lymphadenitis compatible with Kikuchi"s disease. Patient was followed up at 6 weeks & repeat anti phospholipid antibody and anti cardiolipin antibody was positive in significant titre.

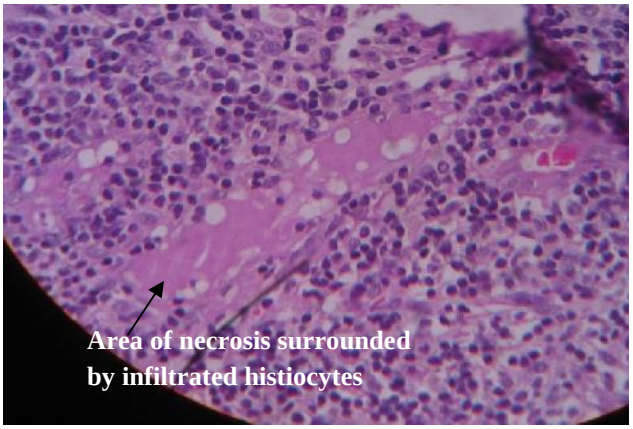

Fig 2: Lymph node histopathology (40X)

CT thorax and abdomen was done which revealed no malignancy. So the complete diagnosis was SLE associated with Kikuchi disease and APLA syndrome and hemophagocytic syndrome.

DISCUSSION

Kikuchi-Fujimoto disease (KFD) is a unique disease which was first described in 1972 in Japan. KFD is a very rare disease and mainly seen in Japan although occasional cases are reported in America and Europe. It is also known as Kikuchi disease[1], histiocytic necrotizing lymphadenitis, phagocytic necrotizing lymphadenitis, subacute necrotizing lymphadenitis.KFD generally affects the cervical lymph nodes. Cause of disease is unknown although infectious and autoimmune etiologies have been discussed as probable etiologies. A genetic predisposition to the proposed autoimmune response cannot be ruled out. Several infectious candidates have been proposed like Mycobacterium szulgai, Yersinia and Toxoplasma. Role of Epstein-Barr virus, as well as other viruses (HHV6, HHV8, Parvovirus B19, HIV- and HTLV-1) in the pathogenesis cannot be ruled out. Serologic tests including antibodies to viruses have not been proven fruitful and viral particles cannot be identified in electron microscopy. KFD generally affects the cervical lymph nodes. It can be confused with

tuberculosis, lymphoma which can have similar presentation it mainly affects young adults (20–30 years), with females outnumbering males[2]. Course of the disease is generally benign and self-limiting. Lymphadenopathy usually resolves within several weeks to months. Recurrence rate is about 4-5%. Mortality is very rare and usually results from hepatic, respiratory, or cardiac failure. SLE is the single most disease associated with this disorder.[3,4] Similar autoimmune states such as polymyositis, juvenile idiopathic arthritis, antiphospholipid syndrome can be associated with KFD. KFD may be an aberrant T-cell mediated immune disoeder in a genetically susceptible individual in response to appropriate stimuli. The exact relationships between SLE and KFD are not known as SLE can coincide, proceed, or follow KFD. Clinical features of SLE and KFD can be identical; fever, lymphadenopathy, fatigue, and joint pain are noted in both. These two diseases are separated by histopathological features; the presence of hematoxylin, plasma cells, and deposition of DNA is seen in SLE only.SLE is probably the most common underlying diseases of APLA syndrome. Kikuchi disease and SLE with APLA syndrome can coexist as documented in literature.[5]

SLE is often complicated by hemphagocytosis syndrome[6] which is also called as Macrophage Activation Syndrome (MAS). Now MAS is called hemophagocytic lymphohistiocytosis (HLH).Criteria for hemophagocytic lymphohistiocytosis (HLH) , which include fever, splenomegaly, cytopenias affecting at least two of three lineages in the peripheral blood, hypertriglyceridemia and/or hypofibrinogenemia, hemophagocytosis in bone marrow, spleen or lymph nodes, low or absent natural killer cell activity, hyperferritinemia, and high levels of sIL-2 receptor. Five of the eight criteria should be fulfilled to make this diagnosis. Patients with a molecular diagnosis of HLH are exempted from fulfilling all the diagnostic criteria. The prevalence of HPS among patients with autoimmune diseases varies but around 3%[4].Incidence is highest in patients with adult onset Still's disease, followed by Sjogren's Syndrome and SLE. Increased mortality is noted in age above 50 years, the presence of coexistent infection, leucocyte count < 5000/mcl, platelet count < 50000/mcl and CRP level < 50 mg/L at the onset of HPS[5] .Current treatment strategy is induction therapy over an eight-week period with dexamethasone, etoposide (VP-16), and intrathecal methotrexate, followed by cyclosporine started at 9 th week . Pulses of dexamethasone and etoposide to be given for one year.[7] This case presents an extremely rare coexistence of SLE, Kikuchi disease, APLA syndrome and finally HPS & highlights the fact that patient may manifest with APLA at earlier stage & later turn into florid SLE in the subsequent disease course, even after years. Whether the HPS in this case was a complication of kikuchi's disease or SLE per se cannot be determined with certainty as both of them are established predisposing factor for HPS.

REFERENCES

1. Kikuchi M. Lymphadenitis showing focal reticulum cell hyperplasia with nuclear debris and phagocytes. Acta haematologica Japonica. 1972;35:379–80.
2. Fujimoto Y, Kojima Y,. Yamaguchi K. Cervical Subacute necrotizing lymphadenitits. Naika.1972, 20:920–27.
3. Khanna D, Shrivastava A, Malur PR, Kangle R. Necrotizing lymphadenitis in systemic lupus erythematosus: is it kikuchi-fujimoto disease? Journal of Clinical Rheumatology. 2010;16(3):123–24
4. Londhey VA, Buche AS, Kini SH, Rajadhyaksha GC. Kikuchi fujimoto disease and systemic lupus erythematosus—a rare association," Journal of Association of Physicians of India. 2010;58(10):642–43.
5. Chen HC, Lai JH, Huang GS. Systemic lupus erythematosus with simultaneous onset of

Kikuchi-Fujimoto's disease complicated with antiphospholipid antibody syndrome: a case report and review of the literature. Rheumatology International. 2005;25(4): 303 –06.
6. Kampitak T. Fatal Kikuchi-Fujimoto disease associated with SLE and hemophagocytic syndrome: a case report," Clinical Rheumatology. 2008;27(8):1073
7. Fukaya S, Yasuda S, Hashimoto T, Oku K, Kataoka H, Horita T, Atsumi T, et al. Clinical features of haemophagocytic syndrome in patients with systemic autoimmune diseases: analysis of 30 cases. Rheumatology (Oxford). 2008;47(11):1686-91