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/cumm; N-69%; L-25%; M-5% ; E-1% , Platelet-41000/cumm , 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%.
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.

**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 disease¹, 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. 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. 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 disorder 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. SLE is often complicated by hemophagocytosis syndrome 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%. 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. 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. 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

5. Chen HC, Lai JH, Huang GS. Systemic lupus erythematosus with simultaneous onset of
