

Leukemoid Reaction in Chikungunya Fever

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ABSTRACT

Chikungunya is a viral illness caused by an arbovirus which is transmitted by *Aedes* mosquito. Fever and polyarthralgia are hallmark of this viral illness. Viral infections are generally associated with leucopenia and bacterial infections with leukocytosis. Leukemoid Reaction (LR) is defined by reactive increase in leukocyte count of more than 50,000/cu mm with increase in mature leukocytes on peripheral blood. Leukocytosis is common in Chikungunya but leukemoid reaction has not been reported in medical literature. Our patient presented with high grade fever and symmetrical polyarthrititis. Blood investigation showed Leukemoid reaction and after extensive work up a diagnosis of chikungunya was made.

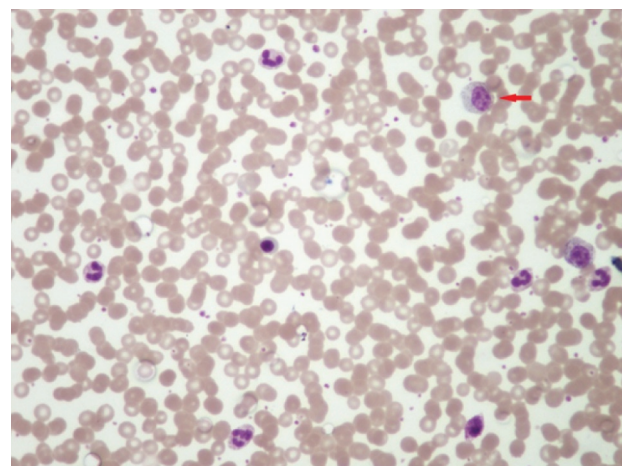
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CASE REPORT

A 55-year-old gentleman presented with chief complaints of multiple joint pain for last one week. He was apparently normal 10 days back when he developed fever which was high grade, continuous and associated with chills and rigors. His fever subsided on third day and on same day he developed pain in his both ankle joints which was associated with swelling. Pain gradually progressed to involve multiple joints of upper and lower limbs symmetrically over next five days. Pain was additive and severe in intensity causing severe limitation of day to day activities. There was no history of dysuria, loose stools and rash in recent past.

On physical examination, he had temperature of 36.4° C, pulse rate was 102 per minute and blood pressure was 110/70 mm Hg. Bilateral ankle, knee, shoulder, elbow, wrist, metacarpophalangeal, proximal and distal interphalangeal joints were swollen and tender. There was no lymphadenopathy but conjunctival injection was present. No organs were palpable on per abdomen examination and rest of the systemic examination was essentially normal.

Blood investigations showed ESR of 45 mm/h, haemoglobin of 13 g/dl, TLC of 52,000/cumm with a DLC of 68% neutrophil, 8% lymphocyte, 2% monocyte, 6% myelocyte, 8% metamyelocyte and 8% stab cells. Platelet count was 1.5 lacs/cu mm. Peripheral smear showed neutrophilic leukocytosis with shift to left and red cells were normocytic normochromic [Table/Fig-1]. Kidney function tests, liver function tests and serum electrolytes were normal. Blood and urine culture were sterile. Serology for Brucellosis, Leptospirosis, parvovirus B19 and dengue were negative. Anti nuclear antibody, Rheumatoid factor and Anti CCP were negative. HbsAg, Anti HCV and HIV were non reactive. A bone marrow examination was planned in view of persistently raised leukocyte count. Bone marrow biopsy showed hypercellular marrow with normoblastic reaction of erythroid series, normal maturation of myeloid series and adequate megakaryocytes. Neutrophil Alkaline Phosphatase (NAP) score was normal. A bone marrow culture was also sent which came sterile. Ultrasound abdomen and chest x ray were normal. IgM ELISA for Chikungunya was positive. CRP levels were significantly raised (21mg/dl). He remained afebrile during his hospital stay and was given oral naproxen for arthritis. His symptoms improved markedly after starting NSAID'S and was discharged on oral naproxen. Repeat leukocyte count done after two and four weeks of discharge were 25,000 and 10,000/cumm respectively.



[Table/Fig-1]: Peripheral smear showing neutrophilic leukocytosis with few myelocytes (arrow).

DISCUSSION

Chikungunya is a viral illness caused by an arbovirus which is transmitted by *Aedes* mosquito. The name Chikungunya in Tanzania means "that which bends up". The causative agent is Chikungunya virus (CHIK virus), which belongs to Alphavirus genus of the *Togaviridae*. *Aedes aegypti* is the common vector in urban areas.

After an incubation period of 2-4 days, CHIK virus causes high grade fever which is abrupt and can be associated with chills and rigor. Fever usually persists for 3-5 days and responds to antipyretic medications. Polyarthralgia begins acutely after two to five days of fever onset. Joints most commonly affected are wrist, small joints of hand, ankle and less commonly axial skeleton. Arthralgia/arthritis is symmetrical and pain can be intense causing complete immobilization. Transient maculopapular rash is seen in 40-60% of patients. Other clinical features include conjunctivitis, lymphadenopathy, oral ulcers, stomatitis and rarely neurological involvement. Common differential diagnosis includes Dengue fever, Leptospirosis, seronegative rheumatoid arthritis and Rickettsial disease. Serology is the most commonly used tool for diagnosis. IgM anti-chikungunya antibodies appear within two weeks of symptom onset, which can be detected by ELISA.

Krumbhaar coined the term 'leukemoid reaction' (LR) in 1926 for various non leukemic conditions having leukaemia like blood

picture [1]. It is defined by leukocyte count greater than 50,000/cu mm, increase in mature leukocytes in the peripheral blood along with differential count showing shift to left [2]. Chronic Myelogenous Leukaemia (CML) and Chronic Neutrophilic Leukaemia (CNL) should be ruled out before a diagnosis of LR is made. LR can be differentiated from CML on clinical and laboratory parameters. Hepatosplenomegaly and bone tenderness is common in CML, not seen in LR. In CML, peripheral blood shows increase in blast cells, immature cells and basophils whereas there are mature leukocytes with left shift in LR. NAP score is low in CML but it can be normal or raised in LR [3].

Bone marrow examination in LR shows increased cellularity with myeloid hyperplasia but in CML there are basophilia, eosinophilia and blasts cells. Presence of bcr-abl translocation is the hallmark of CML. CNL is a rare myeloproliferative disorder and differentiating LR from CNL can be challenging as both of them have almost similar morphological features. Immunophenotyping and serum G-CSF levels can be helpful in differentiating LR from CNL [4].

The common causes of LR are infections, carcinoma, lymphoma, drugs and ingestion of ethylene alcohol [5]. Infections causing LR are bacterial diseases like disseminated tuberculosis [6], clostridium difficile colitis, shigella dysentery and pneumonia. Viral diseases like (HIV, mumps, CMV, EBV, parvovirus B19), parasitic infestation (malaria, trichinosis, visceral larva migrans) and fungal infections (mucormycosis) are the other infections causing LR. Solid tumors (lung, gastrointestinal, genitourinary, pancreas) and Hodgkin's lymphoma are associated with LR [7]. LR can also result from exposure to drugs (steroids, minocycline, recombinant haematopoietic growth factors) and in various stressful conditions (severe pain, trauma) [8].

Haemogram in Chikungunya fever typically shows raised ESR, leucocytosis or leucopenia and rarely thrombocytopenia too. Thiruvengadam et al., in their study on Chikungunya fever in 1964 found leucocytosis (49%), leucopenia (12%), thrombocytopenia (6%) and raised ESR in 40% of cases [9]. Three mechanism for LR

have been proposed; first is bone marrow stimulation by physical, chemical or allergen; second is marrow response in cases of increased demand for leucocytes; third is ectopic haematopoiesis due to bone marrow damage [10]. Possible explanation of LR in this case could be marrow stimulation by CHIK virus or intense pain from arthritis.

CONCLUSION

Chikungunya fever can have various atypical manifestations. Leucocytosis is commonly seen in this viral illness; however, leukemoid reaction has not been reported in medical literature so far. This is the first case report of leukemoid reaction in Chikungunya fever. Any patient with short duration of fever and symmetrical polyarthritis with leukemoid reaction should be evaluated for Chikungunya fever.

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