

Leukemoid Reaction in Chikungunya Fever: A Case Report

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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. Persistent neutrophilia with cell counts of $\geq 30,000$ – $50,000/\mu\text{L}$ is called a leukemoid reaction. Leukocytosis is common in Chikungunya but leukemoid reaction has not been reported. Our patient presented with high grade fever and symmetrical polyarthritis. Blood investigation showed Leukemoid reaction and after extensive work up a diagnosis of chikungunya was made.

Keywords: Chronic myelogenous leukaemia, Chronic neutrophilic leukaemia, Neutrophil alkaline phosphatase, Total leukocyte counts, Differential leukocyte counts, Renal function test, Liver function test, Peripheral blood smear

Introduction

Chikungunya is a viral fever caused by alphavirus and spread by Aedes mosquitoes. Symptoms include fever, maculopapular rash involving limbs and trunk and arthralgia or arthritis affecting multiple joints. Chikungunya fever may cause leucocytosis or leucopenia and mild thrombocytopenia. But in our case

report Leukemoid reaction occur. In our best knowledge only one case has been reported till date.

Case Report

A 70 yr old female patient presented with chief complaints of multiple joint pain for last 2 days. She was apparently normal 7 days back when she developed fever which was high grade, continuous and associated with chills and rigors. Her fever subsided on 5th day and on same day she developed pain in her both ankle joints which was associated with swelling. Pain gradually progressed to involve multiple joints of upper and lower limbs symmetrically over next 2 days. Pain was severe in intensity causing limitation of day to day activities. There was no history of dysuria, loose stools and rash in recent past.

On physical examination, she had temperature of 36.8°C , pulse rate was 94 per minute and blood pressure was 120/80 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.

On admission day 1, blood investigations showed ESR of 40 mm/h, haemoglobin of 12 g/dl and Total

leukocyte count(TLC) of 14000/cumm.On day 5,TLC raised upto 38800/cumm with a DLC(Differential leukocyte counts) of 66% neutrophil, 10% lymphocyte, 2% monocyte, 6% myelocyte, 8% metamyelocyte and 8% stab cells. Platelet count was 1.5 lacs/cu mm. Peripheral blood smear(PBF) showed neutrophilic leukocytosis with shift to left and red cells were normocytic normochromic. Renal function tests(S.urea 87,S.creat 2) and liver function tests(S.bilirubin total-5.4,S.bilirubin direct-4.0,SGOT-87,SGPT-103) were slightly derranged and serum electrolytes were normal. Blood and urine culture were sterile. HbsAg, Anti HCV and HIV were non reactive. Ultrasound abdomen, chest x ray and 2 D Echo were normal. IgM ELISA for Chikungunya was positive. Serology for Brucellosis, Leptospirosis, Parvovirus B19 and Dengue were negative. Anti nuclear antibody, Rheumatoid factor and Anti CCP were negative. A bone marrow examination done. 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.Repeat TLC done on day 7 and day 10 were 28000 and 20000 respectively. Repeat RFT and LFT were normal on day 7 and 10 of admission. 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. After one week of discharge repeat leukocyte count were 7800 and RFT, LFT were also normal .

Discussion

Chikungunya is an infection caused by chikungunya virus(CHIK virus) which is arbovirus and transmitted by Aedes mosquito. The name Chikungunya in

Tanzania means “that which bends up”. CHIK virus belongs to Alphavirus genus of the Togaviridae. *Aedes aegypti* is the common vector in urban areas.Other vector is *Aedes albopictus*.Risk of death is around 1 in 1000.

After an incubation period of 2-10 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. Maculopapular rash may appear at the outset or several days into the illness;its development often coincides with defervescence,which occurs around day 2 or 3 of the disease.Rash is most intense on the trunk and limbs and may desquamate. 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]. Leukocytosis with cell counts of 10,000–25,000/ μ L occurs in response to infection and other forms of acute inflammation and results from both release of the margined pool and mobilization of marrow reserves. Persistent neutrophilia with cell counts of $\geq 30,000$ – 50,000/ μ L is called a leukemoid reaction, a term often used to

distinguish this degree of neutrophilia from leukemia. In a leukemoid reaction, the circulating neutrophils are usually mature and not clonally derived[2].PBF shows increase in mature leukocytes along with differential count showing shift to left .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 basophilis 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 tuberculosis , clostridium difficle 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 [6]. LR can also result from exposure to drugs (steroids,

minocycline, recombinant haematopoietic growth factors) and in various stressful conditions (severe pain, trauma) [7].

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 leukocytosis (49%), leucopenia (12%), thrombocytopenia (6%) and raised ESR in 40% of cases [8]. 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 [9]. 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. Any patient with short duration of fever and symmetrical polyarthritis with leukemoid reaction should be evaluated for Chikungunya fever.

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