Peripheral Blood Leukemoid Reaction: An Unusual Presentation Of Leptospirosis

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Abstract

A spirochetal zoonosis caused by Leptospira species, Leptospirosis is a potentially fatal multisystem illness. Of late, there are many reports of epidemic leptospirosis in the Indian literature. However reports of sporadic leptospirosis are anecdotal. The protean clinical manifestations of the disease make early diagnosis of isolated forms unlikely. A case of leptospirosis with peripheral blood leukemoid reaction is presented with review of literature.

CASE REPORT

A four year old boy was brought for intermittent high grade fever for 5 days, generalized abdominal distention with abdominal pain in right hypochondriac region for 4 days, progressive pallor and jaundice for 3 days, bone pains, facial puffiness and edema of lower limbs for 2 days. On examination, the child was sick, icteric and febrile with clinical signs of moderate dehydration. He had pitting pedal edema, cervical, axillary and inguinal lymphadenopathy. His vitals were heart rate of 120 beats/min, respiratory rate of 24 breaths/min and blood pressure of 120/70mmHg. Abdomen was grossly distended. He had a palpable, tender liver of 7 cm below the right costal margin and a palpable spleen of 7 cm below the left costal margin. On auscultation, there was a grade 2/6 short systolic murmur at the cardiac apex. Neurological examination was normal. His long bones were tender without any other signs of inflammation. Joints were normal. He was commenced on IV Antibiotics (ceftriaxone and ofloxacin) and maintenance fluids. His initial blood picture showed gross anemia (Hb: 7.5 g/dl), leukocytosis (54,000/cumm) and a normal platelet count (1.93 lakhs/cumm). Peripheral smear showed prominence of blasts and atypical cells (24%), about twice the size of a mature lymphocyte with condensed chromatin, scanty cytoplasm, vacuolated granules and suspicious nucleoli. Liver function tests revealed hyperbilirubinemia (total: 4.4mg/dl, direct: 3 mg/dl) and elevated liver enzymes.

Chest radiograph was normal and ultrasound scan of the abdomen showed hepatomegaly with ascites. Renal functions were normal. A bone marrow aspiration was performed and study suggested erythroid hyperplasia with megaloblastic and micronormoblastic maturation. The myeloid series were normal but myeloid: erythroid ratio was 1:1.There were numerous smudge cells and micro megakaryocytes but no definite blast cell prominence (2%). Cytochemistry (myeloperoxidase and PAS) was non contributory. He was extensively investigated for the cause of peripheral blood leukemoid reaction. Infectious mononucleosis was ruled out by a negative Paul Bunnel test. Tests for malaria, tuberculosis and hepatitis viruses A, B and C were all negative. Blood cultures were sterile. A second opinion of the bone marrow examination was sought and it was suggestive of a hypercellular marrow with erythroid myeloid ratio 1.3:1, normal megakaryocytes, normoblastic to megaloblastoid erythropoesis and dyspoetic granulopoesis with few giant band forms. Myelogram showed lymphocytosis, eosinophilia and few reactive lymphocytes. The picture pointed towards a virus induced reactive marrow lymphocytosis. As he continued to remain febrile with increasing facial puffiness and pedal edema and developed generalized maculopapular rash, he was evaluated further for a possible connective tissue disorder, Wilson's disease and leptospirosis. Antibiotics were upgraded to Piperacillin Tazobactum and Tobramycin. Connective tissue disorder was ruled out by a negative Rheumatoid factor, Anti ds DNA and Anti nuclear antibodies and low erythrocyte sedimentation rate. Serum Copper and Ceruloplasmin were well within normal limits. Leptospiral IgM antibody was positive (1.94 index/value) (Normal <1.5). After upgrading the antibiotic to Penicillin group, he became afebrile with decreasing pedal edema, facial puffiness, jaundice and

improving appetite within 48 hours. Antibiotics were continued for a period of 14 days.

DISCUSSION

Leptospirosis [1, 2] is a zoonotic caused by Leptospira species, the rat being the main reservoir of infection. Leptospirosis was first described by Weil in 1886. Inada et al identified the organism in 1916.[3] In India, there are several reports of outbreaks of leptospirosis following floods.[2,4] Bela Varma et al reported four children from Mumbai with leptospirosis who presented with fever, hepatorenal dysfunction and bleeding manifestations[5]. Karande S et al reported an outbreak of leptospirosis in 32 children in Mumbai slums in 2001[6]. Childhood leptospirosis has been reported from Orissa and Tamil Nadu also.[7,8]

Leptospira interrogans, the most important pathogenic species is a 6 to 20 micro m long spirochete, with a terminal hook, identified by dark field examination and silver staining. The organism enters human being through abraded skin or intact mucous membranes by way of contaminated water or animal bites. Human to human transmission is rare. It is an occupational hazard to agricultural laborers, laboratory workers, veterinary doctors etc. The incubation period is 7 to 12 days. The clinical manifestations localizing to various organ systems are secondary to endothelial injury caused by the organism. The clinical syndrome may range from a completely asymptomatic, subclinical infection with seroconversion to a life threatening systemic infection involving the liver, kidneys, heart, skeletal muscles, blood and the meninges.

The initial phase of illness presents as an influenza like illness with fever, chills, lethargy, head ache, nausea, vomiting and severe myalgias. Hepatosplenomegaly, lymphadenopathy, generalized rash, conjunctival suffusion, orbital pain and arthralgias may be present. This is followed by aseptic meningitis after an asymptomatic interval. The neurological involvement is self limiting. The icteric form of the illness termed as Weil's disease shows hepatorenal dysfunction after the initial phase. Bleeding manifestations and thrombocytopenia may be present. The criteria laid down by Indian Leptospirosis Society for clinical diagnosis of leptospirosis include high grade fever, headache and generalized body aches, associated with at least any one of the following a) jaundice, b) oliguria, c) cough, hemoptysis and breathlessness, d) neck stiffness with altered sensorium, and e) hemorrhagic tendencies including conjunctival suffusion and others.[4] Reported mortality rates range from 10 to 25%[4,9] .The case fatality rate is lower in children compared to adults.[10]The most common causes of death are hepatic, renal, respiratory failure and myocarditis.

In the initial phase of the illness, the organism can be isolated from the blood and CSF. Later on antibodies appear and leptospires can be isolated from the urine from the 3rd week onwards.

Diagnosis is based on estimation of anti leptospiral antibodies by ELISA in the blood, which appear by the 12th day of the illness. Rising titres are diagnostic. Though the micro agglutination test is the gold standard, estimation of the levels of IgM antibodies to Leptospiral antigens remains the most useful investigation in the clinical setting, as it is sensitive, specific, easy and cost effective[2,4]. Dark ground microscopy is simple but less sensitive[9]. Warthin Starry silver stain and immuno fluorescent stain and immunohistochemical methods can be used to identify the organism from the body fluids. It can be cultured on rabbit serum or bovine serum albumin and long chain fatty acids.

Penicillin group of antibiotics remains the mainstay of treatment of the infection in children. In adults and those with penicillin allergy, tetracyclines can be used[1].

This child presented to us with fever, pallor, jaundice, anasarca , rash and bone pains all of which are recognized symptoms of leptospirosis. Since isolated forms are rare, leptospirosis was not suspected initially. Commoner conditions like systemic bacterial sepsis, malaria, infectious mononucleosis, tuberculosis, viral hepatitis, connective tissue disorders and Wilson's disease which present with similar features have been ruled out by appropriate investigations. He was anemic and his peripheral smear showed leucocytosis with prominence of blasts and atypical cells with suspicious nucleoli. Bone marrow aspiration performed in view of the peripheral blood leukemoid reaction, ruled out acute leukemia's and infiltrative bone marrow disorders as diagnostic possibilities. In view of the inconclusive evaluation and clinical picture satisfying the diagnostic criteria laid down by the Indian Leptospirosis society, leptospirosis was considered as a differential diagnosis and IgM anti leptospiral antibody titres were positive thus confirming the diagnosis of leptospirosis. Earlier researchers in India have used this test to confirm the diagnosis of leptospirosis in the first week of illness though micro agglutination test is the gold standard for diagnosis [2,4]. Peripheral blood leukemoid reaction is a rare presentation of leptospirosis. Till date, to the best of our knowledge only

one case of leptospirosis with peripheral blood leukemoid reaction has been reported[11]. Bone marrow involvement has been reported with leptospirosis in adults.[12]

There were no other cases of leptospirosis in the city during that period thereby suggesting the sporadic nature of the illness. The source of infection was unknown. He was not exposed to any animals or contaminated water in the period preceding the illness. There was no history of travel. There were no floods or cyclones in the city as was in the case of previous outbreaks of leptospirosis in India. He responded well to Penicillin group of antibiotics with defervescence and significant clinical amelioration within 48 hours. He is on regular follow up now and is doing well.

CONCLUSION

Leptospirosis is not rare in the pediatric population. It can mimic many multi system disorders and clinical suspicion in the absence of an epidemic is exceedingly difficult. Nevertheless response to antimicrobials is substantial and encouraging. Hence a possibility of leptospirosis should be kept in mind when a multisystem illness is encountered if deadly complications are to be avoided.

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