Peripheral Blood Leukemoid Reaction: An Unusual Presentation Of Leptospirosis

N Kharidehal, R Prasad

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

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. Reported mortality rates range from
10 to 25%. The case fatality rate is lower in children
compared to adults. 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. Dark ground
microscopy is simple but less sensitive. 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.

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 leptosomal 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.
Peripheral blood leukemoid reaction is a rare presentation
of leptospirosis. Till date, to the best of our knowledge only
Peripheral Blood Leukemoid Reaction: An Unusual Presentation Of Leptospirosis

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

CORRESPONDENCE TO

Raghavendra Prasad H.V. MD Peds, DNB Peds, MNAMS (India), FRCPCH (UK) Consultant Pediatrician & Intensivist Children's Medical Center KRISHNA INSTITUTE OF MEDICAL SCIENCES 1-8-31/1, Minister Road, Secunderabad, A.P. State INDIA – 500 003 Tel: (0091-40) 2781 4499, Fax: (0091-40) 2784 0980 Mobile: (0091) 98492 91001 E-mail: raghuhv@yahoo.com

References

2. S Karande, M Bhatt, A Kelkar, M Kulkarni, A De and A Varaiya An observational study to detect leptospirosis in Mumbai, India, 2000 Archives of Disease in Childhood 2003;88:1070-1075
10. Suárez HM, Rodríguez MG, Menéndez TO, Marrero AJL, Sánchez JMA Leptospirosis In children living in Cuba Rev Mex Pediatr 2006; 73 (1): 14-17
Peripheral Blood Leukemoid Reaction: An Unusual Presentation Of Leptospirosis

Author Information

Neelima Kharidehal, MD. Peds.
Paediatric Registrar, Children's Medical Center, Krishna Institute Of Medical Sciences

Raghavendra H. V. Prasad, MD Peds, DNB Peds, MNAMS (India), FRCPCH (UK)
Consultant Paediatrician & Intensivist, Children's Medical Center, Krishna Institute Of Medical Sciences