Case of fever with hepatosplenomegaly & thrombocytopenia

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Case 1

- 8 yrs old Master S, from Thiruvallur presented with C/O
  - Fever - 5 days, intermittent, no rashes
  - Abdominal pain - periumbilical, not radiating
  - H/o myalgia
- No H/O vomiting/LS/ altered sensorium/ seizures
- No throat pain, breathing difficulty or urinary tract symptoms
- No joint pain
- No H/O recent travel or contact with pets
• Immunized upto date
• No previous hospitalizations
• O/E - sick looking, febrile, pallor (+), no eschars, generalised lymphadenopathy(+) largest 1.5cm
• Vitals - tachycardic
• P/A - Liver - 4 cm under RCM, firm, nontender
  Spleen - 2 cm along its axis, firm, non tender
• Other systems - WNL
Case 2

- Miss R, 9 yr old from Thiruvallur presented with
- Fever - 6 days, intermittent
- No H/O vomiting/LS/ altered sensorium/
  seizures
- No throat pain, breathing difficulty, abdominal
  pain or urinary tract symptoms
- No joint pain/ rashes
• On examination
• Sick looking, febrile, tachycardic, pallor (+), no eschar
• P/A - liver 3 cm under RCM, firm, non tender, spleen just palpable
• Other systems - WNL
• DD

? Malaria

? Typhoid

? Dengue

? Viral fever
# Master S

<table>
<thead>
<tr>
<th>Inv</th>
<th>09/01 (OP)</th>
<th>13/01</th>
<th>13/01</th>
<th>14/01</th>
<th>15/01</th>
<th>16/01</th>
<th>19/01</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>11.3</td>
<td>10.8</td>
<td>9.8</td>
<td>9.9</td>
<td>10.1</td>
<td>10.8</td>
<td>10.9</td>
</tr>
<tr>
<td>Total count</td>
<td>5100</td>
<td>11300</td>
<td>9800</td>
<td>10100</td>
<td>8810</td>
<td>10960</td>
<td>6820</td>
</tr>
<tr>
<td>Differential</td>
<td>P41L49</td>
<td>P49L44</td>
<td>P43L47</td>
<td>P43L47 M7</td>
<td>P24L61</td>
<td>P20L63</td>
<td>P20L64</td>
</tr>
<tr>
<td>Platelet</td>
<td>1,38,000</td>
<td>8000</td>
<td>19000</td>
<td>17000</td>
<td>14400</td>
<td>13400</td>
<td>20400</td>
</tr>
</tbody>
</table>
• ESR - 54 mm/hr
• LFT, RFT - Normal
• P/S -
  RBC - hypochromic, normocytic cells
  WBC - Lymphocytosis
  Platelet - thrombocytopenia
  No haemoparasites. No abnormal cells
• Mp/Mf by card test - negative
• Dengue Serology - negative
• Scrub typhus IgM - Negative
• Typhi Dot IgM - Negative
• Widal - Negative
• USG abdomen - Hepatosplenomegaly with Enlarged para aortic nodes

• Blood C/S - no growth
Ms R - Inv:

<table>
<thead>
<tr>
<th>Inv</th>
<th>19/01</th>
<th>21/01</th>
<th>23/01</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>10.5</td>
<td>10.4</td>
<td>9.8</td>
</tr>
<tr>
<td>PCV</td>
<td>30.6</td>
<td>30.1</td>
<td>29.9</td>
</tr>
<tr>
<td>Total count</td>
<td>5450</td>
<td>7540</td>
<td>10100</td>
</tr>
<tr>
<td>Differential count</td>
<td>P50L43</td>
<td>P36L52</td>
<td>P29L59</td>
</tr>
<tr>
<td>Platelet</td>
<td>81400</td>
<td>1,00,340</td>
<td>2,50,000</td>
</tr>
</tbody>
</table>
• ESR - 15mm/hr

• Peripheral smear
  RBC - normocytic hypochromic
  WBC - WNL with neutrophilia
  Platelet - agglutination seen
  No hemoparasites. No abnormal cells

• Dengue Serology - Negative

• Mp/Mf by card test - negative

• Typhi Dot IgM - Negative

• Widal - Negative

• Urinalysis - normal

• Blood culture - No growth
• Fever with hepatosplenomegaly with thrombocytopenia
  ? IMN
  ? Leptospirosis
  ? Brucellosis
• EBV - Negative

• Leptospira IgM - Negative

• Brucella IgM (EIA) - Positive
<table>
<thead>
<tr>
<th>Test Description</th>
<th>Observed value</th>
<th>Biological Reference Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serology:</td>
<td>POSITIVE (2.73)</td>
<td>Negative: 0 to 0.8 Ratio</td>
</tr>
<tr>
<td>Brucella-IgM antibody (Serum/EIA)</td>
<td>Rechecked (correlate clinically)</td>
<td>Borderline: 0.8 to 1.1 Ratio</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Positive: Above 1.1 Ratio</td>
</tr>
</tbody>
</table>

End of Report
• Both siblings were positive for brucella and treated with

  Inj Ceftriaxone * 7 days

  Inj Amikacin * 14 days

  Tab Doxycycline * 14 days & discharged on oral

  Tab. Doxycycline
DISCUSSION
Brucellosis

- **Syn**: Undulant fever, Malta fever, Mediterranean fever
- **Zoonoses** - humans accidental host
- **Organism**:  
  - *B. abortus*
  - *B. melitensis*
  - *B. suis*
  - *B. canis*
- **fastidious, aerobic, small, G neg coccobacilli**
• **Modes of transmission:**

  Food borne - ingestion of raw milk or dairy products
  
  Contact infection - direct contact with infected tissue
  
  Air borne
  
  Transplacental
  
  Person to person - extremely rare

• **Incubation period:** 1 - 3 weeks
Major virulence factor - smooth lipopolysaccharide

Brucellosis – Pathogenesis

**Virulence factors**
- Survival & replication inside macrophage
  - Inhibition of the phagosome-lysosome fusion
  - Prevention of toxic enzymes release from intracellular granule (catalase & SOD inactivate $\text{H}_2\text{O}_2$ & superoxide)
  - Endotoxin

**Phagocytised bacteria multiply in macrophages**
- Carried to liver, spleen, bone marrow, lymph nodes, kidneys
- Multiply in cells of the reticuloendothelial system
  - Formation of small granulomas & release of bacteria in systemic circulation ⇒ septicemia
Clinical features

- Fever
- Arthritis/arthralgia
- Hepatosplenomegaly
<table>
<thead>
<tr>
<th>System</th>
<th>Symptoms / Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal &amp; hepatobiliary</td>
<td>Abd. Pain, constipation, hepatomegaly, jaundice, splenomegaly</td>
</tr>
<tr>
<td>Osteoarticular</td>
<td>Sacroilitis, spondylitis, peripheral arthritis, osteomyelitis, monoarticular arthritis</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Endocarditis (Aortic Valve)</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>Glomerulonephritis, orchiepididymitis &amp; renal abscess</td>
</tr>
<tr>
<td>Neurological (1%)</td>
<td>Peripheral neuropathy, chorea, meningoencephalitis, TIA, psychiatric manifestations</td>
</tr>
<tr>
<td>Skin</td>
<td>Erythematous papular lesions, purpura, SJS</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Pleural effusion, pneumonia</td>
</tr>
<tr>
<td>Congenital &amp; neonatal</td>
<td></td>
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</tbody>
</table>
• History – exposure to animals/ ingestion of unpasteurized dairy products
• Complete blood count
  Thrombocytopenia, neutropenia, anemia, pancytopenia
  Leucocytosis (9%)
  Leucopenia (11%)
  Thrombocytopenia (10%)
  Anemia (26%)
• Culture – gold standard
  Blood/BM – long time for isolation (4 wks)
• **Serodiagnosis:**

• **Serum agglutination tests**
  
  Based on reactivity of antibodies against smooth lipopolysaccharide
  
  Detects both IgM & IgG
  
  Cross reacting Ab to other G Neg bacteria - false (+)

• **Enzyme ImmunoAssay:**
  
  High sensitivity but less specificity

• **Other tests**
  
  Polymerase chain reaction
<table>
<thead>
<tr>
<th>AGE AND CONDITION</th>
<th>ANTIMICROBIAL AGENT</th>
<th>DOSE</th>
<th>ROUTE</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥8 yr</td>
<td>Doxycycline</td>
<td>2-4 mg/kg/day; maximum 200 mg/day</td>
<td>PO</td>
<td>6 wk</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rifampin</td>
<td>15-20 mg/kg/day; maximum 600-900 mg/day</td>
<td>PO</td>
<td>6 wk</td>
</tr>
<tr>
<td></td>
<td><strong>Alternative:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Doxycycline</td>
<td>2-4 mg/kg/day; maximum 200 mg/day</td>
<td>PO</td>
<td>6 wk</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Streptomycin</td>
<td>15-30 mg/kg/day; maximum 1 g/day</td>
<td>IM</td>
<td>2 wk</td>
</tr>
<tr>
<td></td>
<td>or</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gentamicin</td>
<td>3-5 mg/kg/day</td>
<td>IM/IV</td>
<td>2 wk</td>
</tr>
<tr>
<td>&lt;8 yr</td>
<td>Trimethoprim-sulfamethoxazole (TMP-SMZ)</td>
<td>TMP (10 mg/kg/day; maximum 480 mg/day) and SMZ (50 mg/kg/day; maximum 2.4 g/day)</td>
<td>PO</td>
<td>4-8 wk</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>15-20 mg/kg/day</td>
<td>PO</td>
<td>6 wk</td>
</tr>
<tr>
<td>Meningitis, osteomyelitis, endocarditis</td>
<td>Doxycycline</td>
<td>2-4 mg/kg/day; maximum 200 mg/day</td>
<td>PO</td>
<td>4-6 mo</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gentamicin</td>
<td>3-5 mg/kg/day</td>
<td>IV</td>
<td>2 wk</td>
</tr>
<tr>
<td></td>
<td>?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
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<td>15-20 mg/kg/day; maximum 600-900 mg/day</td>
<td>PO</td>
<td>4-6 mo</td>
</tr>
</tbody>
</table>
• **Control measures:**

  Early diagnosis and treatment

  Pasteurisation of milk

  Avoid direct contact with infected animals

  Vaccine - not currently available
Behnaz F, Mohammadzadeh M, Mohammadi moghaddam M, 

Background 
Brucella mellitensis, the most invasive strain of brucella, is the predominant Strain of genus brucella in Iran. It causes variety of hematological abnormalities some of which are frequent and causes difficulties in diagnosis.

Objective 
To find hematological abnormalities of brucellosis in hospitalized patients in an endemic area.

Results 
Out of 238 patients diagnosed as brucellosis, hematologic evaluation had been performed for 208 patients. Anemia was detected in (55/119) 46% of male and (35/89) 39.3% of female patients (Pvaule0.383). Leukopenia (WBC < 4300/mm3) was present in (18/208) 8.5%, thrombocytopenia (Platelet < 150.000/mm3) in (24/200) 12% and pancytopenia in (3/200) 1.5% of patients.

Conclusion 
Brucellosis should be considered in differential diagnosis of any patient with disturbances of hematologic findings in endemic areas.

BACKGROUND:

Brucellosis, constituting a major health problem in many parts of the world—particularly in the Mediterranean and the Middle East—is a multisystem disease with a broad spectrum of clinical manifestations. Hematological abnormalities ranging from a fulminant state of disseminated intravascular coagulopathy to subtle hemostatic alterations have been reported in brucella infection. Immunemediated thrombocytopenia is also a clinically important mechanism that can be encountered during brucellosis.

CASE:

A young lady with fever was referred to a university hospital because of thrombocytopenia. The provisional diagnosis was idiopathic thrombocytopenic purpura, as the bone marrow examination showed an increased number of megakaryocytes and the absence of fever after hospitalization. The patient responded well to corticosteroid treatment. However, she was finally diagnosed with brucellosis with positive bone marrow and blood cultures for B. abortus and agglutination test of 1:320. The patient was discharged from the hospital 10 days later in good health on rifampicin and doxycycline therapy. The follow-up of the patient revealed normal hematological findings together with a progressive reduction in the titer of the agglutination test for brucella.

CONCLUSION:

Brucella infection may cause severe thrombocytopenia, mimicking a primary hematological disease that is reversible after appropriate antimicrobial therapy. In cases of brucellosis-induced immune thrombocytopenic purpura, a short-term standard dose of corticosteroid treatment might be an alternative and additional treatment as an urgent approach for thrombocytopenia while initiating antibrucellosis treatment.
• Suleyman Baldane et al, An Atypical Presentation of Brucellosis in a Patient with Isolated Thrombocytopenia Complicated with Upper Gastrointestinal Tract Bleeding: Case Reports in Medicine: Volume 2012, Article ID 473784, 4 pages

• Iftikhar Hussein et al. Brucellosis associated with thrombocytopenia; Saudi Medical Journal 2000; Vol. 21 (9): 877-879
City pediatric meet for the month of March, 2015 will be held in Southern Railway Head Quarters Hospital.

Venue: Auditorium, Radiology Block

Date: 18.03.2015

Time: 2:30 – 4:30 pm

Kindly send your abstract for presentation on or before 8th March to

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Southern Railway HeadQuarters Hospital,
Perambur, Chennai - 600023

Email Id: nibeditamitra1@yahoo.co.in

Mobile no: 9003160535

We look forward to your participation and your presence.