Rickettsial Disease: an unusual cause of severe febrile illness in ICU

**KEYWORDS**
Rickettsioses, rickettsial disease, typhus

**ABSTRACT**
We report a case of a 45yrs male patient admitted in ICU with 12 days H/O fever, headache & myalgias. He had respiratory distress and hypotension requiring mechanical ventilation and inotropic support. Presentation mimicking usual viral or tropical fever but usual fever workup was nondiagnostic. Finally detected to have rickettsial fever. Responded wonderfully to appropriate specific treatment in 48 hours and recovered completely.

Rickettsial Diseases usually are transmitted to humans by arthropods. They are generally incapacitating and notoriously difficult to diagnose; untreated cases can have high fatality rates. Clinical suspicion is important. The Weil Felix and other serological tests are useful. Doxycycline is usually the drug of choice.

**INTRODUCTION:**
Rickettsioses usually are arthropod borne diseases. Patients usually present as fever, rash, myalgia & various systemic features. High index of suspicion is required as untreated cases can have high mortality rates. Clinical presentation often mimics viral or tropical fever. Weil Felix & other serological tests are useful for diagnosis. Drug of choice is doxycycline.

**Case:**
45years/ male, apparently healthy farmer, presented with H/O sudden onset sickness for last 12 days. He complained of high grade intermittent fever with chills. Fever spiking daily. He suffered from severe headache and agonizing generalized muscle pains particularly more in thigh region. Pain was severe enough so as to disturb his daily routine. He gave H/O cough and breathlessness for last 2 days. Breathlessness worsened rapidly over few hours before admission. There were no other significant medical complaints. He had no associated co-morbidities. He had taken treatment from local doctor in the form of analgesics, antipyretics, antibiotics (cephalosporins) but with little relief. Breath sounds were equal. Crepitations were heard all over lung fields. Hepatosplenomegaly was present. There were no signs of meningeval irritation and also no neurodeficit. His SPO2 and PO2 were low. He soon required mechanical ventilation.

**Blood Pressure couldnot be maintained without inotropic support (noradrenalin). We started him with broad spectrum antibiotic (pipera-cillin + tazobactum) and other supportive management. Review of investigations showed normal leukocyte count, mildly deranged Liver function tests, reduced sr. albumin (1.9g/dl) normal renal function tests. Chest X ray showed bilateral crepitations heard all over lung fields.**

**Discussion:**
Rickettsioses can be divided into the following biogroups:

**TABLE I : BIOGROUPS OF RICKETTSIAEAE**

<table>
<thead>
<tr>
<th>Biogroup</th>
<th>Disease</th>
<th>Vector</th>
<th>Host</th>
<th>Organism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spotted fever</td>
<td>Rocky Mountain spotted fever (RMSF)</td>
<td>Tick</td>
<td>Dogs, rodents</td>
<td>R. rickettsii</td>
</tr>
<tr>
<td></td>
<td>Rickettsialpox</td>
<td>Mite</td>
<td>Mice</td>
<td>R. akari</td>
</tr>
<tr>
<td></td>
<td>Indian tick typhus / Boutonneuse fever/ Mediterranean spotted fever (MSF)</td>
<td>Tick</td>
<td>Dogs, rodents</td>
<td>R. conorii</td>
</tr>
<tr>
<td>Typhus</td>
<td>Epidemic louse borne typhus</td>
<td>Louse</td>
<td>Human</td>
<td>R. prowazeki</td>
</tr>
<tr>
<td></td>
<td>Brill-Zinsser disease</td>
<td>Louse</td>
<td>Human</td>
<td>R. prowazeki</td>
</tr>
<tr>
<td></td>
<td>Endemic/Murine flea borne typhus</td>
<td>Flea</td>
<td>Rats</td>
<td>R. typhi</td>
</tr>
<tr>
<td>Scrub typhus</td>
<td>Scrub typhus</td>
<td>Chigger</td>
<td>Rodents</td>
<td>O. tsutsugamushi</td>
</tr>
<tr>
<td></td>
<td>Ehrlichioses and Anaplasmosis</td>
<td>Tick</td>
<td>Deer, dog, rodent</td>
<td>Ehrlichia, Anaplasma</td>
</tr>
<tr>
<td></td>
<td>TIBOLA*</td>
<td>Tick</td>
<td>Wild boar</td>
<td>R. slovaca</td>
</tr>
<tr>
<td></td>
<td>DEBONEL**</td>
<td>Tick</td>
<td>Wild boar</td>
<td>R. slovaca</td>
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</tbody>
</table>

**Potential occupational exposure to anthropods, typical clinical features, negative workup for other viral and tropical diseases, serological tests suggestive of rickettsiosis and rapid defervescence after doxycycline therapy.**

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Rickettsiae take a characteristic red color when stained by the Giemsa or Gimenez stain. Rickettsia parasitize the endothelial cells of the small venous, arterial, and capillary vessels leading to vasculitic process. This process may cause thrombosis, and the deposition of leukocytes, macrophages, platelets may result in loss of intravascular colloid with subsequent hypovolemia and decreased tissue perfusion. Loss of electrolytes is common. The consequence of cell-to-cell spread of rickettsiae maculo-papular rash develops. The vascular injury and subsequent host lympho-histiocytic response correspond to distribution of rickettsiae and systemic features. Platelets are consumed locally.

Clinical Manifestations:
Early signs and symptoms of these infections are nonspecific and mimic benign viral illnesses, making diagnosis more difficult. Clinical presentation may mimic other common infections in the tropics. Incubation period of various rickettsial infections vary between 2-21 days. Fever of undetermined origin is the most frequent presentation of rickettsial disease. Fever is usually abrupt onset, high grade, sometimes with chills, occasionally with morning remissions. Severe frontal headache and generalized myalgia especially in muscles of the lumber region, thigh and calf is seen in variable proportion of cases. Though rash is considered as hallmark of rickettsial disease, it is neither seen at presentation nor in all the patients. Rash usually becomes apparent after 3-5 days of onset of symptoms. Initially rash is in the form of pink, blanching, discrete macules which subsequently becomes maculo-papular, petechial or hemorrhagic. The rash of typhus group rickettsioses is quite atypical, initially appearing on trunk, the lumber region, thigh and calf is seen in variable proportion. A necrotic eschar at the inoculating site is seen in variable frequency. Doxycycline is the drug of choice for treatment of rickettsial disease should be reconsidered. Treatment may be terminated 2-3 days after the patient is afebrile and at least 7 days of treatment are necessary. Jaundice, renal failure, pneumonitis, ARDS, septic shock, myocarditis and meningoencephalitis are known with this disease. Q fever: Complications include chronic Q fever, endocarditis, myocarditis, meningoencephalitis, glomerulonephritis, and SIADH

Pathophysiology:
They are obligate intracellular gram-negative coccobacillary forms that multiply within eukaryotic cells. Rickettsiae take on a characteristic red color when stained by the Giemsa or Gimenez stain. Rickettsia parasitize the endothelial cells of the small venous, arterial, and capillary vessels leading to vasculitic process. This process may cause thrombosis, and the deposition of leukocytes, macrophages, platelets may result in loss of intravascular colloid with subsequent hypovolemia and decreased tissue perfusion. Loss of electrolytes is common. The consequence of cell-to-cell spread of rickettsiae maculo-papular rash develops. The vascular injury and subsequent host lympho-histiocytic response correspond to distribution of rickettsiae and systemic features. Platelets are consumed locally.

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Different Diagnoses:
Dengue, Leptospirosis, Malaria, Measles, Meningococcal Infections, Rubella, Streptococcal Infection, Syphilis, Toxic Shock Syndrome, Vasculitis.

Laboratory Findings:
Thrombocytopenia, hypoaalbuminemia, hypotension and normal to low leucocyte count are certain clues to early diagnosis. Test is based on the detection of antibodies to various proteins and antigens from members of the genus Rickettsia. Even though the WF agglutination test is not very sensitive, when positive, it is a rather specific test. Enzyme linked Immunosorbent Assay (ELISA), Indirect immunoflorescence test (IF), PCR although considered more specific but are not easily available.

Differential Diagnoses:
Following five factors taken together should help in diagnosis, which can then be confirmed with serology. Compatible clinical presentations, Tick bite or tick exposure, Epidemiological data, Suggestive laboratory features, and Rapid defervecence with appropriate antibiotics

Treatment: Adequate antibiotic therapy initiated early in the first week of illness is highly effective. Fever usually subsides within 24-72 hours after starting antibiotic therapy. If fever fails to subside with the use of a suitable antibiotic, the diagnosis of rickettsial disease should be reconsidered. Treatment may be terminated 2-3 days after the patient is afebrile and at least 10 days of therapy has been given. Doxycycline is the drug of choice. Other drugs are chloramphenicol, fluoroquinolones & rifampin. Murine (endemic or flea-borne) typhus: A single dose of doxycycline is the treatment of choice. Thrombocytopenia, hypoalbuminemia, hypotension, and coagulation defects require supportive management.

Prognosis: Rocky Mountain spotted fever (RMSF): Fatalities are mainly caused by delay in diagnosis and treatment. The overall mortality rate currently is 5-7%. Rickettsialdixox is usually self-limited. Louse-borne (epidemic) typhus: Mortality may be uncommon in children younger than 12 years, but rates rise to as high as 60-70% in individuals older than 50 years. Murine typhus although considered a mild illness, at times may prove fatal. Scrub Typhus: Fatalities are rare with use of antibiotics. Q fever: The mortality rate is less than 1%.
REFERENCE