A CASE STUDY OF A MAN WHO RETURNED FROM ABROAD WITH FEVER
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CASE HISTORY

At the General Practitioner’s Clinic
Mr HKY was a 52-year-old Chinese male who presented initially to his general practitioner (GP) with a history of an intermittent fever for 6 days after his return to Singapore from Bintan, an island off Indonesia. This occurred when the Severe Acute Respiratory Syndrome (SARS) outbreak took place in Singapore during May 2003. The GP carried out a full blood count done which showed a haemoglobin (Hb) 11.8 g/dl (13.5-18.0), platelets 259x10^9/L (150-400), total leucocytes 8.1x10^9/L (4.00-11.00), neutrophils 4.9x10^9/L (2.00-7.50), lymphocytes 1.5x10^9/L (1.50-4.00), monocytes 0.78x10^9/L (0.20-0.80), eosinophils 0.75x10^9/L (0.04-0.40), and basophils 0.05x10^9/L (0.00-2.00). His previous Hb was documented as 15.0 g/dl. In view of the significant decline in Hb, his GP referred him to the nearby polyclinic for further management.

If you were the attending polyclinic doctor, how would you manage him at this point of time?
Mr HKY presented three days later, day 9 of his fever to a district polyclinic. He stated that his fever worsened in the evenings. He had no respiratory, abdominal, cardiac and neurological sign and symptoms. Clinical examination was unremarkable. There was no sign of rash, or organomegaly. Full blood count done in the polyclinic showed a Hb of 13.2 g/dl (11.0-18.0), platelets 438x10^3/UL (150-450), total leucocyte count 10.2x10^3/UL (4.5-10.5), lymphocytes 2.3x10^3/UL (1.2-3.4), monocytes 1.0x10^3/UL (0.1-0.6), neutrophils 6.9x10^3/UL (1.4-6.5). Blood film for Malaria parasite was negative. How would you now manage him?
The polyclinic doctor referred Mr. HKY to Tan Tock Seng Hospital (TTSH), the designated SARS hospital, for further investigation for his fever. The provisional diagnosis was malaria in view of his travel history and prolonged fever.

What is typhus?

Empirical treatment with Doxycycline commenced on the third day of hospitalization with subsequent rapid resolution of the fever. He was discharged well on the 5th day of admission. He was diagnosed as a case of typhus.

What is typhus?

Of the wide range of rickettsial diseases, typhus disease is the most commonly recognized entity in South East Asia. In Singapore murine typhus is more prevalent than scrub typhus. Rickettsial diseases are important but often under recognised causes of febrile illness locally.

Rickettsiae are obligate intracellular bacteria that are ecologically associated with an arthropod host. The genus Rickettsia includes three antigenic allied defined groups: spotted fever group, typhus group, and scrub typhus group, but the scrub typhus rickettsia, Orientia (formerly Rickettsia) tsutsugamushi, has no established evolutionary relationship with the other two. However, these diseases have similar target tissues (blood vessels) and organs, with the result that the histopathology has many similarities. These microbiologically distinct pathogens cause diseases with many similar features.

What is the epidemiology of typhus?

Typhus is endemic in South East Asia. A comprehensive study of 1629 hospitalized patients with febrile illnesses in rural Malaysia revealed that scrub typhus was the cause of 19.3% of the febrile patients. As Singapore is a modern urban city with a high standard of public health, typhus was considered a disease of the past. In Singapore, six cases of Murine typhus occurring within a period of three months were reported. Another study conducted at the National University Hospital in Singapore reported 21 cases of typhus between January 1999 and February 2000.

What is the differential diagnosis?
The classical triad of typhus disease was described as fever, headache and rash. Other common symptoms are myalgia, cough and gastrointestinal complaints. Fever was the most consistent feature, followed by headache. Only 1.8% had rash on presentation. Important laboratory clues of typhus disease were a normal total white count with thrombocytopenia and the presence of mild transaminits.

The clinical features of typhus and laboratory findings of typhus thus mimic dengue fever, which is another endemic but
Table 1 of the tabulation of Rickettsial diseases known

<table>
<thead>
<tr>
<th>Disease</th>
<th>Agent</th>
<th>Geographic Distribution</th>
<th>Natural History</th>
<th>Transmission to human</th>
</tr>
</thead>
<tbody>
<tr>
<td>Murine typhus</td>
<td>R typhi</td>
<td>Worldwide, predominantly tropical &amp; subtropical especially coastal California &amp; Texas in the United States</td>
<td>Rattus to rat flea to Rattus; opossum to cat flea to opossum</td>
<td>Flea faeces scratched into skin rubbed into conjunctiva or inhaled</td>
</tr>
<tr>
<td>Scrub typhus</td>
<td>O tsutsugamushi</td>
<td>Japan, southern and eastern Asia, northern Australia, islands of the western and southwestern Pacific</td>
<td>Transovarial transmission in Leptothrombidium chiggers</td>
<td>Chigger bite</td>
</tr>
<tr>
<td>Rocky Mountain spotted fever</td>
<td>R rickettsii</td>
<td>North, Central, and South America</td>
<td>Transovarial maintenance in Dermacentor, Rhipicephalus and Amblyomma ticks; less extensive horizontal transmission from tick to mammal to tick</td>
<td>Tick bite</td>
</tr>
<tr>
<td>Boutonneuse fever</td>
<td>R conorii</td>
<td>Mediterranean basin, Africa, Asia</td>
<td>Transovarial maintenance in Rhipicephalus, Hyalomma, and Amblyomma ticks; role of horizontal transmission is not clear</td>
<td>Tick bite</td>
</tr>
<tr>
<td>North Asian tick typhus</td>
<td>R sibirica</td>
<td>Russia, China, Mongolia, Pakistan, Kazakhstan, Tadzhikistan</td>
<td>Transovarial maintenance in Dermacentor, Haemaphysalis, and Hyalomma ticks; horizontal transmission from tick to mammal to tick</td>
<td>Tick bite</td>
</tr>
<tr>
<td>Oriental spotted fever</td>
<td>R japonica</td>
<td>Japan</td>
<td>Presumably a transovarial tick host; the role of horizontal transmission is not clear</td>
<td>Tick bite</td>
</tr>
<tr>
<td>Queensland tick typhus</td>
<td>R australis</td>
<td>Eastern Australia</td>
<td>Transovarial transmission in Ixodes ticks; the role of horizontal transmission is not clear</td>
<td>Tick bite</td>
</tr>
<tr>
<td>Rickettsialpox</td>
<td>R akari</td>
<td>United States, Ukraine, Croatia, possibly worldwide</td>
<td>Transovarial transmission in Liporosoides sanguine mites; horizontal transmission from mite to Mus musculus to mite</td>
<td>Mite bite</td>
</tr>
<tr>
<td>Murine typhus-like illness</td>
<td>R felis</td>
<td>California, Texas</td>
<td>Transovarial transmission in cat flea; role of horizontal transmission is not clear</td>
<td>Presumably flea feaces</td>
</tr>
<tr>
<td>Epidemic typhus</td>
<td>R prowazekii</td>
<td>South America, Africa, Asia, Central America, Mexico</td>
<td>Human to Pediculus corporis humanus louse to human</td>
<td>Louse faeces scratched into skin</td>
</tr>
<tr>
<td>Sylvatic typhus</td>
<td>R prowazekii</td>
<td>United States</td>
<td>Flying squirrel to louse and flea ectoparasites to flying squirrels</td>
<td>Ectoparasites of flying squirrels to humans</td>
</tr>
<tr>
<td>Recrudescent typhus</td>
<td>R prowazekii</td>
<td>Worldwide</td>
<td>Reactivation of latent human infection years after acute illness</td>
<td>None</td>
</tr>
</tbody>
</table>

Toxoplasmosis and scrub typhus has been found in Singaporeans with occupational or recreational epidemiological risks. This is significant in the context for the above patient as onset of symptoms took place within days of returning from his foreign travel. Thus typhus must be considered in tourists and travellers returning from endemic regions and presenting with a febrile illness.

What is the diagnostic test for typhus?
Currently two types of test are used to diagnose typhus. The Weil-Widal Felix (WWF) is known to lack specificity and sensitivity in diagnosing typhus disease. It yields false positive results with Leptospirosis, malaria, Proteus infections and other febrile illnesses. The indirect immunoperoxidase test (IIP) is the gold standard in diagnosing typhus disease. The IIP is sensitive and specific for typhus fever but it is limited by complexity of the test and cost much more than the WWF test.
How do you manage typhus?

As typhus is easily treatable with a course of tetracycline, Dr Chen et al\(^1\) recommended that an empirical course of Doxycycline, which would serve as a quick and effective diagnostic tool in clinically suspected typhus fever. After 72 hours of drug initiation, close to 90\% of infected patients had resolution of their fevers\(^7\). A therapeutic course of Doxycycline currently is significantly less expensive than rickettsial serology using IIP. In addition, such an approach cuts short the clinical course of the disease, which while usually benign, has been known to result in serious complications for example hepatic, renal failure, aseptic meningitis and encephalitis, and pneumonitis with respiratory failure\(^3\).

REFERENCES