Meliodosis and scrub typhus co-infection in a patient presenting with acute undifferentiated febrile illness
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Case Report

INTRODUCTION

Melioidosis which is caused by non-lactose fermenting gram-negative rods, *Burkholderia pseudomallei* is a typical environmental community-acquired febrile illness in Malaysia.1 Scrub typhus, on the other hand, is caused by the obligately intracellular organism, *Orientia tsutsugamushi*, is transmitted via bites from the larvae of Trombiculid mites; known as chiggers to humans. The bites may elicit eschars in which if present may assist in early clinical recognition.2,3 Both melioidosis and scrub typhus may cause
severe infections with multiorgan dysfunctions such as pneumonitis, meningitis, septic shock and death.\textsuperscript{1-10} Unlike melioidosis, scrub typhus remains an under-appreciated and under-diagnosed disease, likely due to non-specific clinical presentation and the laborious nature of its diagnostic requirements.\textsuperscript{11, 12} We describe a patient who had presented with undifferentiated febrile symptoms with acute kidney injury who had initially been diagnosed with melioidosis before a co-infection of scrub typhus was made.

**Case report**

During the rainy season in May 2016, a 60-year-old Malay man from Teluk Intan, Perak (Northwest of Peninsular Malaysia) complained of 7 days of fever which was associated with a headache. He had no vomiting, visual complaints, confusion or neck pain. He was a farmer working on paddy fields. There was no report of recent travel and involvement in forest activities. His medical history included poorly controlled type 2 diabetes mellitus with recent Hba1c of 10.8%.

On physical examination, he was alert and enterally orientated. His vital signs include an oral temperature of 39°C, blood pressure of 110/77 mmHg with the pulse rate of 100 beats per minute, respiratory rate of 18 breaths per minute with oxygen saturation of 98% on room air, with total qSOFA scores of 0 (13). Skin examination was unremarkable with no visible eschars seen. Eyes were normal, and there were no palpable cervical lymph nodes, mouth ulcers or myositis elicited. The cardio-respiratory examination was unremarkable and abdominal examination failed to demonstrate organomegaly. Central nervous system examination did not isolate any focal neurological abnormalities.

The initial laboratory parameters demonstrated leukocytosis with white cell counts of 20.2 x 10\textsuperscript{9} cell/L (reference range 4.0-12.0 x 10\textsuperscript{9} cell/L) and platelet of 252 x 10\textsuperscript{9} cell/L (reference range 150-440 x 10\textsuperscript{9} cell/L). He was not known to have chronic kidney disease and his serum creatinine level was markedly elevated at 561 µmol/L (reference range 62-106 µmol/L) with normal liver enzymes with alanine aminotransferase of 27 IU/L (reference range 10-50 IU/L) and aspartate aminotransferase of 42 IU/L (reference range 10-40 IU/L) and normal total bilirubin level of 7.9 µmol/l (reference range < 21 µmol/l). C-reactive protein (CRP) was elevated at 154 mg/l (reference range < 5mg/l).

Blood culture taken on admission showed the presence of non-lactose fermenter Gram-negative bacillus that was later identified as *Burkholderia pseudomallei* by Vitek 2 Compact (BioMerieux, Inc. USA). Antibiotic susceptibility test by disc diffusion method showed resistant to ceftazidime and susceptible to imipenem. Thorax and abdominal computed tomography scans were normal with no evidence of lungs or intraabdominal abscesses. Despite imipenem, he remained febrile on the ward. Serum MAT for leptospirosis and PCR targeting the LipL32 gene in Leptospiral were both negatives. Dengue NS1 and IgM by ELISA and blood film for malaria were non-reactive as well. Patient’s serum was tested positive using the InBios Scrub Typhus Detect IgM Rapid Test which later was confirmed by nucleic acid detections assays by polymerase chain reaction using the forward primer (AACTGATTTTATCAACTAATGCTGCT) and reverse primers (TATGCCTGAGTAAGATACRTGAATRGAATT) against the 47-kDa was positives with DNA copies of 1800 copies/ml.\textsuperscript{14} Doxycycline 200mg loading followed by 100mg twice a day was commenced. He became afebrile within 48 hours of starting with the anti rickettsial treatment. The patient completed 14 days of imipenem and seven days of doxycycline and with normalization of blood parameters and was subsequently discharged well (Figure 1).

**Ethics statement**

This study had been approved by the Malaysian National Medical Research and Ethics Committee (1 September 2015). Informed consent was signed by the patient.
DISCUSSION

To our knowledge, this is the first reported case of co-infection with melioidosis which was confirmed by blood culture and scrub typhus diagnosed by scrub typhus rapid test kit, with subsequent confirmation via molecular assays in Malaysia. Unlike melioidosis which can be diagnosed readily by conventional culture methods, diagnosis of scrub typhus by culture requires cellular culture method which is often unfeasible due to laborious techniques and potentially requiring biosafety level-3 laboratory containment (based on the risk assessment), which is costly. Clinically, symptoms of melioidosis and scrub typhus often are unspecific and may mimic each other. Whilst eschar which is the vasculitic skin reaction following bites from the infected chiggers may assist in diagnosis of scrub typhus, not all cases were accompanied by the skin lesion as demonstrated by Paris et al. where the author postulates that in the setting of multiple exposures with chigger bites, incidence of eschar is much less due to impaired cellular immunity of the host.

Studies in Southeast Asia countries and their surrounding areas have demonstrated the considerable prevalence of scrub typhus as an important, treatable acute febrile illness especially within rural areas. Doxycycline is an effective antibiotic for scrub typhus. Hence we suggest that in an area where the zoonotic infections co-circulate, it should be the first line antibiotic agent in suspected cases of scrub typhus.

In conclusion, scrub typhus should remain high in the list of differential diagnoses when faced with undifferentiated clinical symptoms and signs as clinical parameters alone hardly discriminate between scrub typhus and others, thus a need for high index of clinical suspicion coupled with reliable confirmatory tests. Rapid tests are promising which may aid in early diagnosis, however more studies are required to evaluate its reliability in endemic regions.

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