CASE REPORT

Scrub typhus with central nervous system involvement: A case report with CT and MR imaging features

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Abstract

A 40 year old resident of Kuala Lumpur presented with acute febrile illness two weeks following a forest camping trip in the National Park, Pahang. There was presence of eschar, jaundice, anaemia with evidence of hepatitis and renal impairment. The patient was confused with no focal neurological signs. The serological study confirmed the diagnosis of scrub typhus with a significant IgM titre and rising IgG titres using indirect immunoperoxidase test. The patient responded dramatically to doxycycline. CT scan during the acute illness showed multiple low density lesions at the corpus callosum and periventricular white matter which improved after treatment. MRI showed a small ring enhancing lesion, with multiple areas of hyperintensities at periventricular and deep white matter with T2 and FLAIR sequences. The radiological changes are consistent with the known pathology of scrub typhus, which is vasculitis involving the small vessels causing microinfarctions and ischaemia. The distribution of the lesions is consistent with the predominant involvement of small vessels.

Key words: scrub typhus, Orientia tsutsugamushi, Rickettsia, CNS infection, CT, MRI

INTRODUCTION

The aetiologic agent of scrub typhus is Orientia (formerly Rickettsia) tsutsugamushi and is acquired from the bites of infected chiggers or mite larvae. It is probably one of the most common infections in Asia. A recent seroepidemiological survey among the rural rubber estate workers in Slim River, Peninsular Malaysia showed a seroconversion rate for IgM against O tsutsugamushi of 5.7% over a four months period. A comprehensive study of 1629 hospitalised patients with febrile illnesses in rural Malaysia revealed that scrub typhus accounted for 19.3% of these fevers. A serological survey in a rural Thai village has shown a 52% prevalence of antibody against O tsutsugamushi among children below 10 years of age. A one-year nation-wide study of acute fevers of unknown origin in Thailand showed that 9.6% of these fevers were caused by scrub typhus. The infection is acquired through agricultural activities in the oil palms, rubber plantations, rice-fields; recreational activities in the woods or mountainous areas. Most of the infections are asymptomatic. For those who are symptomatic, the incubation period is 6-21 days. The clinical manifestations are: fever, headache and non-specific symptoms such as vomiting and myalgia. Eschar, a crusted black sore at the site of insect bite is a cardinal feature. However, it is uncommon among South East Asian patients as compared to Caucasians. Complications may develop especially among the non-immune individuals. They include pneumonitis, meningo-encephalitis, jaundice, renal impairment and myocarditis. The infection responds well to chloramphenical, tetracycline and doxycycline. Although CNS involvement in scrub typhus is well described, there has been no previous documented study of CT scan and MRI changes in the infection. This is a case report of scrub typhus presenting with encephalitis with CT scan and MRI changes.

CASE REPORT

A 40 year old Malay technician who lived in Kuala Lumpur was admitted to the University Hospital, Kuala Lumpur, with a five day history
of fever, headache, vomiting and cough followed by one day history of drowsiness. He had gone camping in the forest area in the National Park, Pahang two weeks before the onset of symptoms. Other than a three years history of diabetes mellitus on oral hypoglycaemics, there was no other previous medical history of relevance. There was also no history of insect bites or rashes. Physical examination revealed a temperature of 39.5°Celsius. He was pale and jaundiced with no other systemic signs. Laboratory investigations showed Hb was 12 g/l, peripheral white cell count was 13.3 x 10⁹/l with neutrophil of 85%, platelet count was 81 x 10⁹ /l, blood urea was 10.4 mmol/l and creatinine 195 μmol/l. The liver function tests revealed an albumin level of 17 g/l, total bilirubin of 50 μmol/l (predominantly conjugated), alkaline phosphatase was 221 IU/l, alanine transferase was 70 IU/l, AST was 123 IU/l and ESR was 115 mm/hr. Other tests which were normal included urine analysis, blood and urine cultures, blood films for malarial parasites, coagulation profile, chest x-ray and an abdominal ultrasound. The patient was initially treated for leptospirosis and meliodosis with intravenous crystalline penicillin, ceftriaxone and subsequently, ceftazidime without improvement. The patient became confused but without focal neurological signs.

CT scan of the brain (Fig 1) at day six of admission revealed multiple low attenuation lesions at left corpus callosum, both periventricular and deep white matter. A lumbar puncture revealed an opening pressure of 24 cm H₂O, white blood cell count of 10/mm³, glucose level of 5.2 mmol/l (blood glucose 10 mmol/l) and protein 100 mg/l. Indian ink stain and antigen test for Cryptococcus, stain for acid fast bacilli and culture for bacteria were all negative. An eschar was then noted over the right buttock and the patient was immediately commenced on oral doxycycline 100 mg b.d. The patient improved dramatically. He became afebrile and orientated within 48 hours. The liver and renal function gradually normalised. He was discharged a week later. A repeat CT scan after two weeks showed the low attenuation lesions became less pronounced. MRI (Fig. 2,3) performed four weeks post-treatment on a Siemens 1.5 Tesla machine revealed a small ring enhancing lesion of 3mm in the left corpus callosum with multiple areas of hyperintensities on FLAIR and T2-weighted in both periventricular and the deep

![FIG. 1: Pre-treatment axial non enhanced CT brain showing well defined hypodense area in the left corpus callosum.](image-url)
white matter. Some of these lesions align perpendicular to the lateral ventricle.

During follow-up after a month, the patient was well, having returned to work while the eschar had healed considerably. Indirect immunoperoxidase (IPP) test as described by Kelly et al. showed the IgM titre for scrub typhus was 1:1280. Paired IgG sera for scrub typhus revealed a fourfold rise in the titre from 1:160 to 1:640. Serological tests for melioidosis, dengue, leptospirosis and HIV were all negative.

**DISCUSSION**

The clinical features of this 40 years old man with acute fever, eschar, confusion, hepatitis
and renal impairment responding rapidly to doxycycline are consistent with the diagnosis of scrub typhus. This is confirmed by the high IgM and rising IgG titres. The patient was likely to have acquired the infection while camping in the National Park.

CNS involvement is a known complication of scrub typhus which ranges from aseptic meningitis to frank meningoencephalitis. The name "typhus" itself, is derived from the Greek work, "typhos", which means "stupor". Silpajakul reported nine of 72 patients with scrub typhus from Southern Thailand had CNS complications which was mainly aseptic meningitis. The neurological complications in scrub typhus are attributed to involvement of the small vessels which occurs throughout the body. Post-mortem examinations in the brains revealed macrophage, lymphocyte and plasma cell infiltrates of the meninges. The reaction of the brain parenchyma were typified by the "typhus nodules" which were composed of glial cells, lymphocytes, plasma cells and macrophages collected around the walls of capillaries. The arteries were less involved. The CT changes of multiple low attenuation lesions at corpus callosum and periventricular white matter which resolved after treatment, and the MRI changes of small ring enhancing lesion, with multiple areas of hyperintensities at periventricular and deep white matter, is consistent with the pathological changes. They are likely to represent breakdown in blood-brain barrier, microinfarction and oedema secondary to vasculitis. The predominant involvement of periventricular and deep white matter is also consistent with small vessel predilection of the disease.

Although clinical features of scrub typhus are well described, there has been no previous documentation of a systematic neuroradiological study, despite its high prevalence in parts of rural Asia. Neuroradiological appearances of other rickettsial infections have previously been analysed for Rocky Mountain spotted fever caused by Rickettsia rickettsii, a tick-borne disease found in the United States and Canada. Abnormalities in CT and MRI of the brain consisted of infarctions, cerebral oedema, meningeal enhancement and prominent perivascular spaces. The changes are more common in the MRI as compared to the CT scan. The neuroradiological changes are associated with a poorer outcome. However, comparative pathological studies between scrub typhus and other rickettsial diseases have shown that there is less microinfarction in scrub typhus as compared to Rocky Mountain spotted fever. There may be differences in the CT and MRI changes between Rocky Mountain spotted fever and scrub typhus. Systematic studies of neuroradiological changes in scrub typhus is thus necessary.

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REFERENCES