

## CASE REPORTS

# Encephalomyelitis as the first manifestation of scrub typhus

Chen Wang *MD PhD*, Naian Xiao *MD*, Yihong Zhan *MD*, Qilin Ma *MD*

<sup>1</sup>*Department of Neurology, The First Affiliated Hospital, School of Medicine, Xiamen University, Xiamen, Fujian, China*

### Abstract

Scrub typhus is a zoonotic disease caused by *Orientia tsutsugamushi*. We report here a middle-aged man with 3 days history of mild fever, dysphagia, and anarthria. On examination, he had nystagmus, quadriparesis, and a fresh eschar in the left scrotal region. Cerebrospinal fluid (CSF) and serum samples were positive for tsutsugamushi antibody. The magnetic resonance images (MRIs) showed T2 lesions in the brainstem, basal ganglia, frontal, corona radiate and spinal cord. After treatment with chloramphenicol and prednisolone, the clinical symptoms and signs improved. Our case highlights that encephalomyelitis may be caused by rickettsial disease such as scrub typhus.

**Keywords:** Scrub typhus, encephalomyelitis, postinfectious encephalomyelitis, infectious disease, zoonotic disease

### INTRODUCTION

Scrub typhus is a zoonotic rickettsial disease caused by *Orientia tsutsugamushi* and is characterized by fever, headache, muscle pain, rash, cough, gastrointestinal symptoms, interstitial pneumonia and meningoencephalitis.<sup>1</sup> In spite of its decreasing incidence, rickettsioses remains a public health threat in many regions of the world. In tropical and subtropical regions in China, such as the southern part of Fujian province, the incidence of scrub typhus remains high. Patients with scrub typhus often present with systemic symptoms and sometimes with encephalopathy. However, presentation with acute disseminated encephalomyelitis (ADEM) in scrub typhus has rarely been described. We report here such a case seen recently in our Center.

### CASE REPORT

A 58-year-old man presented with nausea and vertigo, dysphagia, loss of speech, generalized weakness, and mild fever with a peak temperature of 37.8°C that developed over three days. The patient visited his hometown in the southern part of the Fujian province (? Is it correct) to help in the paddy fields one week before admission. On admission, neurologic examination revealed bilateral sixth, ninth and tenth cranial nerve

palsies; bilateral gaze evoked nystagmus, anarthria and quadriparesis. Muscle power was decreased in all four limbs (grade 3/5). Hyperesthesia was detected for all sensory modalities below C4. The plantar response was extensor both sides. There was a 15 × 10 mm eschar on the left scrotal region (Figure 1). His white blood cell count was  $12.1 \times 10^9/L$  and neutrophils  $8.1 \times 10^9/L$ . Cerebrospinal fluid (CSF) analysis showed elevated protein content (0.53 g/L), normal sugar level, white cell



Figure 1. An ecchymotic 20 × 15 mm plaque with a 15 × 10 mm scarlet eschar was present on the left scrotal region.

*Address correspondence to:* Chen Wang, Qilin Ma and Yihong Zhan, Department of Neurology, The First Affiliated Hospital, School of Medicine, Xiamen University, Zhenhai Road No.55, Siming District, Xiamen, 361003, Fujian, China. E-mail: wangchen1986xm@163.com (C. Wang), qilinma@yeah.net (Q. Ma), and yihongzhan@163.com (Y.H. Zhan).

counts  $17 \times 10^6$  cells/L with 88.2% lymphocytes and 11.8% neutrophils. Immunofluorescent antibody test of CSF and serum samples revealed *Orientia tsutsugamushi* IgG antibody titers of 1:380 and 1:3,140. The findings of the rest of the physical examination and laboratory tests were normal.

MRI brain and spine demonstrated T2 hyperintense lesions in the frontal cortex, corona radiata, thalamus, pons, medulla oblongata, cervical and thoracic spinal cord (Figure 2). The hyperintense lesions in the medulla oblongata were mainly located in the mid and dorsolateral

regions, and the spinal cord lesions mainly involved the central gray matter.

The patient was treated with chloramphenicol (500 mg/d) and tapering doses of prednisolone (120-80-40 mg/d) for 17 days. After the treatment, he was alert and could walk with assistance. The anarthria, dysphagia, sensory symptoms have all improved, and his motor power of both upper and lower extremities recovered to grade 5/5. The follow-up T2-weighted MRIs showed the abnormal hyperintensities has reduced.

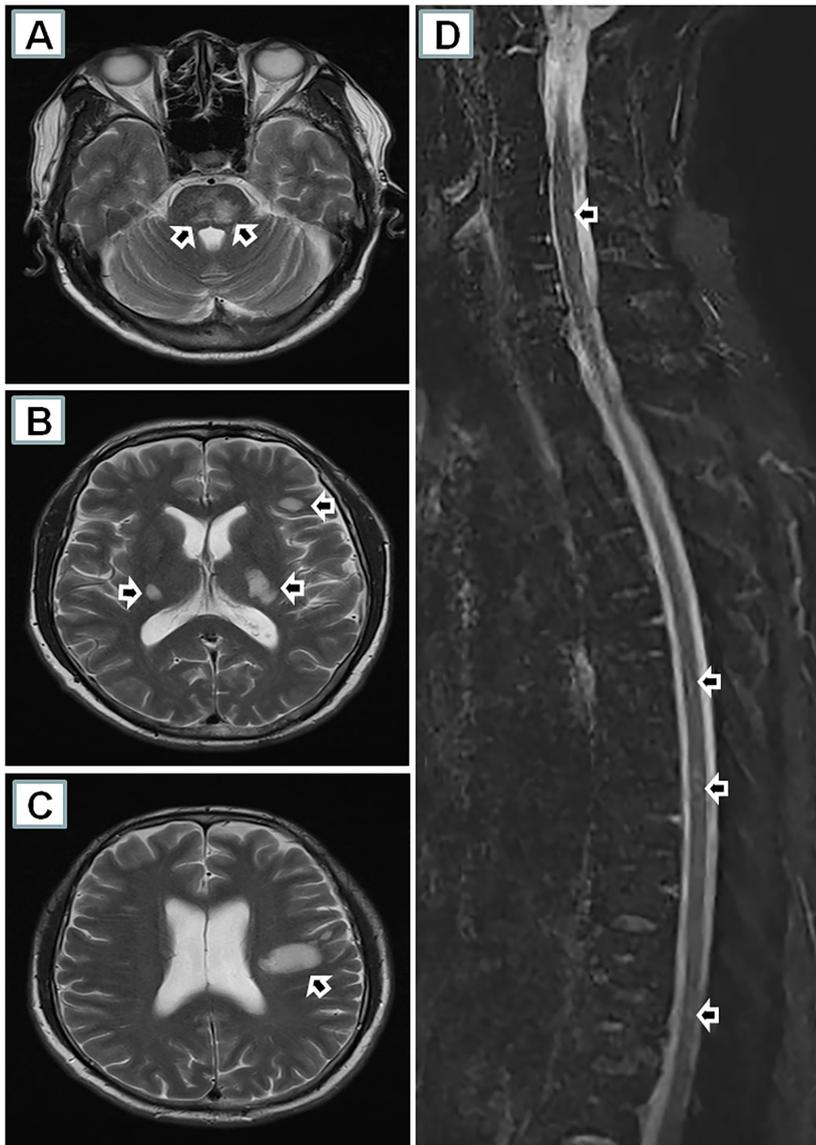


Figure 2. Neuroimaging obtained four days after symptom onset of acute disseminated encephalomyelitis caused by scrub typhus. (A, D) T2 weighted magnetic resonance images (MRIs) show abnormal high signal intensities within the brainstem, cervical and thoracic spinal cord (arrows). (B, C) T2 weighted MRIs show abnormal high signal intensities of basal ganglia, frontal and corona radiata (arrows).

## DISCUSSION

In our patient, the systemic symptoms in the presence of eschar with raised *Orientia tsutsugamushi* antibody titers support the diagnosis of scrub typhus. The diagnosis of typhus was also alerted by the recent travel and work in the region endemic of typhus in the southern part of the Fujian province. Scrub typhus is a zoonosis caused by *Orientia tsutsugamushi*, which is increasingly recognized as an important cause of bacterial infection in Asia with an estimated one million infections occurring each year.<sup>2</sup> Non-specific clinical manifestations of this disease and limited access to health care mean that many patients are undiagnosed and untreated, and the true burden of the infection, including morbidity and mortality rate, remains unknown. The presence of an eschar is a useful sign to support the diagnosis. However, the serology test is particularly important in patients who do not present with an eschar.

Scrub typhus is commonly associated with an acute inflammation of the vascular endothelial lining, vascular wall and perivascular tissue, with resultant hemorrhage and even intravascular coagulation. Other than the common systemic symptoms of fever, myalgia, headache, gastrointestinal dysfunction, myocarditis, lymphadenopathy, skin rash and respiratory symptoms; in recent studies, meningitis, meningoencephalitis, encephalitis, encephalopathy, and seizure were common central nervous system (CNS) manifestations, together with stroke as rare manifestation. In addition, some rare immune mediated neurological manifestations such as optic neuritis, myelitis, mononeuritis multiplex, brachial plexopathy, Guillain-Barre syndrome and acute disseminated encephalomyelitis (ADEM) have also been described.<sup>3,4</sup> In our patient, the clinical presentation of quadriparesis, rapidly progressive bulbar paralysis, MRI changes and good outcome following the use of antibiotics and steroid fit the diagnosis of ADEM, although the short latency of 3 days from fever to onset of neurological symptoms was atypical. We thought the alternative pathology of vasculitis was less likely. ADEM has also been associated with other infection caused by viruses, bacteria and other pathogens, including mycoplasma<sup>5</sup>, which is also known as postinfectious encephalitis.

In summary, we describe a patient with encephalomyelitis associated with scrub typhus.

## ACKNOWLEDGMENTS

We thank the Department of Radiology of the First Affiliated Hospital of Xiamen University to supply the MR images. This work was supported by the Natural Science Fund of Fujian province (2019J01576) and Young Scholars Fund of The First Affiliated Hospital of Xiamen University (XYY2016015).

## REFERENCES

1. Watt G, Parola P. Scrub typhus and tropical rickettsioses. *Curr Opin Infect Dis* 2003; 16:429-36.
2. Taylor AJ, Paris DH, Newton PN. A systematic review of mortality from untreated scrub typhus (*Orientia tsutsugamushi*). *PLoS Negl Trop Dis* 2015; 9:e0003971.
3. Nam TS, Choi SM, Park KH, Kim MK, Cho KH. Opsoclonus associated with scrub typhus. *Neurology* 2010; 74:1925.
4. Misra UK, Kalita J, Mani VE. Neurological manifestations of scrub typhus. *J Neurol Neurosurg Psychiatry* 2015; 86:761-6.
5. Pohl D, Alper G, Van Haren K, et al. Acute disseminated encephalomyelitis: Updates on an inflammatory CNS syndrome. *Neurology* 2016; 87:S38-45.