

# Unusual neurological manifestations of scrub typhus

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Scrub typhus is a zoonotic disease caused by *Orientia tsutsugamushi* (Rickettsia family) and is transmitted by the bite of Trombiculid mites. *O. tsutsugamushi* invades endothelial cells to produce disseminated vasculitic<sup>1</sup> and perivascular inflammatory lesions, which results in significant vascular leakage and ensuing end-organ injury of various organs such as the lung, heart, and kidney.<sup>2</sup> The central nervous system findings in the affected patients include a focal or diffuse mononuclear cell exudate in the leptomeninges and typhus nodules (clusters of microglial cells) that are spread throughout the brain.<sup>3</sup> Eschars are the characteristic skin lesions of scrub typhus. They lead to the production of several cytokines such as granulocyte-macrophage colony stimulating factor, tumor necrosis factor  $\alpha$ , and interferon  $\gamma$ . Both the cytotoxic T lymphocytes and the natural killer T cells play a major role in the destruction of infected host cells.

During the 1960s and 1970s, scrub typhus was endemic in many parts of India. However, with the widespread use of insecticides in the later years, it was almost completely eradicated in our country. In recent years, a resurgence and re-emergence of the disease have been noted.<sup>4</sup>

A 55-year-old woman from Burdwan, India, presented with high fever for 12 days, vomiting for 10 days, and progressive gradual deterioration of consciousness for 7 days. On examination, the patient was found to be drowsy with a Glasgow Coma Scale score of 12 out of 15, and meningeal signs were present. Eye examination showed multiaxial, involuntary, saccadic movements of both eyes, suggestive of opsoclonus. There was no limitation of voluntary eye movements, with a full range of uniocular and conjugate eye movements. The patient was unable to maintain tongue in protruded state and the tongue moved in and out, suggestive of tongue dyskinesia. The rest of the cranial nerves examination was normal. The respiratory system

examination revealed bilateral diffuse crepitations throughout both lung fields.

Cerebrospinal fluid study and magnetic resonance imaging of the brain were done. Antibiotics and antivirals targeting meningitis were started empirically. Cerebrospinal fluid showed 10 cells/mm<sup>3</sup>, of which 80% were lymphocytes and 20% were polymorphonuclear neutrophils. Cerebrospinal fluid contained a protein concentration of 48 mg/dl and a glucose concentration of 53 mg/dl. Adenosine deaminase, polymerase chain reaction for the detection of *Mycobacterium tuberculosis*, herpes simplex virus, and Japanese encephalitis virus were all negative. Magnetic resonance imaging findings were also unremarkable.

While the complete blood count revealed neutrophilic leukocytosis, the liver function tests showed increased conjugated bilirubin and raised alanine transaminase and aspartate aminotransferase levels. The alanine transaminase levels were greater than aspartate aminotransferase. Chest X-ray showed bilateral diffuse areas of reticulonodular opacities (FIGURE 1A), and ultrasonography of the abdomen revealed hepatosplenomegaly. High-resolution computed tomography of the thorax showed bilateral ground-glass opacities (FIGURE 1B). All tests to rule out Dengue fever (NS<sub>1</sub> antigen and dengue IgM), malaria, and enteric fever (typhidot IgM) were negative. Further tests were done to investigate the cause, which ultimately revealed scrub typhus IgM to be positive.

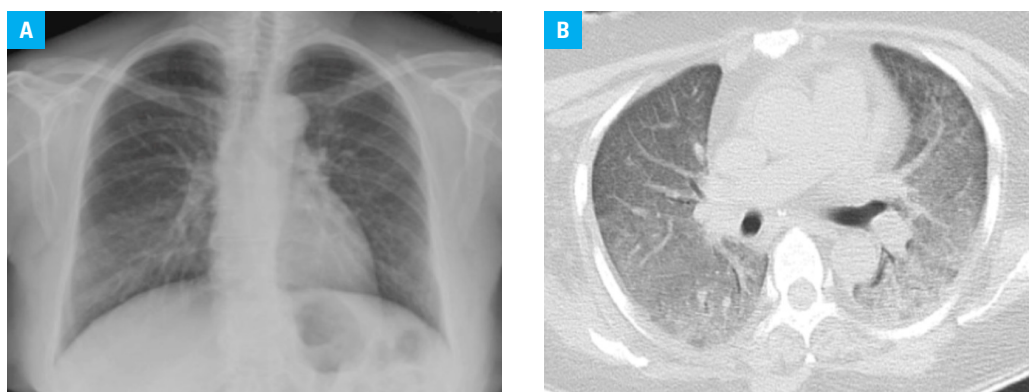
The patient was started on doxycycline 100 mg twice daily for 15 days after which she gradually recovered and was discharged on day 26 of admission.

Opsoclonus is characterized by rapid, involuntary, multivectorial, unpredictable, conjugate fast eye movements without intersaccadic intervals. It is also referred to as saccadomania or reflexive saccade. The potential causes of these symptoms may be parainfectious brainstem encephalitis. The most probable cause of opsoclonus in this case is the immune-mediated disinhibition

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**FIGURE 1** **A** – chest X-ray showing bilateral diffuse areas of reticulonodular opacities; **B** – high-resolution computed tomography of the thorax showing bilateral ground-glass opacities



of the fastigial nucleus of the cerebellum.<sup>5</sup> Opsoclonus is a rare neurological manifestation in scrub typhus, usually occurring in association with myoclonus, cerebellar dysfunction, or extra pyramidal symptoms.

Tongue dyskinesia, in our case, is believed to be due to the involvement of the neurotransmitter dopamine and the immune-mediated inhibition of its receptors.

Serological investigations are essential to establish a diagnosis of scrub typhus. Although the Weil-Felix OX-K test is cost-effective, it lacks sensitivity and specificity. The scrub typhus IgM is an ELISA test which may be used instead.

In our case, the patient was diagnosed as having scrub typhus with meningoencephalitis and involvement of the lungs, specifically, the alveoli. Treatment with doxycycline allowed prompt recovery of our patient.

## ARTICLE INFORMATION

**NOTE** This paper won the 1st award at the 2021 Best Case Report Contest; MIRCIM, June 18, 2021.

**CONFLICT OF INTEREST** None declared.

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