Cerebral venous sinus thrombosis in scrub typhus infection: A rare presentation

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Received - 30 October 2018 Initial Review - 17 November 2018 Accepted - 31 December 2018

ABSTRACT

Scrub typhus is an acute febrile infectious illness caused by Rickettsia species Orientia tsutsugamushi. Scrub typhus has diverse clinical manifestations ranging from a non-specific febrile illness to severe multiorgan dysfunction. A spectrum of neurological complications in scrub typhus includes aseptic meningitis, meningoencephalitis, cerebellitis, myelitis, cerebral hemorrhage, and cerebral infarction. This report describes the case of a scrub typhus with cerebral venous sinus thrombosis, an unreported complication of scrub typhus to the best of our knowledge.

Key words: Cerebral venous thrombosis, Endothelial damage, Scrub typhus

Rickettsial diseases are prevalent worldwide, but maximum prevalence is found in countries of the Asian-Pacific region. Scrub typhus or “tsutsugamushi disease” is a life-threatening zoonotic disease caused by Orientia tsutsugamushi which is an obligate intracellular, Gram-negative bacteria [1]. Scrub typhus is transmitted by the bite of the larval “chigger” of the trombiculid mite which is the reservoir as well as the vector of the disease. On bite, a characteristic eschar is found in 40–50% cases [2]. O. tsutsugamushi invades the central nervous system (CNS) as a part of systemic infection and is found in the endothelial cell of the blood vessel and in circulating phagocytes.

The clinical picture of scrub typhus is associated with fever, rash, myalgia, and diffuse lymphadenopathy but typically not found in all patients. Reported severe clinical manifestations or complications of scrub typhus include interstitial pneumonia, acute renal failure, meningoencephalitis, gastrointestinal bleeding, multiple organ failure, and typical CNS manifestations such as a headache, meningitis, meningoencephalitis, cerebellitis, seizures, and altered sensorium. However, isolated involvement of cerebral venous sinuses is rare [3]. We report a rare case of a scrub typhus with cerebral venous sinus thrombosis (CVT) as an unreported complication of scrub typhus.

CASE REPORT

A 17-year-old young male admitted in the neurology department with complaints of throbbing headache, high-grade fever and periorbital pain for 15 days. There was no history of vision difficulty. On examination, no focal neurological deficit was present, and general physical examination was unremarkable. Fundus examination was also normal and vitals were stable.

Hematological analysis showed an increased leukocyte count ($22 \times 10^9$ cells/mm$^3$), hemoglobin 12.8 g%, serum bilirubin 0.8 mg/dl, serum urea 34 mg/dl, serum creatinine 1.1 mg/dl, and international normalized ratio (INR) was 1.13. Ultrasound abdomen showed mild hepatomegaly. Liver function test and renal function test were normal. IgM antibody was positive for scrub typhus by enzyme-linked immunosorbent assay method. Antinuclear antigen was 12.5 units, antiphospholipid antigen was negative, Vitamin B12 level was 296 pg/ml, and homocysteine was 15.2 units. Magnetic resonance venogram brain showed acute thrombus in the superior sagittal sinus, T2W, and fluid-attenuated inversion recovery images of magnetic resonance imaging brain showed white matter edema in the bilateral high frontoparietal region (Figs. 1 and 2).

The patient was managed with doxycycline 100 mg BD for 7 days and azithromycin 500 mg OD for 5 days along with subcutaneous low-molecular-weight heparin and nicoumalone. After a few days, targeted INR was achieved, the condition of the patient was improved and his headache along with fever was significantly reduced. On follow-up, the patient headache resolved and baseline INR maintained.

DISCUSSION

Scrub typhus is a tropical disease caused by O. tsutsugamushi which enters the CNS by an invasion of endothelial cells in the blood vessels. Cytokines are released by acutely inflamed vascular endothelial cells secondary to the invasion which damages endothelial integrity causing fluid leakage. There is localized platelet aggregation, polymorphs, and monocyte proliferation, leading to focal occlusive and angiitis causing microinfarcts in various tissues. This localized process can also cause venous thrombosis and peripheral gangrene [4-6].

The most commonly reported neurological manifestation of scrub typhus meningoencephalitis [7]. A study was done by Misra...
et al., in 2012, found meningoencephalitis as the most common presentation of scrub typhus [2].

A study done in Korea evaluated 89 patients with severe complications and 119 without severe complications due to scrub typhus [3]. In the group with severe scrub typhus, 23 (11.3%) patients had meningoencephalitis [3]. Rana et al. conducted a study on 323 patients from 2013 to 2014 also found meningoencephalitis as the most common symptom in CNS manifestations of scrub typhus patients [8]. One case report published from Manipal Hospital found scrub typhus as a cause of cerebellitis [5]. An occurrence of CVT is rare in scrub typhus, only one case reported from CMC, Vellore [9]. We excluded other causative factors by investigations and postulated that venous stasis and hypercoagulability due to extensive endothelial damage caused by O. tsutsugamushi could be responsible for CVT.

**CONCLUSION**

This case highlights the significance of rare presentation/association of scrub typhus with CVT. Early search and prompt management of scrub typhus and CVT may be rewarding since scrub typhus is a treatable disease and so is CVT.

**REFERENCES**