

Case Report**Splenic infarction secondary to probable scrub typhus**

A Mathur, S Srivastava, A Mishra

*Sri Lankan Journal of Infectious Diseases 2023 Vol.13(2): E43:1-7*DOI: <https://10.4038/sljid.v13i2.8568>**Abstract**

A mite-borne infection, scrub typhus is endemic in India. It causes a myriad of complications with multisystemic involvement like meningoencephalitis, acute respiratory distress syndrome (ARDS), myocarditis and is also known to cause abdominal complications like hepatomegaly, gastrointestinal haemorrhage, acute pancreatitis, and acute renal failure. Among the abdominal organs, splenic involvement is considered to be very rare and the usual presentation in such cases is splenomegaly. Splenic infarcts are a lesser known complication of scrub typhus which has been sparsely reported in the literature. We report a case with a rare presentation of scrub typhus in a 39-year-old male who reported to our hospital with fever and gastrointestinal system related complaints and was ultimately diagnosed to have multiple splenic infarcts secondary to scrub typhus.


Keywords: *Scrub typhus, splenic infarct, scrub typhus IgM antibody*

Introduction

Scrub typhus is a vector borne disease caused by *Orientia tsutsugamushi* and is transmitted by a bite of a trombiculid mite. It has a high case fatality rate with a global burden of about a million cases reported annually.¹ Historically, the endemicity was believed to be limited to the “Tsutsugamushi triangle” which represented an extensive area of Asia-Pacific that includes Korea and far east Russia in the north, northern Australia in the south and Afghanistan-Pakistan in the west which further extends to include islands of the western pacific oceans such as Japan, Philippines, Indonesia, Indian subcontinent and Sri Lanka. There is growing evidence that the disease may not be restricted to the Tsutsugamushi triangle, with cases being reported from Eastern Africa. The analysis of sero-epidemiological data has suggested that the seroprevalence of *Orientia tsutsugamushi* infection across Asia ranges from 9.3% to 27.9%. It is prevalent in the Indian subcontinent and accounts for 30%–40% hospitalisations for undifferentiated fever.² The disease can show multisystemic involvement with complications including meningoencephalitis, acute respiratory distress syndrome, and myocarditis. It can also involve abdominal organs like the liver, gall bladder, pancreas, and kidneys. Scrub typhus has a mean incubation period of 10 to 12 days and usually presents with sudden onset fever with chills and headache, generalised body aches and lymphadenopathy. An eschar at the site of the chigger bite is also seen often in association with the febrile illness. Common laboratory indicators are

Command Hospital Udhampur, India

Address for correspondence: Dr Abhishek Mishra, Radiologist, Command Hospital Udhampur, India

Email: zoom.honey@gmail.com: Telephone: +919674913117  <https://orcid.org/0000 0002 8434 426X>

Received 27 January 2023 and revised version accepted 29 June 2023. Published on 25.8.23



This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

thrombocytopenia, elevated liver enzymes and leucocytosis. Serological assays are the main diagnostic tool and consist of the Weil-Felix test, an indirect immunofluorescence assay (IFA), enzyme-linked immunosorbent assays (ELISA) and rapid diagnostic assays.

Case report

A 39-year-old male with no previous history of any significant medical comorbidity reported to the medical division of this hospital with low to moderate grade continuous fever without any chills or rigors and loss of appetite for one week. He also complained of nausea, vomiting, loose stools and pain in the epigastrium and left hypochondrium and non-productive cough for the previous two days. There was no complaint of yellow discolouration of eyes or urine, no dysuria, no skin rashes, or any cutaneous eschar. There was no history of a recent blood transfusion. Clinical examination findings along with vital parameters at the time of admission are given in Table 1.

Table 1: Detailed systemic and local examination

Systemic examination	Abdomen	Liver and spleen palpable four cm below the costal margin, spleen was firm on palpation and not crossing the midline. Abdomen was soft and non-tender
	Cardiovascular system	First and second heart sounds heard, no cardiac murmurs
	Central nervous system	No abnormality detected
	Respiratory system	Fine basal crackles (+) bilaterally
Local examination	No cutaneous eschar No pallor, cyanosis, clubbing, icterus, oedema on feet, venous engorgement of neck vein, or yellowish discolouration of eyes	
Vital parameters	Blood pressure: 90/59 mm Hg bedside Respiratory rate: 22/min Temperature: 98.4 °F SpO ₂ : 100% at room air	

A baseline electrocardiogram (ECG) was normal. He was admitted and haematological and biochemical workup was requested. The lab parameters and radiological investigations during the hospital stay are given in Table 2a and 2b.

With these results, the patient was started on medical management for suspected enteric fever with IV ceftriaxone alone, IV fluids, antiemetics and antipyretics. A repeat per abdomen clinical examination showed liver and spleen palpable four fingers below the costal margin and spleen appearing firm on palpation. An ultrasound of abdomen on fourth day of admission reported liver (16.8cm right lobe cranio-caudally) and spleen (15cm) to be enlarged with multiple bizarre geographical pattern hypoechoic lesions in peripheral splenic parenchyma, largest measuring about 30 x 17mm in the inferior pole, thought to be either splenic infarcts or abscesses.

Table 2a: Laboratory investigations

Relevant laboratory investigations		Results
Haematology	Haemoglobin	13.7 gm %
	Total leucocyte count	9.7 cells/m ²
	Neutrophils	80%
	Lymphocytes	16%
	Platelet count	1x10 ⁵ cells/ul
Liver function tests	Serum bilirubin	0.46mg%
	AST	384 IU/L
	ALT	319 IU/L
	ALP	389 IU/L
Coagulation profile	Prothombin time	14 Sec
	PT/INR-	1.00(14/14)
	d-dimer	>10,000ng/ml
Serum biochemistry	Blood urea	52mg/dl
	Serum creatinine	1.3 mg/dl
Acute phase reactants	C reactive protein	8.2mg/dl
	Erythrocyte sedimentation rate (ESR)	28mm/hour
Serology	Dengue	Negative
	HIV	Negative
	Anti HCV	Negative
	HBs Ag	Negative
	Scrub typhus rapid test for IgM and IgG antibodies to <i>Orientiatsutsugamushi</i> (Immunochromatography based) (sample was sent on 8 th day of admission)	Detection of IgM antibodies
Urine routine and microscopy		Protein (1+)
Peripheral blood smear for malarial parasite		Negative
Blood and stool culture		Sterile

Table 2b: Radiological investigations

Chest Radiograph (Erect)	Normal
Ultrasonography - Abdomen <i>(4th day of admission)</i>	Hepatomegaly (Right lobe 16.8cm cranio-caudally) Splenomegaly (15cm) with multiple bizarre geographic hypoechoic lesions in peripheral splenic parenchyma, thought to be either splenic infarcts or abscesses.
Computed tomographic pulmonary angiogram (CTPA) Contrast enhanced computed tomography of abdomen(CECT) <i>(8th day of admission)</i>	Negative for pulmonary thrombo-embolism (PTE) Hepatosplenomegaly with peripheral wedge shaped non-enhancing intraparenchymal splenic lesions, likely infarcts. No focal hepatic lesions were seen. The pancreas and kidneys were also normal. No mesenteric or retroperitoneal lymphadenopathy was noted. The small and large bowel loops and ileo-cecal junction were reported as normal. No ascites was reported
Repeat Ultrasonography of Abdomen <i>(14th day of admission)</i>	Hepatosplenomegaly regressed.

¹ (CTPA: computed tomographic pulmonary angiogram, PTE: pulmonary thromboembolism, CECT: contrast enhanced computed tomography)

On the seventh day of admission, he developed high grade fever (103.6 °F) without chills or rigors. He also had sinus tachycardia (116 beats per minute).

On the next day he developed difficulty in breathing with a respiratory rate of 24-26 per minute. Keeping in view of sinus tachycardia and difficulty in breathing, an urgent d-dimer test was requested which reported as >10,000 ng/ml. A computed tomography of pulmonary arteries (CTPA) and contrast enhanced computed tomography (CECT) of abdomen was requested to rule out pulmonary thrombo-embolism and to further investigate the nature of splenic lesions. The CTPA was negative for pulmonary thromboembolism. However, it revealed subtle patchy asymmetric ground glass opacities in peripheries of basal zones. No pulmonary infarcts were noted in the CTPA. In CECT abdomen, the liver (17.3cm right lobe cranio-caudally mid clavicular line) and spleen (splenic index: 1310cm³) were enlarged with multiple intraparenchymal peripheral non-enhancing wedge shaped hypodense lesions in the splenic parenchyma, the largest measuring about 3.4 x 1.9cm near its inferior pole. The intervening splenic parenchyma was normal with no evidence of an abscess. The splenic lesions were characterized as infarcts in the CECT of abdomen (**Figure 1A&B**).

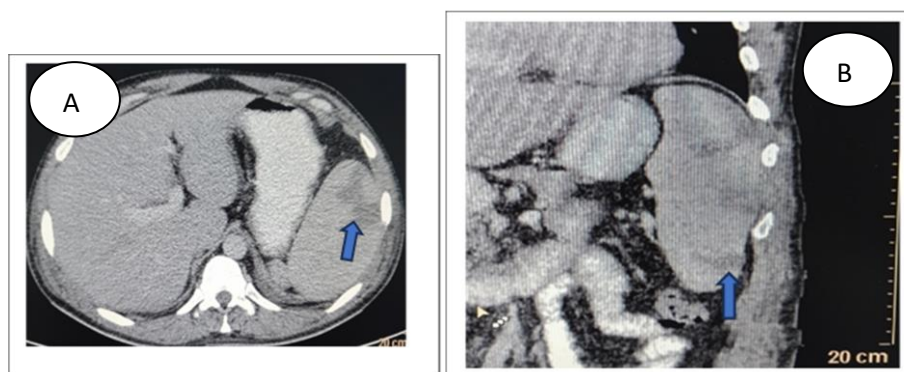


Figure 1 A & B: CECT Abdomen axial and coronal sections show non-enhancing peripheral wedge shaped intraparenchymal lesions. (blue vertical up arrows) in spleen suggestive of infarcts.

The possibility of the patient developing acute respiratory distress syndrome and with splenic infarcts in the CECT abdomen, an alternative diagnosis was explored and a serological evaluation for scrub typhus was requested on the eighth day of admission and doxycycline was added for the first time and continued for the next two weeks. On the ninth day of admission, a qualitative serological assay for detection of IgG and IgM antibodies to *Orientia tsutsugamushi*, detected IgM antibodies by immunochromatography (ICT) based card test. The card test was an invitro rapid diagnostic test with the make number labelled as REF SRTS010 SCRUB TYPHUS RAPID TEST.

A possibility of infective endocarditis was excluded clinically since there was no previous history of any medical comorbidity in particular valvular heart disease, his baseline ECG at the time of admission was normal and no abnormal heart sounds or any cardiac murmur was appreciated in a detailed systematic examination by the cardiologist.

Thus, a clinical diagnosis of scrub typhus with splenic infarcts was made. The patient was continued on doxycycline. On the fourteenth day of admission, after taking oral doxycycline for seven days, the patient became afebrile, and his appetite further improved. A repeat ultrasound of abdomen on the same day showed regression in hepatic and splenic enlargement. No significant changes in the size of the splenic parenchymal lesions were noted and these lesions had assumed a more heterogeneous sonological appearance by then. The largest of these

lesions measured 26 x 14mm in the repeated scan. The hepatic (16cm right lobe cranio-caudally) and splenic (14cm) enlargement also regressed.

He was discharged home in a comfortable state after three weeks of hospital stay after completing a two week course of oral doxycycline. His vitals were normal, and he was feeding normally at the time of discharge with complete resolution of his abdominal complaints nausea, vomiting and loose stools, that might have occurred as a result of peritoneal irritation.

Figure 2 shows the timeline of his disease.

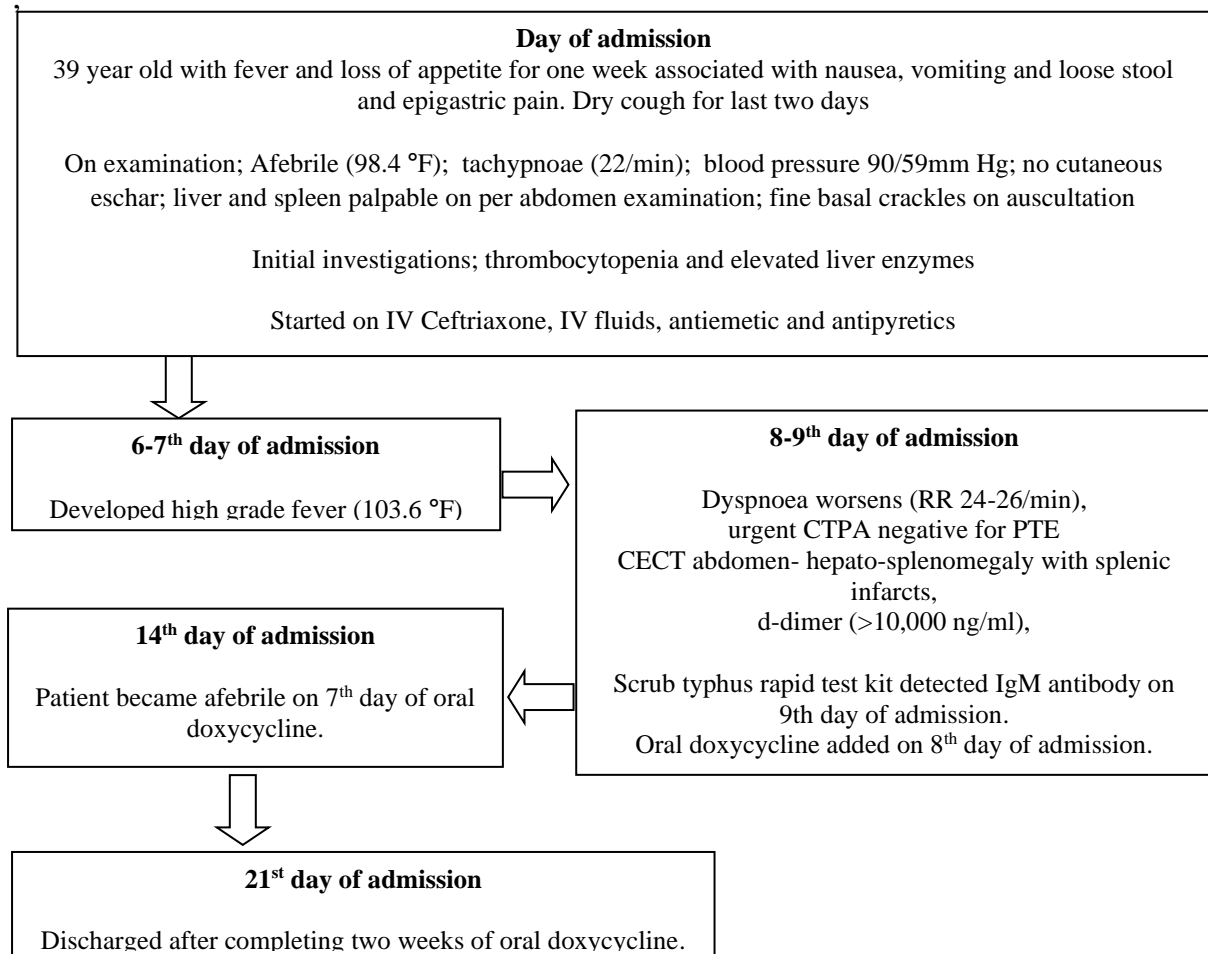


Figure 2: Timeline of infection during the hospital stay.

Discussion

Scrub typhus is a vector borne disease caused by the Gram negative bacillus *Orientia tsutsugamushi* and is transmitted by a bite of the trombiculid mite. It was reported first in China in 313 AD. It is geographically distributed across tropical and subtropical countries like India, Pakistan, Sri Lanka, Indonesia, and Japan. If misdiagnosed and not treated timely it can lead to fatal outcomes due to multi-organ failure.³

The standard line of management is treatment with a course of antibiotics such as doxycycline or azithromycin.⁴ The disease shows a predisposition for pulmonary involvement and usually

presents with interstitial pneumonia. The abdominal involvement is usually manifested as organomegaly, acute renal failure, acute pancreatitis and gastrointestinal bleeding and such patients usually present with abdominal complaints like nausea, vomiting, loose stools, and gastrointestinal bleeding in association with fever. These abdominal complaints can be seen in about 1/4th of patients.³ The understood pathogenetic mechanism is vasculitis and perivasculitis in most of the associated complications of scrub typhus. Corresponding to this pathologic finding, haemorrhage, and infarction in various organs such as atraumatic haemoperitoneum⁵, gastrointestinal tract bleeding⁶ and cerebral haemorrhage and infarctions have been reported.^{7,8} The underlying pathogenetic mechanism is understood to be disseminated or focal gastrointestinal vasculitis with phagocytic invasion of the endothelial cells occurring as an immune response of the body to the rickettsial antigen(s). Splenic infarction in scrub typhus is attributed to compromised vascular supply, which also points towards vasculitis as the underlying pathophysiology.⁹

Since the clinical features may overlap with other febrile illnesses like dengue, typhoid fever, leptospirosis, and murine typhus, in the absence of a classical eschar it is difficult to obtain a correct diagnosis clinically. Laboratory examinations are more reliable and accurate, and diagnosis is obtained either through direct isolation and culture of the bacterium in cell lines like L929, Hela cells or BHK21 or using genetic markers for DNA diagnosis through the polymerase chain reaction. Indirect methods of diagnosis based on serological assay include the Weil Felix test, enzyme linked immunosorbent assays (ELISA), immunofluorescence assays (IFA) and rapid diagnostic assays. Diagnostic imaging findings are variable and non-specific and are more suited for ruling out complications like ARDS, meningo-encephalitis, hepatosplenomegaly, pancreatitis, acute renal failure and lymphadenopathy.

Take home message:

Scrub typhus if not diagnosed timely may potentially lead to fatal outcomes because of the multisystemic nature of involvement. A thorough physical examination for eschar and high index of suspicion in cases with pyrexia of unknown origin is recommended for timely diagnosis with confirmatory laboratory findings. Serological assays like ELISA, IFA and rapid diagnostic assays are usually employed for early detection and diagnosis. Splenic involvement is considered rare in patients with scrub typhus and can be picked up by detailed imaging using ultrasonography and computed tomography which is recommended in patients developing features of multiple organ dysfunction and persistent pyrexia without a clear aetiology.

Declarations

Acknowledgement: None

Conflicts of Interest: There were no conflicts of interest.

Funding: No funding and any other support was from any source.

Ethics statement: Ethical approval was not required for this manuscript. The patient's consent was taken to display imaging.

Authors' contributions: All the authors contributed in patient management and preparing manuscript. Dr Ankit Mathur and Dr Sachin Srivastava were actively involved in the manuscript preparation.

References

1. Taylor AJ, Paris DH, Newton PN. A Systematic Review of Mortality from Untreated Scrub Typhus (*Orientia tsutsugamushi*). *PLoS Negl Trop Dis*. 2015; 14;9(8):e0003971. doi: <https://doi.org/10.1371/journal.pntd.0003971> ; *PMCID: PMC4537241*.
2. Devamani CS, Prakash JA, Alexander N et al. Hospitalisations and outpatient visits for undifferentiated fever attributable to scrub typhus in rural south India: retrospective cohort and nested case-control study. *PLoS Negl Trop Dis* 2019; 13:e0007160.

doi: <https://doi.org/10.1371/journal.pntd.0007160>

3. Chrispal A, Boorugu H, Gopinath Ket al. Scrub typhus: An unrecognized threat in South India — Clinical profile and predictors of mortality. *Trop Doct* 2010; 40(3):129–33.
doi: <https://doi.org/10.1258/td.2010.090452>
4. Taylor AJ, Paris DH, Newton PN. A systematic review of mortality from untreated scrub typhus (*Orientia tsutsugamushi*). *PLoS Negl Trop Dis* 2015; 9:e0003971.
doi: <https://doi.org/10.1371/journal.pntd.0003971>
5. Lin WY, Lin GM, Chang FY. An unusual presentation of scrub typhus with atraumatic hemoperitoneum. *Am J Gastroenterol* 2009; 104:1067. doi 10.1038/ajg.2009.8
6. Thap LC, Supanaranond W, Treeprasertsuk S et al. Septic shock secondary to scrub typhus: characteristics and complications. *Southeast Asian J Trop Med Public Health* 2002; 33:780-6.
doi: <https://pubmed.ncbi.nlm.nih.gov/12757226/>
7. Chung JH, Yun NR, Kim DM et al. Scrub typhus and cerebrovascular injury: a phenomenon of delayed treatment? *Am J Trop Med Hyg* 2013; 89:119-22
doi: <https://doi.org/10.4269/ajtmh.13-0094>
8. Kim JH, Lee SA, Ahn TB, et al. Polyneuropathy and cerebral infarction complicating scrub typhus. *J Clin Neurol* 2008; 4:36-9. doi: <https://doi.org/10.3988/jcn.2008.4.1.36>
9. Raj SS, Krishnamoorthy A, Jagannati M et al. Splenic infarct due to scrub typhus. *J Glob Infect Dis* 2014; 6:86-8. doi: <https://doi.org/10.4103%2F0974-777X.132055>