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CASE REPORT **OPEN ACCESS**

Scrub typhus with massive reversible splenomegaly and gastroduodenal ulcers

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A B S T R A C T

Background: Scrub typhus, a zoonotic illness caused by Orientia tsutsugamushi, is a significant cause of acute undifferentiated febrile illness in endemic regions. While hepatosplenomegaly is a common feature, massive splenomegaly and gastrointestinal ulceration are rare.

Case Presentation: We report the case of a young adult male who presented with high-grade fever, jaundice, abdominal pain, hypotension and melena. Examination revealed massive splenomegaly and hepatomegaly. Laboratory findings showed cytopenias, liver dysfunction and acute kidney injury. Imaging confirmed massive splenomegaly, and upper gastrointestinal endoscopy revealed gastric and duodenal ulcers. Extensive workup for common causes of massive splenomegaly, including malaria and leishmaniasis, was negative. Serology for scrub typhus came out positive. The patient was started on doxycycline, resulting in rapid clinical improvement, resolution of organ dysfunction and normalization of spleen size.

Conclusion: Scrub typhus should be considered in the differential diagnosis of fever with massive splenomegaly, especially in endemic areas. When encountering massive splenomegaly, thorough investigation is imperative to determine its cause. Before resorting to invasive procedures, it's crucial to rule out infectious causes. Scrub typhus, for instance, can manifest as fever with reversible massive splenomegaly upon appropriate therapy.

Keywords: Scrub typhus, Infectious disease, Massive splenomegaly, Reversible splenomegaly, Gastrointestinal ulcers **,**India

BACKGROUND

Scrub typhus is an acute febrile zoonotic illness caused by the intracellular pathogen *Orientia tsutsugamushi*. The pathogen is transmitted by the bite of larval mites belonging to the genus Leptotrombidium.[1] Scrub typhus is a common cause of fever of unknown origin in its endemic areas, which are collectively referred to as the Tsutsugamushi triangle. Clinical signs and symptoms of scrub typhus in humans are largely nonspecific and if infection is not treated promptly and appropriately, it carries a high mortality rate.[1]

In our country, patients with scrub typhus usually present with complaints of fever, diffuse lymphadenopathy, myalgia, rash, jaundice, thrombocytopenia, capillary leak syndrome, hepatomegaly and splenomegaly. A black eschar mark at the bite site is pathognomic. The disease can also have severe complications like acute respiratory distress syndrome (ARDS), acute liver failure, acute kidney injury (AKI) and myocarditis.[2] Though some form of hepatosplenomegaly is common, massive splenomegaly is uncommon in these patients.

Mild gastrointestinal symptoms like nausea and vomiting are common in scrub typhus, but there are barely any reports of severe gastrointestinal involvement and ulcer formation. Though uncommon, the vasculitis-like effects of this disease can lead to the formation of ulcers in the gastrointestinal tract, which can even lead to severe life-threatening bleeds in a few cases.[3]

The common infectious causes of massive splenomegaly with fever in our country are malaria and leishmaniasis, with malaria being the most common.[4] This case highlights the need for screening for atypical infections in these patients. This becomes more important as the number of patients presenting with massive splenomegaly due to malaria and leishmaniasis decreases in the wake of effective treatment and a health programme.[5]

CASE PRESENTATION

This case is of a young adult male in his twenties who presented to a tertiary care centre in northern India. He presented with a continuous fever of 101°F associated with chills, progressive yellowing of the skin and sclera, dull aching abdominal pain and malaise since 7 days. He complained of pruritis but denied any history of insect bites. The patient did not have any chronic illnesses. There was no significant family history and no history of weight loss, substance abuse, chronic medication intake or any high-risk behaviour. On examination, he was febrile (100.6°F), had a low volume pulse with tachycardia (126 bpm) and his blood pressure was 74/42 mm Hg. Systemic examination revealed massive splenomegaly, 13 cm below the costal margin, which was firm in consistency with a smooth surface and a palpable notch. Also noted was hepatomegaly, palpable 3 cm below the costal margin and no associated lymphadenopathy or ascites. Cardiac and pulmonary examinations were unremarkable.

Laboratory analysis showed a normocytic normochromic anaemia, neutrophilic leukocytosis and thrombocytopenia. Kidney function and liver function tests were deranged with azotemia and direct hyperbilirubinemia, respectively. Initial screening for malaria by peripheral smear and typhoid fever with IgM antigen was negative. An ultrasound of the hepatobiliary system was performed, which showed hepatosplenomegaly (liver 16.6 cm and spleen 20.3 cm) with normal echotexture of the liver and normal calibre of the portal vein and common bile duct. The chest radiograph was unremarkable. Further investigations for human immunodeficiency virus (HIV), hepatitis B, C, A and E were all negative. Stool for occult blood was done on account of malena and it showed positivity. 2D echocardiography (2D ECHO) revealed normal valves without any vegetations. A contrast-enhanced computed tomography (CECT) scan could not be done due to AKI and therefore a magnetic resonance cholangio-pancreatography (MRCP) was done, which revealed hepatomegaly of 17.8 cm in craniocaudal extent and massive splenomegaly of 21.8 cm in craniocaudal dimension with normal morphology and signal intensity (Figure 1). No focal lesion was noted. The splenic vein dimension near the hilum was 12 mm. A splenoportal doppler was also done and it revealed massive splenomegaly with a dilated splenic vein at the hilum with normal portal vein, hepatic and splenic artery flow. UGIE was done to look for the cause of malena and it showed multiple deep ulcers in the stomach and multiple superficial ulcers in the duodenum with variable sizes and inflammatory exudate visible over them.(Figure 2). A biopsy taken from the ulcers was suggestive of acute gastritis with ulceration; however, no evidence of *Helicobacter pylori* could be detected in these specimens (Figure 3). Blood and urine cultures were repeatedly sterile. A bone marrow aspiration and biopsy were done to look for hemological causes, but they too revealed normally cellular marrow for age without any atypical features. Serological tests were then sent for atypical infections and these came out to be positive for scrub typhus. (Table 1)

The patient was started on broad-spectrum antibiotics at initial presentation along with ionotropic support. Antimalarial therapy was also given. Despite these therapies, symptomatic improvement was absent. On the eighth day of admission, scrub typhus was diagnosed and the patient was started on oral doxycycline (200 mg/day in two divided doses) for a duration of 7 days. After the initiation of doxycycline, the patient improved symptomatically and his fever subsided in 2 days. The patient also had improvement in jaundice with resolution of azotemia and malena. (Table 1) Ultrasonography done on day 8 of the therapy showed a normal hepatobiliary system with a normal splenic size.

DISCUSSION

Scrub typhus is caused by the intracellular gram negative bacterium *Orientia tsutsugamushi*. It is transmitted by the bite of trombiculid mites.[6] This infection is endemic in the Tsutsugamushi triangle, which consists of northern Japan and far eastern Russia in the north, northern Australia in the south and Pakistan in the west.[7] India makes up a large part of this area and its tropical climate provides habitat for the vector. The mite acts both as a reservoir and vector for the bacterium. Classically, the bite from the insect results in the formation of a black eschar at the site; however, it is found in only 14% of patients.[2] Humans are dead-end hosts for the disease and transmission occurs through the bite of the insect with no human-to-human transmission.[1] In India, among patients presenting with acute undifferentiated fever, scrub typhus was found to be the cause in 10.8% of cases.[8] It frequently occurs as seasonal local outbreaks. Though the most common presenting symptoms are high grade fever with chills and rigour (85%), shortness of breath (42%) and

jaundice (32%), serious complications like AKI (32%), ARDS (25%) and multiple organ dysfunction syndrome (20%) are also present. This disease carries with it a high risk of mortality approaching 13.6 percent. The disease typically improves within a day after initiation of treatment with doxycycline, azithromycin or chloramphenicol.[2]

Massive splenomegaly is defined as a spleen palpable 8 cm below the costal margin or more than 1000 grams of drained weight.[9] Massive splenomegaly further narrows down the differentials to myeloproliferative neoplasms, lymphoma, sarcoidosis and infections like malaria and leishmaniasis.[10] Scrub typhus is commonly associated with splenomegaly in 11% of patients but massive splenomegaly is rare but rapidly reversible after treatment. Gastrointestinal ulcers are most commonly caused by *Helicobacter pylori*, chronic NSAID abuse and chronic alcoholism. In this case stress ulcers were also a possibility because of the severity of disease at presentation. They are usually located in fundus and body of the stomach and are mostly limited to the superficial layer. Clinically important GI bleed occurs in 2.6 % of the patients admitted to the intensive care unit. The risk factors for clinically important GI bleeding were three or more coexisting diseases, co-existing liver disease, use of renal replacement therapy, coexisting coagulopathy, acute coagulopathy, use of acid suppressants and higher organ failure score.[11] Acute infective processes leading to gastritis and ulceration are limited and very few reports of it being caused by scrub typhus are available. These can present as hyperaemia, purpura, erosion or ulceration of the gastric wall. These lesions are most commonly located in the antrum and duodenum but can involve any site in the GI tract.[12] The severity of gastric involvement is directly related to the severity of scrub typhus at presentation. The pathogenesis of scrub typhus is best described as disseminated vasculitis and perivasculitis due to infiltration of endothelial cells and the subsequent release of cytokines by the infected cells.[3] This is the cause of the various manifestations of the disease like massive splenomegaly and GI ulcers as seen in this case.

Scrub typhus is becoming an important cause of acute, undifferentiated febrile illness in our country.[8] As effective government programmes are in place for diseases like malaria and other vector-borne diseases, these previously atypical infections are now becoming a major concern. Though India makes up a large part of the Tsutsugamushi triangle, the unique presentation of this case with massive splenomegaly and malena made us consider other diagnoses rather than scrub typhus. In India much of the healthcare is provided by public sector hospitals and many of the patients treated there have financial constraints. The serological tests for scrub typhus are available only at selected centres in the public sector and that too in endemic districts and even fewer have the polymerase chain reaction test. This combined with the time required for transportation and logistics can inadvertently delay the diagnosis and therefore it should be kept as a differential early in the course, especially in cases not responding to initial empirical antibiotic therapy.

CONCLUSION

When encountering massive splenomegaly, thorough investigation is imperative to determine its cause. Before resorting to invasive procedures, it's crucial to rule out infectious causes. Scrub typhus, for instance, can manifest as fever with reversible massive splenomegaly upon appropriate therapy. Additionally, in patients presenting with severe disease, this condition may present with gastrointestinal ulceration and bleeding.

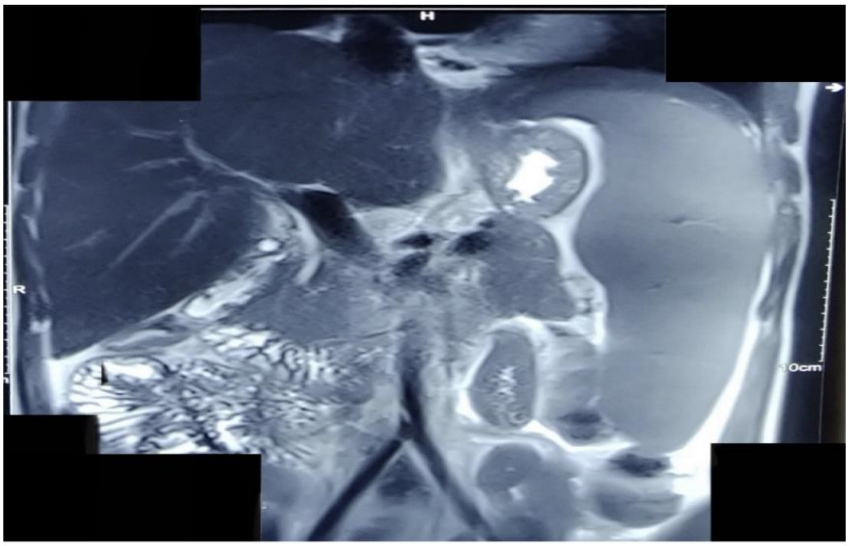

Figure 1) MRCP image showing hepatomegaly with massive splenomegaly

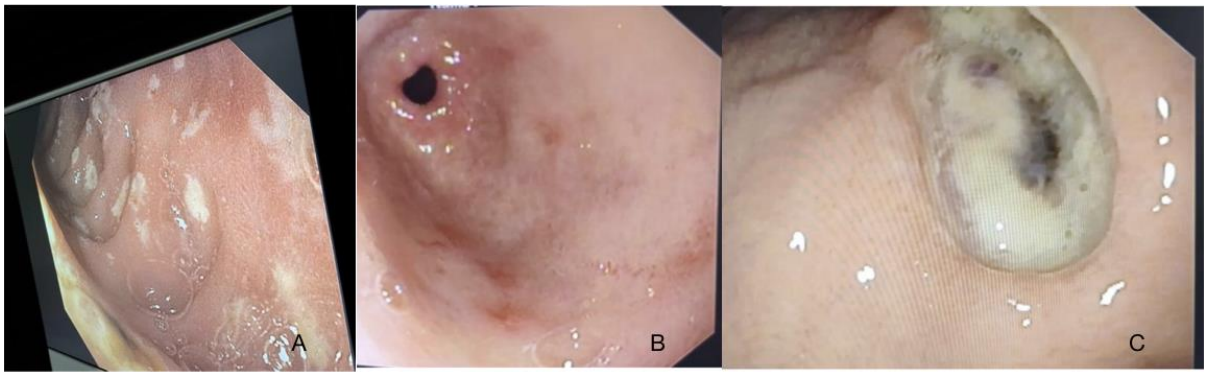

Figure 2) A: Multiple superficial ulcers in the duodenum; B: Diffuse erythema and superficial erosions in the antrum; C: Largest deep ulcer of 15x20 mm with overlying whitish exudate in the body

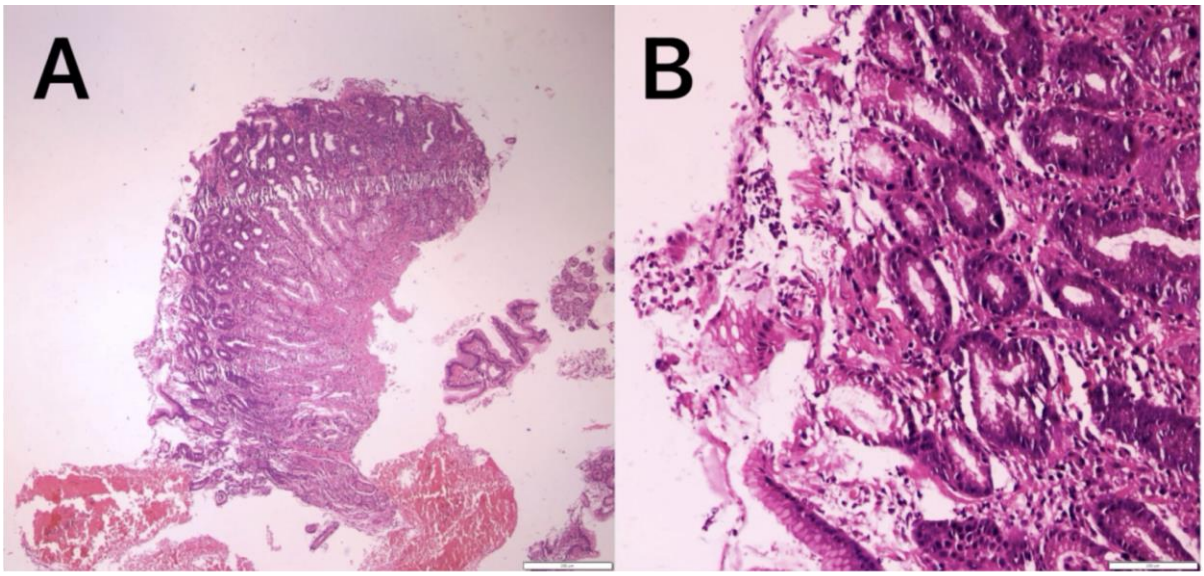

Figure 3) Acute gastritis with ulceration, 10x (A) and 20x (B)

Table 1: Investigations of the patient during hospital stay

On admission		**On 8th day of doxycycline therapy**	
Parameter	**Value**	**Parameter**	**Value**
Hemoglobin (g/dL)	8.1	Hemoglobin (g/dL)	10.1
WBC count (× 10^3/μL)	15450	WBC count (× 10^3/μL)	6400
Platelet count (×10^3/μL)	91(150-350)	Platelet count (×10^3/μL)	165(150-350)
Procalcitonin (ng/ml)	18.2(<0.5)	Procalcitonin (ng/ml)	0.03(<0.5)

Blood Urea(mg/dl)	210(19-43)	Blood Urea(mg/dl)	27(19-43)
Serum creatinine (mg/dL)	2.14(0.66-1.25)	Serum creatinine (mg/dL)	0.5(0.66-1.25)
Total bilirubin (mg/dL)	16.96(0.2-1.3)	Total bilirubin (mg/dL)	1.1(0.2-1.3)
Direct bilirubin (mg/dL)	15.26(0-0.3)	Direct bilirubin (mg/dL)	0.8(0-0.3)
AST(IU/L)	543(17-59)	AST(IU/L)	46(17-59)
ALT(IU/L)	329(5-50)	ALT(IU/L)	38(5-50)
ALP (IU/L)	235(38-126)	ALP (IU/L)	112(38-126)
Additional workup			
Erythrocyte Sedimentation Rate (mm/h)	32	INR	1.06
C-Reactive protein(mg/dL)	85.9(0-5)	LDH (IU/L)	216(120-246)
Indirect Coombs test	Negative	Urine routine microscopy	Normal
Direct Coombs test	Negative	Stool for occult blood	Positive
Malarial antigen (pLDH)	Negative	HIV ELISA	Non-reactive
Peripheral smear for malaria	Negative	Hepatitis B surface antigen	Non-reactive
NS1 and Dengue IgM/IgG	Negative	Hepatitis C antibody	Non-reactive
rk39	Negative	Hepatitis A	Negative
Typhoid IgM/IgG	Negative	Hepatitis E	Negative
Blood culture	Negative	Mantoux	4mm
Urine culture	Negative	Leptospira	Negative
EBV	Negative	Weil Felix test OX2 OX19 OXK	 Negative Negative 1:160
CMV	Negative		
HSV	Negative	Scrub Typhus IgM by IFA	Positive
ECG	Sinus tachycardia		
Bone marrow aspirate	Erythrocyte hyperplasia with megaloblastic reaction. No granuloma, parasite or atypical cell seen		
2D ECHO	Normal echocardiographic study with ejection fraction of 60%.		
Chest X-ray	Bilateral costophrenic angle and lung fields clear. No evidence of cardiomegaly seen.		

UGIE	Esophagus- normal Body- multiple deep ulcers of varying size with largest being 15x20 mm with overlying whitish exudate. Antrum- Diffuse mucosal erythema and superficial erosions D1- multiple superficial ulcers of varying size of 5mm to 10mm with overlying whitish exudate.

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Data availability: Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

REFERENCES

1. Saluja M, Vimlani H, Chittora S, Sen P, Suman C, Galav V, Meena D. Scrub typhus: Epidemiology, clinical presentation, diagnostic approach, and outcomes. Journal, Indian Academy of Clinical Medicine. 2019; 20(1):15-21.
2. Sharma N, Biswal M, Kumar A, Zaman K, Jain S, Bhalla A. Scrub Typhus in a Tertiary Care Hospital in North India. The American Society of Tropical Medicine and Hygiene. 2016; 95(2):447-451.
3. Kim SJ, Chung IK, Chung IS, Song DH, Park SH, Kim HS, Lee MH. The clinical significance of upper gastrointestinal endoscopy in gastrointestinal vasculitis related to scrub typhus. Endoscopy. 2000; 32(12):950-5.
4. Sundaresan JB, Dutta TK, Badrinath S, Jagdish S, Basu D. A hospital-based study of splenomegaly with special reference to the group of indeterminate origin. Journal of the Indian Medical Association. 2008; 106(3):150-2.
5. Rahi M, Sharma A. Malaria control initiatives that have the potential to be gamechangers in India's quest for malaria elimination. The Lancet Regional Health-Southeast Asia. 2022; 2.
6. Sharma P, Kakkar R, Kaore SN, Yadav VK, Sharma R. Geographical distribution, effect of season & life cycle of scrub typhus. Jk Science. 2010; 12(2):63.
7. Xu G, Walker DH, Jupiter D, Melby PC, Arcari CM. A review of the global epidemiology of scrub typhus. PLoS neglected tropical diseases. 2017; 11(11):e0006062.
8. Boda S, Goutham VVN. Clinical spectrum of acute undifferentiated fever - an experience from a tertiary care centre. International Journal of Contemporary Medical Research [IJCMR]. 2019; 6(9).
9. Chapman J, Bansal P, Goyal A, Azevedo AM. Splenomegaly. In: StatPearls. Treasure Island (FL): StatPearls Publishing 2021.
10. Luo EJ, Levitt L. Massive splenomegaly. Hosp Physician. 2008; 44:31-8.
11. Krag M, Perner A, Wetterslev J, Wise MP, Borthwick M, Bendel S, et al. Prevalence and outcome of gastrointestinal bleeding and use of acid suppressants in acutely ill adult intensive care patients. Intensive care medicine. 2015; 41:833-45.
12. Lee J, Kim DM, Yun NR, Kim YD, Park CG, Kim MW. The correlation of endoscopic findings and clinical features in Korean patients with scrub typhus: a cohort study. Plos one. 2016; 11(5):e0155810.