

A study of Scrub typhus vasculitis causing pan-digital gangrene in the ambit of General Medicine: An Unusual Phenomenon

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Abstract

Introduction: Scrub typhus is a mite-borne infectious disease caused by *Orientia Tsutsugamushi*. This disease is mostly seen in cattle grazing people in rural areas and in farmers which forms approximately two-third of all reported cases. Severity of infection varies from mild signs and symptoms to multi organ failure. The chief target of the organism is the vascular endothelium of various organs. There is inflammation in and around the blood vessels that causes endothelial damage resulting in vascular leakage and organ dysfunction.

Case report: A 65yr old female, farmer by occupation was admitted with complain fever, myalgia and headache, subsequently developed gangrene of digits in both hands. We investigated the patient for infectious and non-infectious causes of vasculitis leading to gangrene. Cause of gangrene due to vasculitis as scrub typhus was evidenced by the presence of eschar and positive serology. The patient recovered with antibiotics and her digits were salvaged which was managed conservatively.

Conclusion: While going through various literature reviews it was observed that case reports of gangrene caused by scrub typhus has been rarely reported in Rajasthan and therefore pan-digital gangrene can be considered as an unusual complication of scrub typhus. Hence has to be ruled out in patients presenting with this complication.

Keywords: Pan-digital gangrene, Scrub Typhus, Vasculitis

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I. Introduction:

Scrub typhus, caused by *Orientia Tsutsugamushi*, is transmitted to humans by an arthropod vector of the trombiculidae (mites) family. Scrub typhus, also known as tsutsugamushi disease, is caused by the arthropod borne gram-negative obligately intracellular bacillus *Orientia Tsutsugamushi*. It affects people of all ages including children. Humans are accidental hosts in this zoonotic disease. Mite can serve as both the vector and the reservoir. In India, the presence of scrub typhus and other Rickettsial diseases has been known for several decades. Scrub typhus is grossly under diagnosed in India due to its nonspecific clinical presentation, limited awareness and low index of suspicion among clinicians, and lack of diagnostic facilities.

The incubation period may range from 5 to 21 days. Common symptoms are flu-like symptoms, fever, rash, eschar at the bite site, headache, myalgia, cough, generalized lymphadenopathy, nausea, vomiting, and abdominal pain. Fever and headache are the most common features among scrub typhus patients. The eschar is the single most useful diagnostic clue and is pathognomonic for *O. Tsutsugamushi*.

Scrub typhus is a serious public health problem in the Asia-Pacific area including, but not limited to, Korea, Japan, China, Taiwan, India, Indonesia, Thailand, Sri Lanka, and the Philippines. It threatens one billion people globally, and causes illness in one million people each year.

An eschar at the site of chigger feeding is a classic clinical feature of scrub typhus. It begins as a papule at the site of chigger feeding and then ulcerates and forms a black crust like a skin burn from a cigarette. When present, it occurs prior to the onset of fever and other symptoms. The presence of eschar varies from patients depending on the geographic areas.

Severe complications such as multi organ failure occur in some cases. The severe multi organ manifestations include jaundice, acute renal failure, pneumonitis, acute respiratory distress syndrome (ARDS),

myocarditis, septic shock, meningoencephalitis, pericarditis, and disseminated intravascular coagulation (DIC). The lung is one of the main target organs for *Orientia*, leading to pulmonary complications of variable severity.

The case fatality can be up to 30±70% if no appropriate treatment is received while the median case fatality rate for untreated patients is 6% and for treated patient is 1.4%.

II. Case Report:

A 65 years old female, farmer by occupation presented to the General Medicine OPD with high grade fever with chills for 5 days. Initially she was admitted in a nearby local hospital with no improvement. Within 3 days she noticed blackening of digits of fingers in both hands with decreased sensation. Later she was referred to RNT Medical College Udaipur, for further management.

On examination: She was febrile (102⁰f) and tachypneic with a respiratory rate of 30 per minute. Her pulse rate was 104 per minute and her blood pressure 120/70 mm of Hg. She had an eschar in her left thigh (figure 5). She proceeded with the following investigations as given (tables No. 1 & 2.)

Etiology work up for fever, ARDS and viral parasitic serology was done.

Patient was initially managed with broad spectrum antibiotics – meropenem and azithromycin. After serology report of scrub typhus being positive she was started on doxycycline 100mg BD. On day two of admission blackening of terminal digits of both hands which was rapidly progressive in nature and ultimately developed into dry gangrene over 3 days. (figure 2,3)

However, her peripheral pulses were felt normally. Vasculitis work up like ANA, dsDNA, C-ANCA, P-ANCA, LE-CELL, RA factor, Antiphospholipid antibody, Anticentromere antibody, sickling test were negative. Vascular surgeon's opinion was sought and the patient was started on LMWH and aspirin.

After 6 days of Azithromycin & Doxycycline therapy patient showed gradual improvement in clinical condition and was weaned off from oxygen therapy. Patient developed mild pain in her both upper limb digits near gangrene area.

For the limb digits near gangrene area, she received several analgesics including paracetamol, tramadol. When her platelets increased by 1.05 lakh/cumm, LMWH was given and after the cessation of LMWH, she was further given Aspirin, Pentoxifylline, Cilostazol.

Table No. 1

Hb	10gm/dl
HCT	31.1%
MCV	85.2 fl
MCH	27.2pg
DIFFERENTIAL COUNT	
Neutrophil	68.7%
Lymphocyte	23.6%
Platelet count	10000/ul
Peripheral smear	Normochromic normocytic cells, thrombocytopenia
Urea	62 mg/dl
Creatinine	1.19mg/dl
Total bilirubin	1.0 mg/dl
Direct bilirubin	0.718mg/dl
SGOT	48 U/L
SGPT	57U/L
Total protein	5.7 g/dl
Albumin	2.1g/dl
ALP	157 mg/dl
Calcium	8.3 mg/dl
Cholesterol	112mg/dl
Triglyceride	293mg/dl
HDL	39mg/dl
LDL	26mg/dl
Sodium/Potassium	138/3.5Meq/L

SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamic pyruvic transaminase; ALP : Alkaline phosphatase; HDL: High density lipoprotein; LDL : Low density lipoprotein.

Table No. 2

MP-QBC Antigen	Negative
RT-PCR for H1N1;Throat swab	Negative
Serology for scrub typhus	Positive
IGM Antileptospiral Antibody	Negative
IGM Dengue Antibody	Negative
HIV	Negative
AntiHbs Antigen	Negative
AntiHCV	Negative
Blood culture	No growth
Urine culture	No growth
CSF culture	No growth
ECG	Normal
Echocardiogram	No evidence of IE,EF-65 %
D-DIMER	25.0 ng/mL (0 – 500)
Color doppler study-	Thickened and edematous bilateral upper limb arterial system. ? inflammatory Decreased peak systolic velocity in bilateral distal radial arteries. Long segmental echogenic material in lumen of right & left cephalic vein from mid arm to mid forearm. ? venous thrombosis

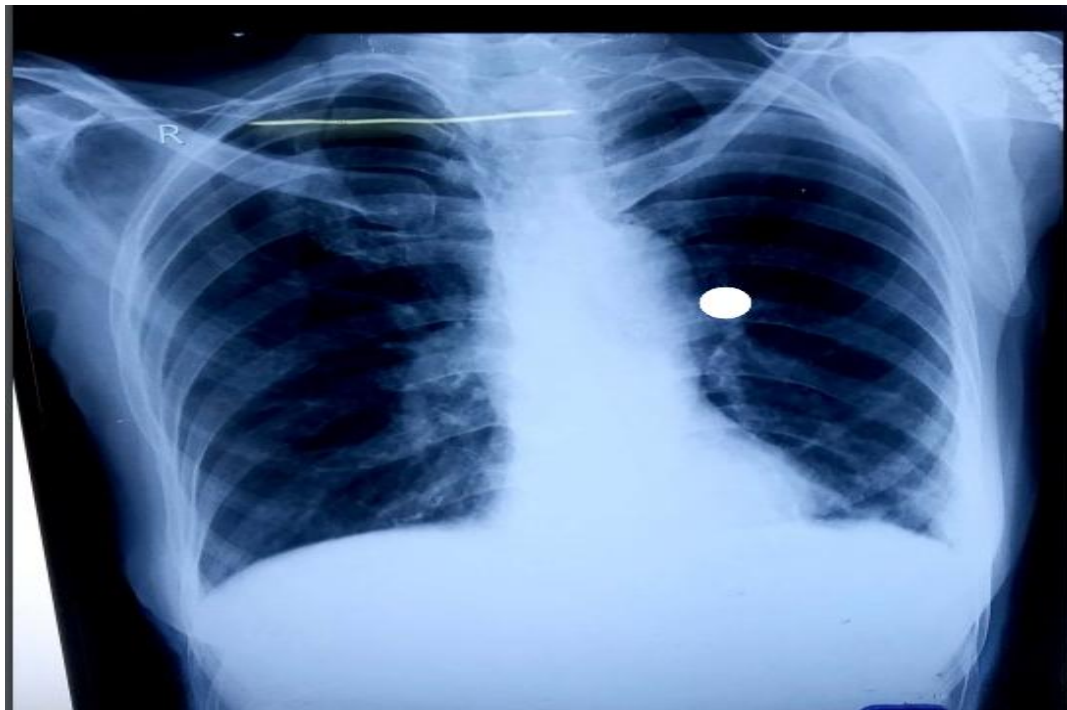


Figure 1 (X-ray PA Chest)



Figure 2



Figure 3

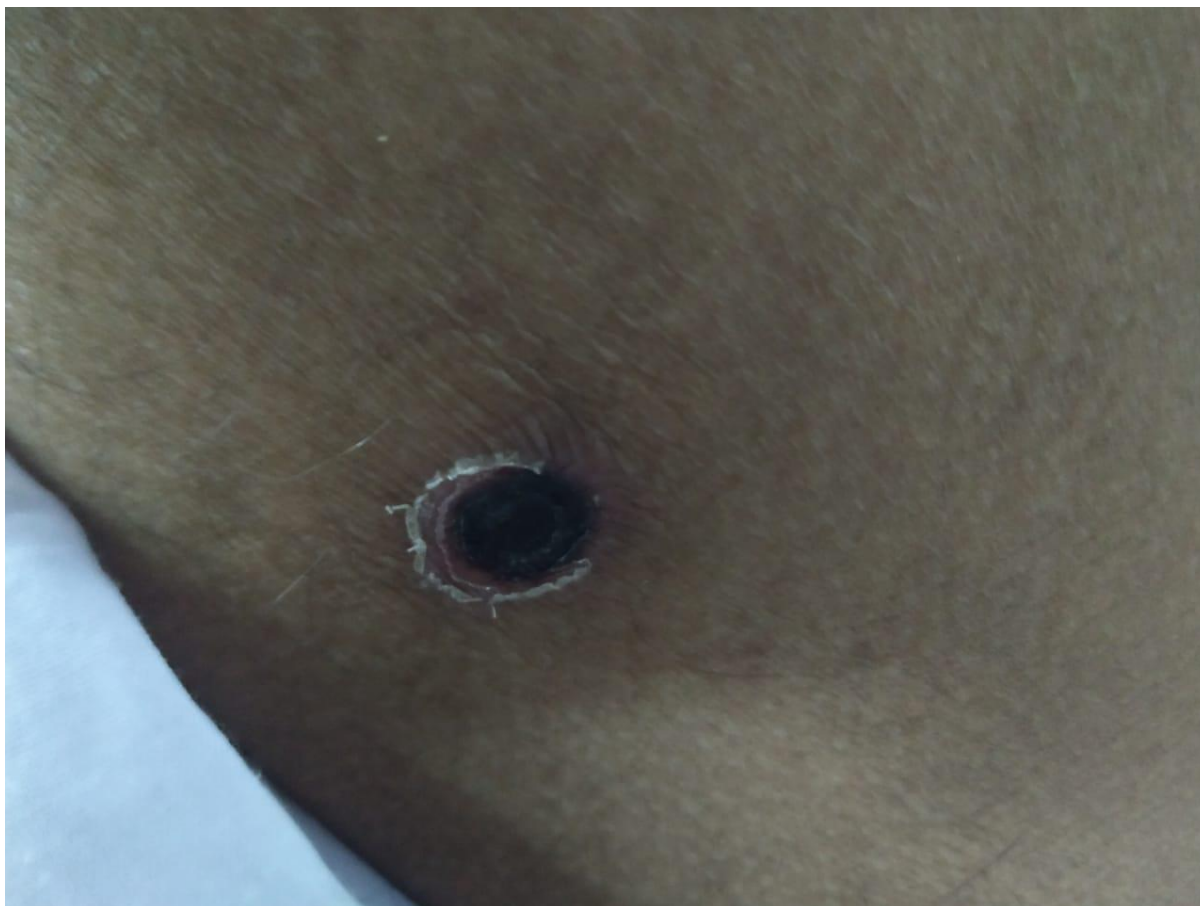


Figure 5 (Eschar on left thigh)

III. Discussion:

Scrub typhus infections may present as mild illness or can lead to fatal complications like ARDS, meningoencephalitis, AKI, myocarditis, hepatic dysfunction and multi organ involvement. Complication usually occurs after first signs of illness. Due to non-specific clinical nature of scrub typhus it is grossly under diagnosed, though it is a growing and emerging disease which can lead to life threatening illness. Thus, initiation of treatment should be early and prompt based on clinical suspicion.

Most of the affected patients were from rural areas. This may be due to the reason that they are more involved in outdoor activities like farming, fishing or collecting firewood from the jungle that expose them to mites infected area or vegetation.

Orientia Tsutsugamushi proliferates in the endothelium of small blood vessels that result in cytokine release. This cytokine causes endothelium damage leading to leakage of fluid and aggravation of platelets, and proliferation of polymorph and monocytes leading to focal micro infection, which eventually leads to venous thrombosis and peripheral gangrene. Various organs like skin, skeletal muscles, kidney, lungs, brain and cardiac muscles are affected by this processes. *O. Tsutsugamushi* infection spreads to multiple organs through blood stream and lymphatics. Mainly targets macrophages present in the spleen and liver. Endothelial cell causing inflammation by this mechanism called oxidative stress leads onto local and systemic vasculitis. Despite that fact endothelial infection occurs in scrub typhus incidence of vasculitis is quite rare.

Systemic vasculitis causing gangrene can occur due to both infectious and non-infectious cause. Among the infections caused, viruses are leading organisms that lead to systemic vasculitis. Hepatitis B virus is associated with polyarteritis nodosa. Hepatitis C related mixed cryoglobulinemia causes systemic vasculitis. Few others viruses like HIV, Parvo virus B19, VZV, HTLV-1 and Cytomegalovirus. Bacteria, fungi or parasites also cause vasculitis which could be by direct invasion of blood vessels or by septic embolization. Syphilitic aortitis or cerebrovascular disease and rickettsial disease are other more specific.

The importance of differentiating infectious and non-infectious caused by vasculitis is necessary because the treatment strategies are different. Infectious causes are treated with appropriate antimicrobial agents. Combination of antiviral drugs, steroids and plasma exchanges are effectively tried for HBV, HCV, HIV related vasculitis.

With risk factors, such as smoking, hypertension, diabetes, obesity, hyperlipidemia atherosclerosis has become the leading causes of peripheral disease. Commonly associated with digital gangrene-Homocysteinemia, Primary systemic vasculitis, Burger's disease, rheumatoid arthritis, Scleroderma, Raynaud's Phenomenon, SLE, medium vessels and large size vasculitis can also lead to digital gangrene, such as Giant Cell Arteritis and Takayasu's Arteritis.

Looking into the infective causes as in this case, the diagnosis of scrub typhus should be made by excluding other viral infectious causes like dengue fever, infectious mononucleosis, HIV and bacterial disease causing typhoid, leptospirosis, meningococcal disease causing vasculitis. These infections were excluded by appropriate investigations. As serology for scrub typhus done by ELISA was positive, we thought about the association of scrub typhus as the cause of vasculitis. Patient subsequently developed pan digital gangrene in both hands. This was confirmed by the presence of eschar and positive scrub typhus serology. Hence we concluded that the patient developed pan digital gangrene in both hands secondary to scrub typhus vasculitis.

IV. Conclusion

There are so many conditions causing vasculitis, but it is essential to differentiate infective from non-infective causes as the treatment for each is entirely different. From this case, one can learn that pan digital gangrene in both hands may be developed due to the unusual complication of scrub typhus.

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