



Scrub typhus - A case report
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Abstract :

Scrub typhus is an acute febrile illness caused by *Orientia tsutsugamushi* (*O.tsutsugamushi*). The disease is of greatest public health importance in southern India and Northeastern states of India. The clinical manifestation of the disease ranges from subclinical to an organ failure. There may be development of complications like liver failure, renal failure, pneumonitis, acute respiratory distress syndrome (ARDS), septic shock, myocarditis and meningio-encephalitis in untreated case. This is a case report of 32 year old farmer with scrub typhus, who presented with multiorgan dysfunction and recovered completely with proper diagnosis and treatment.

Keyword :

Scrub typhus, *O. tsutsugamushi*, acute febrile illness, multiorgan dysfunction, agglutination test, ELISA

Introduction:

Scrub typhus is an acute febrile zoonosis caused by an obligate intracellular bacteria *O. tsutsugamushi*. The natural reservoir of this rickettsial infection is the adult mite from which the organism passes to the larva by transovarian transmission. The larval mite usually feed on the wild rats of the subgenus *Rattus*. It is transmitted by the bite of a larval stage trombiculid mite or chiggers. Human beings usually get infected when they accidentally encroach upon the mite infested areas, known as mite islands mainly in rural and suburban areas.^{1,2} The incubation period varies from 6-21 days. It presents as either a nonspecific febrile illness with constitutional symptoms such as fever, rash, myalgia and headache or with organ dysfunction. Scrub typhus is generally under diagnosed in India due to its nonspecific clinical presentation, limited awareness and low index of suspicion. Clinicians should suspect scrub typhus during the outbreak of many fevers such as Dengue, Chikungunya, Leptospirosis and other viral fevers.³ It is also difficult to distinguish scrub typhus from other common acute febrile illness like Typhoid and Malaria, delay in diagnosis and treatment of scrub typhus results in development of complications after 1st week. Mortality due to this disease is 7-30%.⁴

Case report:

A 32 year old farmer was referred to Government Rajaji Hospital for high grade continuous fever for more than 10 days with

headache, arthralgia, jaundice, facial puffiness, abdominal distention and bilateral pedal edema. He had breathing difficulty, decreased urine output and reduced platelet count for 2 days. His recent past history revealed continuous fever for a week for which he sought medical care at a private health facility. Since fever did not subside, he was treated as an inpatient at a government hospital.

He was on antibiotics and supportive measures. Laboratory evaluation done while at admission revealed raised bilirubin, elevated blood urea and serum creatinine with low platelet count. He was then referred to tertiary care hospital-Government Rajaji Hospital attached to Madurai Medical College for further management. He had an occupational history of working in forest areas where his main job was clearing of bushes around silk cotton trees and he had insect bite during his work.

On admission, the patient presented with fever, tachypnea, jaundice, facial puffiness, hepatosplenomegaly, ascites and bilateral pitting pedal edema. There was no rash, purpura, petechiae and eschars in body surfaces. The cardiovascular system and central nervous system examination was normal. The vitals, temperature was 40, respiratory rate 36/minute, heart rate 110/minute, blood pressure 100/80 mmHg and PCO₂ >90 in room air.

The investigation report done at referral hospital showed Hb-13.6 mg%, platelet count-39000 cells/cmm, blood urea-152 mg%, serum creatinine-5.7mg%, serum bilirubin-total 5.5mg%,direct 2.5mg% and indirect 3.0mg% and SGOT-144IU/l,SGPT-84IU/l.

The patient was managed in Intensive Medical Care Unit(IMCU) and simultaneously evaluation of acute febrile illness done. The panel of investigation were bacterial and fungal culture of blood and urine, serological tests for Enteric fever, Brucellosis, Rickettsial infections and viral infections such as Dengue, Chikungunya and viral hepatitis. Peripheral smear study was done for malarial parasite.

Hematological parameters were evaluated. Serial monitoring of renal parameters-blood urea, serum creatinine and serum bilirubin were done.

Table-1: Bacteriology and serology test reports.

S. No	Name of the disease	Test done	Result	Remarks
1	Bacterial sepsis	Blood culture (Enteric and nonenteric)	No growth after 48 hours	
2	Urinary tract infection	Urine culture	No growth after 24 hours	
3	Malaria	Peripheral smear study	No parasites seen	
4	Enteric fever	WIDAL test ^a	No agglutination	Significant titers: O:1:100 H:AH.BH:200
5	Brucellosis	Standard Agglutination Test (SAT)	No agglutination	Significant titers 1:160
6	Rickettsial infections	Weil-Felix test ^c		
		OX19	No agglutination	Significant titers 1:160
		OX2	No agglutination	Significant titers 1:160
		OXK	granular clumps up to 1:40 dilution	Significant titers 1:160
7	Dengue	IgM capture ELISA ^d	Negative	
8	Chikungunya	IgM capture ELISA ^e	Negative	
9	Leptospirosis	IgM capture ELISA ^f	Negative	
10	Scrub typhus	IgM capture ELISA ^g	Positive	
11	Viral hepatitis	Rapid card test for HAV, HBsAg and HEV ^h	Negative	
12	Fungal sepsis	Blood and urine culture	No growth after 4 weeks	

a-Tube agglutination test, antigens used- S.typhiO, S.typhiH, S.paratyphiAH, S.paratyphiBH, King institute of preventive medicine, Guindy, Chennai, dilutions-1:25 to 1:400, **b**-Tube agglutination test, antigens used- B.melitensis, B.abortus, King institute of preventive medicine, Guindy, Chennai, dilutions-1:10 to 1:1280, **c**-Heterophile agglutination test, antigens used- OX 19, OX 2, OX K strains of Proteus species, King institute of preventive medicine, Guindy, Chennai, dilutions-1:20 to 1:640, **d**-NIV DEN MAC-ELISA kit, Pune, **e**- NIV CHICK MAC-ELISA kit, Pune, **f**- PanBio Lepto Mac Elisa kit, **g** in BrisTypus Mac ELISA kit, **h**- latex agglutination test kit, SD BioLine HAV, HBsAg, HEV Peripheral smear study: Total count-10000 cells/cmm Differential count:P-82%,L-15%, E-2%, M-1% Platelet count-94000cells/cmm Evaluation of acute febrile illness revealed infection with O. tsutsugamushi and scrub typhus fever was diagnosed. Patient was put on C.Doxycycline 100mg orally twice a day for 10 days. Patient became afebrile with improvement in platelet count, but the renal functions deteriorated and bilirubin level was increasing.

Table-2: Platelet count

Date of test	11th day of illness (on admission)	13th day of illness	15th day of illness	17th day of illness	19th day of illness	21st day of illness
Platelet count (cells/cmm)	39000	80000	1.46 lakhs	1.5 lakhs	1.6 lakhs	2.0 lakhs

Table-3: Renal parameters and serum bilirubin.

Name of the test	Day of the test done						
	11th day of illness (admission)	13th day of illness	15th day of illness	17th day of illness	19th day of illness	21st day of illness	23rd day of illness
Blood urea (mg%)	152	184	212	154	146	98	80
Serum creatinine (mg%)	5.7	4.2	4.7	4.0	4.2	3.0	1.5
Serum bilirubin (mg%)							
Total	5.5	14.1	18.8	21	20	16	9.2
Direct	2.5	8.6	11	12	12	10	5.8
Indirect	3	5.5	7.8	9	8	6	3.4

Therefore hemodialysis was done on 16th, 18th and 20th day of illness, patient managed meticulously to prevent liver failure and hepatic encephalopathy. There was a good clinical improvement and the renal and liver functions were normal on 15th day after admission (blood urea- 42 mg%, serum creatinine-1.2mg%, serum bilirubin-total 1.5mg%, direct 1mg% and indirect 0.5mg%). Patient was discharged on 3rd week in a good clinical condition.

Discussion

The rickettsiae are intracellular parasites. They are small Gram-negative bacteria that live freely in the cytoplasm of their infected eukaryotic host cells and released when the heavily infected host cell membrane are destroyed. **5** Scrub typhus is endemic and reemerging in eastern and southern Asia, Northern Australia and islands of the western Pacific and Indian oceans. The classic case descriptions includes an eschar where the chigger has fed, regional lymphadenopathy and maculopapular rash- signs that are seldom seen in indigenous patient. **6** Scrub typhus may be mild or fatal depending on host factors and presumably the virulence of the infecting strain. The target cells for O.tsutsugamushi are endothelial cells and macrophages. It disseminates into the multiple organs through endothelial cells via macrophages and lymphocytes and predominantly locates in the macrophages of liver and spleen. The bacteria then cause focal or systemic vasculitis and perivasculitis in multiple organs, with various complications. The complications of scrub typhus usually develop after one week if untreated and the various complications are acute renal failure, acute hepatic failure, interstitial pneumonitis, ARDS, septic shock, myocarditis, pericarditis, meningoencephalitis and acute hearing loss. **7** Hepatic injury in scrub typhus is usually mild. Liver involvement with jaundice and abnormal liver function test may result from sinusoidal infiltration, pericholangitis, and perivascular lesion in the portal area of liver. **8** An acute renal failure is rare in scrub typhus and proposed mechanism include prerenal azotemia resulting from hypotension and volume depletion. It can be a part of DIC, and there may be acute tubular necrosis due to direct invasion of O.tsutsugamushi. **9** Tropical acute febrile illness are a common cause of acute kidney injury (AKI) in the developing countries.

The common tropical acute febrile illness that cause AKI are scrub typhus (51%), falciparum malaria, mixed malaria, enteric fever, dengue, leptospirosis, vivax malaria, rickettsial spotted fever and Hantaan virus infection. **10** Laboratory diagnosis of scrub typhus is difficult. Culture is 100% specific, it can be cultured in embryonated eggs or in tissue culture and the risk of laboratory-acquired infection is extremely high, limiting the availability of culture to a few specialized laboratories. Conventional and quantitative real time PCR assays for detection of O. tsutsugamushi in blood, eschar tissue and CSF have been developed, but there is a great difficulty in the accessibility in rural endemic areas. **11** Antibodies appear in the second week of illness, when the patient is usually on the way of recovery. Serology is therefore not suitable for early diagnosis but it is used mainly to confirm the diagnosis. Weil-Felix test is inexpensive and easy to perform but it is less reliable because of poor sensitivity and specificity. Immunofluorescence (IFA) and immunoperoxidase IgM and IgG antibody test have been commonly used, but these are expensive. Commercial ELISA kits are available for rapid and sensitive diagnosis. **12** Weil-Felix test, a heterophile agglutination test is based on cross reactions which occur between antibodies produced in acute rickettsial infections and the antigens of Proteus species. Principle of the test is sharing of an alkali stable carbohydrate of some rickettsiae with non motile strains of Proteus, P.vulgaris OX2, OX2 and P.mirabilis OXK. Dilutions of patient's serum are tested against

suspensions of the different *Proteus* strains. *Proteus* OXK strain agglutinins are produced in scrub typhus, but it give some percentage of false negative results. False positive results are also obtained in leptospirosis, relapsing fever, *Proteus* infections and brucellosis.¹³ The preferred drugs in the treatment include doxycycline and chloramphenicol. Doxycycline usually given as 100 mg PO twice daily for 7 to 14 days. The alternate drugs used in scrub typhus include rifampicin and azithromycin. Macrolides have been reported to be effective for the treatment of uncomplicated scrub typhus in children and pregnant women. For short exposure, chemoprophylaxis with doxycycline (200 mg weekly) can prevent the disease but permits infection. No effective vaccines are available.¹⁴

Conclusion:

Diagnosis of scrub typhus should be largely based on a high index of suspicion and careful clinical, laboratory and epidemiological evaluation. Residential area, travel history, occupation, contact history with animals, nature of water sources and mosquito and insect bite history are also considered in the evaluation of tropical acute febrile illness. An early diagnosis and treatment shows better outcome, delay is independently associated with major complication like multi-organ dysfunction. This study emphasizes the need for increased awareness of rickettsial infections in rural Southern India. Use of empiric treatment should also be considered to reduce the high mortality observed with the disease.

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