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Research Article

A CASE SERIES ON SCRUB TYPHUS

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ABSTRACT

Scrub typhus is a rickettsial disease caused by *Orientia tsutsugamushi*. It is transmitted to humans via infected chiggers (larva of trombiculid mite). Eschar is a characteristic feature for the diagnosis of scrub typhus and other mite or tick-borne rickettsiosis. Immunofluorescence Antibody (IFA) test is the gold standard for the diagnosis, and doxycycline is the drug of choice for treatment of scrub typhus. We present a case series of scrub typhus in three patients from South India. All three patients presented with high grade fever and IgM scrub typhus was positive status in all cases. Doxycycline 100 mg twice daily for 7 days along with supportive care was effective in all the cases. Serum creatinine levels dropped to normal and renal status of all patients improved well with antimicrobial treatment. Early diagnosis of the infection is necessary as the disease as it can have multiple system involvement and serious complications.

KEY WORD: Scrub typhus, *Orientia tsutsugamushi*, Eschar, Rickettsiosis

INTRODUCTION

Scrub typhus is a rickettsial disease caused by infected larval mite bites or chiggers of trombiculidae family and Leptotrombidium genus. An acute febrile condition with elevated fever, headache and rash are characteristic manifestations. The causative organism is *Orientia tsutsugamushi*, and is commonly seen in Japan, Thailand, Korea and other South Asian countries.[1, 2] Infection occurs when chiggers infected with O. tsutsugamushi bite and ingest human tissue fluid. The bite often leaves an eschar at the site. Clinical symptoms include fever, headache, chills, maculopapular rash and lymph node enlargement [1,2,3]. Presence of eschar has been shown to be a significant finding for diagnosis of scrub typhus.[4] It can also affect CNS, CVS, renal and respiratory systems causing complications such as AKI, myocarditis, pneumonia ,encephalitis and septic shock. The gold standard for diagnosis is Immunofluorescence Antibody (IFA). Other tests include Immunochromatography Test (ICT) and nested PCR techniques which detect specific antibodies for scrub typhus[5,6]. Treatment regimen includes doxycycline 100mg twice daily for 7 days and other antibiotics such as tetracycline and chloramphenicol[7,8] The infection can be prevented by the use of mite repellents such as permethrin, wearing long clothing's and protective coverings.

INFORMED CONSENT

Informed consent was taken from the subjects prior to participation in study.

CASE SERIES

CASE 1

A 64-year-old female homemaker presented to the casualty with an acute febrile illness since one week. She was in her usual state of health until one week back when she developed a high-grade fever; acute in onset, continuous, not associated with chills or rigor. There was no cough or shortness of breath; no dysuria or altered bowel habits; no other symptoms of cardiac or neurological system involvement. Five days into her fever she complained of decreased urine output. No complaints of associated abdominal discomfort or breathlessness. A detailed history was taken as to any medication intake within the past month, contact with any sick patient, animals or work in farmlands. Past history did not reveal any significant illnesses or hospitalisations. On admission, the patient was ill looking, with high grade fever (103 deg.). She was tachypnoeic, with tachycardia and hypotension (heart rate: 104/'; BP:94/64). No pallor, jaundice or pedal edema was noted. Her sensorium was intact, chest auscultation, abdominal examination was unremarkable. A SARS-CoV2 infection was ruled out primarily with a negative TRUNAT report. Two sets of blood culture were drawn before starting her on an empirical antibiotic coverage. A complete routine blood investigation and a urine routine was done. Total WBC Count -11,400cells /cumm; Hb-11g/dl; platelet count-1.8lac; ESR-76mm/hr; CRP-135mg/dL; AST-104U/L; ALT-61U/L; ALP-144U/L; S.CREATININE-2.9 mg/dl; S.UREA- 75mg/dl. Urine routine examination was normal. A chest X-ray was normal with normal lung fields and no cardiomegaly. An USG abdomen was performed-which showed bilateral increased renal cortical echotexture with accentuated corticomedullary differentiation (CMD). The AKI was secondary

to dehydration and improved well with adequate fluid resuscitation. A 48-hour blood and urine culture were sterile. An IgM LEPTOSPIRA antibody and a rapid. The malarial antigen test also came out negative. On her 3rd day of admission, she was still breaking into spikes of high-grade fever.

In search of rare causes of fever, a keener examination was performed. This was when a characteristic eschar was identified just beneath her left breast of which the patient was completely oblivious. An IgM scrub typhus test was immediately sent. Two days later the IgM scrub typhus card test was found to be reactive (>0.585). The antibiotic coverage was changed from empirical therapy to doxycycline 100 mg twice daily for 7 days and ceftriaxone 1gm iv injection . Hypokalaemia was corrected with KCL iv infusion, and other vitamin supplements were administered. The symptoms saw a dramatic improvement and no further fever spikes were recorded. After five days of the antibiotic therapy, she was completely symptom free. Her serum creatinine decreased to 1.8 mg/dl after she had resumed normal diet and hydration. Inflammatory markers also came down.

Figure 1: Eschar on left axilla region

CASE 2

A 60-year-old female presented with complaints of fever, abdominal distension, decreased urine output, constipation and bone pain. She was a known case of diabetes and DKD. Patient was admitted, routine evaluation was done which showed anaemia, elevated creatinine, ESR, CRP, LDH,D- dimer, and S. Ferritin. Peripheral smear showed normocytic normochromic anaemia. SARS –CoV-2 IgG test was found to be negative.

Echo Cardiography was within normal limits, USG abdomen showed hepatomegaly with minimal coarse echotexture, HRCT showed minimal fibrotic changes in both lungs protein electrophoresis was done and no M - band seen. Blood C &S was sterile, IgM Scrub typhus was done and detected positive. After detailed evaluation, the patient was diagnosed to have scrub typhus with AKI.

Empirical antibiotic therapy was changed to doxycycline 100mg twice daily for 7 days and cefoperazone sulbactam 1gm iv injection. The renal status of the patient improved, and serum creatinine levels dropped from 5.4 to 2.7 mg/dl.

CASE 3

A 61-year-old male presented to the casualty with complaints of high-grade fever of one week duration. No other complaints were reported. No significant medical illnesses were reported in the past except for a history of dyslipidemia for which he was taking statins.

System examination was performed and was well within normal limits. HR was 102/-, BP - 130/80, sPO2 - 97% in room air, febrile with a temperature of 101-degree Fahrenheit. Chest was clear with normal heart sounds. Abdomen was soft, non-tender with no palpable organomegaly. Neurological examination was also normal. A black necrotic lesion was noted over the right upper eyelid resembling an eschar.

Routine blood investigations were done and were unremarkable. Blood and urine C & S was sterile. Peripheral smear was normal, and no malarial parasite was observable. IgM scrub typhus was sent for which turned out to be positive. Treatment with Tab Doxycycline 100 mg bd along with supportive care was given which promptly treated his fever. He became asymptomatic within two days of treatment and was found to be clinically better on follow up.

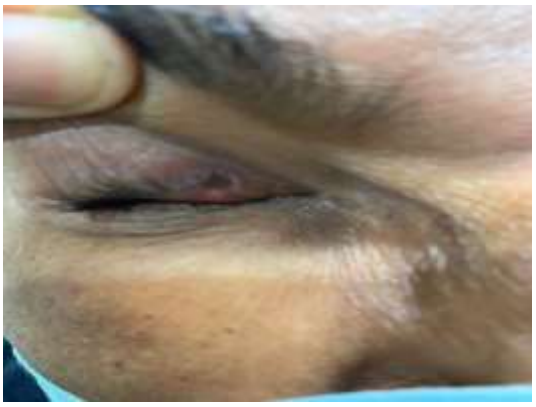

Figure 2: Eschar on right eye lid

DISCUSSION

Scrub typhus is usually characterised by fever and eschar formation. It can result in multiple organ failure leading to fatal complications such as myocarditis, pneumonia and AKI. Differential diagnosis of scrub typhus includes malaria, leptospirosis and dengue fever. Most of the cases remain undiagnosed after ruling out these conditions. Gold standard for diagnosis is Immuno fluorescence test. (IFA) Nested PCR and ICT can also be performed to confirm the antibodies. The drug of choice for this infection includes Doxycycline 200mg/day. Other antibiotic regimens for this infection include chloramphenicol, azithromycin and rifampicin.

In the first case, pneumonia with sepsis, leptospirosis was suspected initially. Malarial antigen test was found to be negative. A detailed history of travel and other comorbidities was negative. No clinical improvement was recorded, so another detailed examination of the patient revealed the eschar beneath her breast. The second case showed features of acute febrile illness without eschar. In both cases, IgM scrub typhus card test was found to be reactive with features of AKI. The empirical antibiotic therapy was promptly changed to doxycycline and ceftriaxone. AKI was resolved with fluid resuscitation and high creatinine levels also dropped to normal. The patients showed good progress in renal status and no further fever spikes were observed.

The third case presented with a tell-tale sign of an eschar on the face which prompted an IgM scrub typhus investigation.

Table 1

	High Grade Fever	AKI	Eschar	Relief with Doxycycline
CASE 1	+	+	+	+
CASE 2	+	+	-	+
CASE 3	+	-	+	+

CONCLUSION

Early diagnosis of the infection is necessary as the complications may be fatal, which include acute renal failure gastrointestinal bleeding, encephalitis ,pneumonia and myocarditis. In the first case, a keen physical examination revealed a characteristic eschar. The second case was presented with features of acute febrile illness with an AKI. All other suspected infections were ruled out and an antibody test was done immediately. Patients received right treatment without delay and were found to be clinically stable after starting Doxycycline. The third case had the patient presenting with the characteristic eschar with high grade fever which prompted an antibody test for scrub typhus.

The infection responds very well with the antimicrobial therapy and can prevent further complications. It is prudent to propose empiric therapy in developing countries having limited diagnostic facilities, in cases of undifferentiated febrile illness with multiple system involvement.

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