



TYPHUS TACTICS: DOMINATING WITH MULTIORGAN DYSFUNCTION SYNDROME

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ABSTRACT

Scrub typhus is a vector borne rickettsial disease caused by *Orientia tsutsugamushi*[1]. It is endemic in southeastern and far eastern countries of Asia [India, Sri Lanka, Pakistan, Japan, Thailand and Korea], also extending from Afghanistan down to north Australia so called tsutsugamushi triangle[1]. Unlike other gram negative bacteria, *Orientia tsutsugamushi* lacks lipopolysaccharide and express low levels of unclassical peptidoglycans[2]. The pathophysiology of scrub typhus is not fully understood though in general it is thought to be caused by focal/disseminated vasculitis[1]. In some individuals, scrub typhus can cause a severe illness with multiorgan dysfunction[1]. If left untreated, mortality rates can be high as 30%[1]. Here we present a case of scrub typhus with multiorgan dysfunction syndrome in a 60-year-old male patient. Awareness of unusual manifestations will guide clinicians towards diagnosing the condition early and initiating appropriate management[1]. **Introduction:** Scrub typhus presents as fever with little to distinguish it clinically from co-endemic diseases such as typhoid, leptospirosis and dengue fever[3]. The disease was first described in Japan in 1899 and the term tsutsugamushi is derived from separate Japanese words 'tsutsuga' meaning something small and dangerous and 'mushi' meaning creature[4]. Annually one million cases have been reported and an estimated one billion people are at risk of contracting the illness[5]. In India, typhus has been reported in many states which includes Tamilnadu, Himachal Pradesh, Pondicherry, Andhra Pradesh, Kerala and Meghalaya[4]. Trombiculid mites are the natural host of the organism and the disease is transmitted to humans during feeding by the mite in its infected larval stage[1]. Agricultural workers in the endemic region are known to have a higher risk for acquiring scrub typhus[5]. The incubation period in humans is around 10-12 days and can vary between 6-21 days[1]. It usually presents as an acute febrile illness with high fever, headache, malaise and cough[1]. The most characteristic finding of scrub typhus is the presence of eschar at the site of the bite[1]. The presence of eschar is highly variable between 7-80%[1].

KEYWORDS : SCRUB TYPHUS, MULTIORGAN DYSFUNCTION SYNDROME.

CASE REPORT:

A 60-year-old gentleman farmer by occupation residing in Nellore, known hypertensive presented with the chief complaints of high grade fever associated with myalgia for ten days. History of vomiting and loose stools for the past 2 days. History of altered sensorium and decreased mobility for the past 2 days. History of high coloured urine for the past 2 days. Patient got admitted for further management.

On admission patient was confused, GCS-E3V3M6. His blood pressure was 140/70mmHg, pulse rate-108/minute, respiratory rate-24/minute, temperature-97.5 Fahrenheit and SPO2-98% under room air. An eschar was found on the right thigh. There were no palpable lymph nodes and palpable organomegaly. Patient was started on antibiotics, IV fluids and oxygen support. He was shifted to intensive care unit for further management. Hemogram showed HB-11.8 g/dl, white cell count-19,730 and platelet-1,40,000. Blood biochemistry showed urea-69mg/dl, creatinine-1.9mg/dl, aspartate transaminases-144IU/L, alanine transaminases-162U/L, Alkaline phosphatase-162mg/dl, Gamma-glutamyl transpeptidase-173mg/dl, albumin-2.7g/dl and total bilirubin-5.2mg/dl [indirect-1.4 and direct-3.8]. Meanwhile urine analysis showed 11-13 RBC/HPF, 1-3 WBC/HPF and no proteinuria. ECG showed sinus tachycardia. Chest x-ray showed multiple in-homogenous opacities in bilateral lung fields. Ultrasound abdomen showed grade 1 fatty liver. Computed tomography brain showed normal brain parenchyma.

Patient developed respiratory distress and started on high flow nasal cannula. Computed tomography of chest showed diffuse interstitial septal thickening with ground glass opacities in both the lung fields, dependent subpleural consolidation in bilateral postero-basal segments and minimal bilateral pleural effusion. Two dimensional echo-cardiography showed ejection fraction of 65% and no regional wall motion abnormalities. NT PRO-BNP level was 5549 pg/ml and patient was started on injection Lasix. Dengue serology, MPQBC, leptospirosis IgM, respiratory syncytial virus, SARS-COV-2, influenza A and B polymerase chain reaction were negative. Scrub typhus IgM was positive. Patient's encephalopathy resolved on day 4 of admission. Acute kidney injury resolved on day 5 of admission. Patient was gradually weaned off from oxygen support on day 8 and shifted to ward. Patient received 8 days of doxycycline 100mg twice

daily and Azithromycin 500mg twice daily. Patient was discharged with liver supportive medications and fluid restricted diet.



Figure:1 Chest X-RAY Showing Multiple Inhomogenous Opacities



Figure:2 Eschar In The Right Thigh

DISCUSSION:

The clinical spectrum of scrub typhus ranges from mild and probably subclinical to severe and prostrating courses^[6]. Myalgia, headache and fever begin about 1-3 weeks after a bite by an infected mite^[6]. The eschar starts as a small papule which enlarges and undergoes central necrosis then turn to black^[1]. The commonest sites of eschar are groin, axilla, waist, neck and other exposed parts of the body^[1]. Additionally a non pruritic maculopapular rash initially starting on the trunk and radiating outwards occurs in one half of the patient along with constitutional symptoms^[6]. Generalised and regional lymphadenopathy can also occur^[6]. Most of the systemic manifestations start towards the beginning of the second week^[1].

The presence of pneumonitis may be a marker of severe disease^[1]. Other clinical manifestations include pulmonary oedema, pleural effusion, pulmonary haemorrhage and pneumonia^[1]. Acute respiratory distress syndrome is a uncommon complication of scrub typhus^[1]. Initial presentation of dyspnoea, cough, white cell count, haematocrit, total bilirubin and delayed use of appropriate antibiotics were independent predictors of ARDS^[7]. Bilateral reticular opacities, air space nodules and pleural effusion are the most common radiological features of scrub typhus^[1]. Other radiological manifestations include

ground glass opacities, consolidation, septal lines, mediastinal and hilar lymphadenopathy^[1].

Relative bradycardia is the most common cardiovascular manifestation of scrub typhus and it is seen in over 50% patients^[1]. Heart failure, myocarditis and acute myocardial infarction due to scrub typhus have been rarely reported^[7]. Acute kidney injury is a complication of scrub typhus and it is a mortality predictor^[1]. Meningitis, meningoencephalitis, encephalitis, encephalopathy and seizures are the common neurological manifestations^[4]. The rare immune mediated manifestations include optic neuritis, myelitis, acute disseminated encephalomyelitis, Guillain-Barre syndrome and neuropathies[sixth nerve, seventh nerve, mononeuritis multiplex and brachial plexopathy]^[4].

Diarrhoea is not unusual in scrub typhus^[1]. Abnormalities of liver function are common, transaminases elevation appears to be more common than raised bilirubin^[1]. Liver failure is rare^[1]. Splenomegaly is a common feature in scrub typhus^[1]. Hemoperitoneum, pancreatitis, acalculous cholecystitis and intestinal bleeding have also been reported. Disseminated intravascular coagulation is a well known complication of scrub typhus and it is associated with high mortality^[1]. Haemophagocytic syndrome is rare but it has been reported^[1]. Endocrinology manifestations like adrenal insufficiency and subacute thyroiditis has also been reported^[1].

The mainstay of scrub typhus diagnosis remains serology^[3]. The oldest test is the Weil-Felix OX-K agglutination reaction and it lacks specificity and sensitivity^[3]. The other methods of diagnosis include Indirect immunofluorescence assay, Indirect immunoperoxidase assay, enzyme linked immunosorbent assay and immunochromatographic methods^[8]. Among all serological assays, the most reliable test is IgM-ELISA based method^[8]. The genetic variation among the strains of *Orientia tsutsugamushi* are the biggest defiance for scrub typhus diagnosis through polymerase chain reaction method even though it has more specificity and sensitivity^[8].

Doxycycline therapy is associated with rapid abatement of clinical manifestations and oral doxycycline is the currently standard treatment for mild scrub typhus cases^[9]. Macrolide antibiotics such as Azithromycin is an appropriate alternative in areas where doxycycline resistant scrub typhus is prevalent and in children under 8 years of age and pregnant women where doxycycline is contraindicated^[9]. In India, among scrub typhus patients admitted to an intensive care unit 85% of patient had dysfunction of three or more organ systems^[1].

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