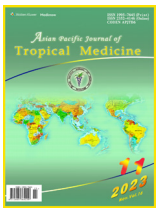

Letter to Editor

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Myocarditis in scrub typhus-An uncommon presentation

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Scrub typhus is a disease caused by bacteria *i.e. Orientia tsutsugamushi* and spreads through bites of infected larval mites rapidly emerging particularly in Asia-Pacific countries[1]. The disease became severe with organ involvement due to vascular injury, interstitial pneumonia, encephalitis, and renal or liver failure[2]. Myocarditis is an uncommon complication and leads to mortality if associated with ischemic heart disease and acute heart failure[3]. Here we report a series of 5 cases presenting the complications of myocarditis, which were managed by timely diagnosis and prompt therapeutic action (Institutional Ethical Approval-KIIT/KIIMS/IEC/1434/2023).

A 37-year-old female presented to the hospital with symptoms of fever for 8 days, dyspnoea and body swelling for 4 days. High-grade fever with chills and whole body swelling were observed after 8 days. There was no history of rashes, cough, chest pain, palpitations, syncope, decreased urine output, abdominal distension, jaundice, abnormal bowel habits, or altered sensorium. The patient had a history of hypothyroidism. No addictions or allergies were reported. Menstrual history was unremarkable. Her blood pressure was 110/70 mm Hg, pulse rate 120/min, respiratory rate (RR) 48 breaths/min, oxygen saturation 56% at room air. Pallor and pitting edema in all four limbs and facial puffiness were observed by physical examination. Jugular venous pressure was 5 cm above the sternal angle. There was no icterus, cyanosis or clubbing. Respiratory examination by chest X-ray revealed diffuse non-homogenous opacities in bilateral lung fields (Supplementary Figure 1A). Cardiovascular examination revealed normal intensity of first and second heart sounds with no third or fourth heart sound or murmurs. Based on the diagnostic possibilities of respiratory failure due to heart failure with acute pulmonary edema or bronchopneumonia complicated by acute respiratory distress syndrome or sepsis, the patient was admitted to the intensive care unit for ventilation and treated with intravenous broad-spectrum antibiotics, diuretics, nebulization with bronchodilators and other supportive medications. Echocardiogram (ECG) report showed sinus tachycardia ST depressions and T wave inversions (Supplementary Figure 1B). Scrub typhus was diagnosed and confirmed by IgM test and PCR test.

As a treatment, doxycycline 100 mg at 12 hours was given intravenously with the ongoing treatment. Respiratory distress and hemodynamic parameters were managed by mechanical ventilation with vasopressor support and norepinephrine. Myocardial injury was evident from a rise in cardiac troponin levels and ECG changes as confirmed by two-dimensional (2D) echocardiography. The diagnosis revealed global hypokinesia of left ventricle with ejection fraction of 30% (Supplementary Figure 1C and 1D). The patient was treated with carvedilol 3.125 mg ½ tablet twice daily, ramipril 2.5 mg once daily, eplerenone 25 mg once daily, trimetazidine 35 mg twice daily, aspirin 75 mg daily, atorvastatin 80 mg once daily and ivabradine 5 mg twice daily.

After five days, the cardiorespiratory and hemodynamic conditions improved, 2D echocardiography revealed no regional wall motion abnormality and an ejection fraction of 60%. The patient was discharged in a hemodynamically and clinically stable state. Follow-up was unremarkable.

Similarly, four cases such as two females (46 years old and 56 years old) and two males (16 years old and 49 years old) of scrub typhus had tachycardia on admission but atrial fibrillation was seen in the last case while the other two cases had normal sinus rhythm (Table 1). All four of them had also have elevated cardiac troponins

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Table 1. Case summaries of the five patients.

Investigations	Case 1	Case 2	Case 3	Case 4	Case 5
Age, years	37	47	16	52	49
Sex	Female	Female	Male	Female	Male
Complaints, duration, days					
Fever	8	12	15	-	10
Cough	-	-	2	10	-
Comorbidities	Nil	Nil	Nil	Nil	Nil
Vitals					
Pulse rate, /min	120	112	116	126	114
Blood pressure, mm Hg	110/70	130/70	100/60	84/50	130/80
Respiration rate, /min	48	20	28	20	18
Temperature, °F	99.0	99.7	100.6	99.7	98.8
Eschar	Absent	Present	Absent	Absent	Present (on penile shaft)
Physical examination	Pallor and edema of all four limbs and facial puffiness	Unremarkable	Unremarkable	Unremarkable	Unremarkable
Complete blood count					
Total leucocyte count, /mm^3	13400	8500	6800	7200	8900
Hemoglobin, g/dL	10.4	12	11.8	12	12.3
Total platelet count, /mm^3	60000	120000	60000	90000	150000
Renal function test					
Urea (U), mg/dL	69.9	47	24	29	18
Creatinine (Cr), mg/dL	0.81	0.96	0.71	0.95	0.88
Sodium (Na), mEq/L	129	130	120	134	133
Potassium (K), mEq/L	3.5	4.7	4.4	4.0	4.4
Liver function test					
Total bililubin, mg/dL	0.88	6.23	0.55	0.26	0.66
AST, U/L	227	373	111	72	64
ALT, U/L	92	255	43	59	57
GGT, U/L	260	404	21	88	275
ALP, U/L	104	581	63	194	301
Scrub PCR/IgM					
PCR	Positive	Positive	Positive	Positive	Positive
IgM	3.55	2.56	2.77	3.03	3.01
Others					
IgM/NS1 dengue	Negative	Negative	Negative	Negative	Negative
MP-ICT	Negative	Negative	Negative	Negative	Negative
Typhi dot IgM	Negative	Negative	Negative	Negative	Negative
Leptospira IgM	Negative	Negative	Negative	Negative	Negative
NT pro BNP	16000 pg/mL	1200 pg/mL	998 pg/mL	1258 pg/mL	805 pg/mL
Troponin I	0.206 ng/mL	0.473 ng/mL	0.58 ng/mL	0.35 ng/mL	0.94 ng/mL
2D echocardiography	Global hypokinesia of left ventricle with ejection fraction of 30%	Atrial fibrilation noted	Mild to moderate left ventricle systolic dysfunction	Mild left ventricle systolic dysfunction (ejection fraction-40%)	Atrial fibrillation noted during study, concentric left ventricle hypertrophy, normal left ventricle systolic function (ejection fraction-58%), mild mitral regurgitation

-: not found; AST: aspartate transaminase; ALT: alanine transaminase; ALP: alkaline phosphatase; GGT: gamma glutamyl transaminase; NT pro BNP: N terminal pro B type natriuretic peptide; PCR: polymerase chain reaction; 2D: two-dimensional.

and 2D echocardiography suggestive of left ventricle systolic dysfunction. The scrub typhus in all the five cases were confirmed by IgM test and RT-PCR test. All were treated as cases of myocarditis due to scrub typhus and managed along similar lines as in the first cases. Case 4 had hypotension, which was managed by intravenous fluids and vasopressor support in the form of noradrenaline. Atrial fibrillation in case 2 and 5 was managed with amiodarone. All of them responded to treatment and were discharged in stable states with normalization of myocardial function as evident by 2D echocardiography.

A series of five cases of scrub typhus presenting myocarditis evident clinically by tachycardia in all of them, atrial fibrillation in cases 2 and 5, hypotension in cases 1 and 4. In all cases, cardiac troponins was elevated and subnormal left ventricular function evident by 2D echocardiography. The first case developed heart failure with cardiogenic shock. All of them responded to conventional treatment guided by case to case basis.

Scrub typhus is an infectious disease caused by *Orientia tsutsugamushi* and transmitted through bites of infected chiggers (larvae of the trombiculid mites). The chiggers inoculate the organism into the skin when they come in contact[2]. After an incubation period of 6-21 days, onset begins with fever,

constitutional symptoms, cough, and gastrointestinal symptoms with or without eschar, regional lymphadenopathy or maculopapular rashes[2]. Meningoencephalitis, interstitial pneumonia, acute respiratory distress syndrome, acute renal failure, liver failure, sepsis, shock and rarely myocardial involvement are the clinical manifestations. As the organism penetrates vascular endothelial cells causing diffuse vasculitis and microvascular ulcerations, it may lead to organ failure. The case-fatality rate for untreated classic cases is 6%[2]. The involvement of cardiovascular in the form of myocarditis, pericarditis or arrhythmias, may lead to an increase in mortality[3]. A rare case of scrub typhus with biopsy-proven acute fulminant myocarditis has been described, which progressed very rapidly to cardiac arrest and was treated successfully with extracorporeal cardiopulmonary resuscitation[4].

Myocarditis in scrub typhus is often overlooked until it presents in fulminant form. Previously, it has not been reported as a manifestation of scrub typhus because the incidence appears to be very low. Early diagnosis by serological tests and polymerase chain reaction are needed, but some time, the results do not always correlate and are affected by prior antibiotic treatment[5,6]. Thus ECG, 2D echocardiography and troponin I marker test are advisable in complicated atrial fibrillation conditions. Doxycycline or tetracycline are the most common drug used for treatment, chloramphenicol is an alternative. In children and pregnant women, azithromycin is an alternative when doxycycline resistance is suspected.

In conclusion, myocarditis is a recognised although uncommon presentation of scrub typhus. The presence of tachycardia, hypotension, worsening dyspnoea or arrhythmias should prompt towards estimation of biomarkers of cardiac injury, troponins, and echocardiographic assessment of myocardial function to suggest the possibility of myocarditis. Early detection and aggressive monitoring can help to institute timely life-saving measures which can prevent or mitigate catastrophic complications like heart failure or conduction disturbances.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

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Authors' contributions

RPBR and LM conceptualized and managed all the five cases. AJ and SS collected all the data. All the authors contributed in the data collection and analysis.

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