



## Case Series

# Rocky mountain spotted fever- A case series

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### ABSTRACT

Rocky mountain spotted fever caused by *Rickettsia rickettsii*, is a life threatening tick transmitted infection, which is the most prevalent rickettiosis. It remains a diagnostic challenge because of its varied clinical presentation and the overlap of signs and symptoms with other diseases. Under diagnosed and misdiagnosed rickettsial infections are important public health problems. There is neither an effective vaccine nor an assay that is diagnostic during the early stages of the disease when treatment is most effective. Here, we report three cases with varied clinical manifestations.

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## 1. Introduction

Rocky Mountain spotted fever (RMSF) is one of the most severe of all infectious diseases. It was first recognized on the frontier of the American West. Efforts to elucidate the rickettsioses have been diverted by wars, epidemics, and other newly recognized infections. This zoonosis is firmly entrenched in the tick host, which maintains the rickettsiae in nature by transovarian transmission. Although the incidence of disease fluctuates in various regions and nationwide.<sup>1</sup>

The development of antimicrobial agents that are effective when given early in the course of infection and the cyclic waning of disease incidence, as occurred concurrently in the late 1940s, led many to conclude incorrectly that the problem had finally been solved. Resurgence in the incidence, difficulty of clinical diagnosis, defined populations at higher risk of fatal outcome, and increased general use of antimicrobial agents that lack antirickettsial activity are persistent factors leading to misdiagnosis and death. Failure of vaccines to confer protective immunity

and the lack of a generally available laboratory diagnostic test during the acute stage of illness provide overwhelming evidence that the old problems of prevention and diagnosis of RMSF still need attention.<sup>1</sup>

High-risk locations include wooded, shrubby, or grassy areas. Approximately half of patients with infection do not recall tick exposure. Symptoms can include fever, headache, photo phobia, malaise, myalgias, and a petechial rash that begins on the wrists and ankles and spreads to the trunk. Rash may not occur in  $\leq 15\%$  of patients, and the classic triad of fever, headache, and rash is also not definitive. Laboratory evaluation may demonstrate hyponatremia, anemia, thrombocytopenia, abnormal liver enzymes, and elevated coagulation tests. Antibody testing can be helpful, but these results are not typically available to the emergency clinician. Doxycycline is the treatment of choice in adults, children, and pregnant patients. Patients should be advised about prevention strategies and effective techniques for removing ticks.<sup>2,3</sup>

RMSF is a potentially deadly disease that requires prompt recognition and management. Focused history, physical examination, and testing are important in the diagnosis of this disease. Understanding the clinical

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features, diagnostic tools, and proper treatment can assist emergency clinicians in the management of RMSF.<sup>4</sup>

## 2. Case History

### 2.1. Case 1

A 58 year old diabetic hypertensive male from Chikkaballapur, presented with history of fever, easy fatigability, reduced appetite since 1 week and hiccups since 2 days. On day 3 of admission, patient developed maculo - papular erythematous rashes over the palms soles followed by the trunk and painful peripheries suggestive of neuropathy. Patient was haemodynamically stable with good glycaemic control. Other system examination was unremarkable except for hyperaesthesia over the distal extremities. On laboratory investigations, patient's reports were as follows.

**Table 1:**

	19/2/21	22/2/21	27/2/ 21
<b>CBC – Haemoglobin</b>	11.8	10.3	9.3
<b>RBC count</b>	3.79	3.28	3.13
<b>PCV</b>	34.1	30.03	28
<b>MCV</b>	89.9	91.4	89.6
<b>WBC</b>	11,600	10,560	6,300
<b>Platelets</b>	1.24	1.97	2.64
<b>LFT – TB / DB / TP / ALB</b>	0.66 / 0.45 / 5.9 / 2.8 / 91 / 80		
<b>/ AST / ALT / ALP</b>			/ 300
<b>RFT – Urea / Creat</b>	78 / 2	26 / 1	
<b>Serum Electrolytes – Na / K / Cl</b>	125 / 4.1 / 94	129 / 4.6 / 98	
<b>TSH</b>	1.22		
<b>Urine routine</b>	Pale yellow, pH – 5, Alb + , Pus cells 2 – 3, Ep cells 1 -2 , No casts, RBCs		
<b>Fever profile – Dengue profile</b>	Negative		
<b>PS for MP</b>	Negative		
<b>IgM leptospira</b>	Negative		
<b>Widal test</b>	Negative		
<b>HIV, HCV, HbsAg</b>	Negative		
<b>Radiology – CXR – PA view</b>	WNL		
<b>Ultrasound abdomen and pelvis</b>	No definitive sonological abnormality detected		
<b>NCS</b>	Normal		

Patient was treated with empirical third general cephalosporin, anti – malarials , insulin , pregabalin and other supportive measures. However, patient continued to have high grade fever spikes.

### 2.2. Case 2

A 55 year old hypertensive female from Sultanpalya, Bangalore presented with fever of 15 days duration ; vomiting, loose stools, spasmodic type of intermittent

abdominal pain, yellowish discoloration of sclera and altered sensorium since 5 days.

**Table 2:**

<b>Vitals</b>	Temperature – Febrile Pulse rate – 104 bpm BP – 160 / 90 mm of Hg RR – 18 cpm spO 2 – 95 % RA
<b>General Physical Examination</b>	Icterus + Facial puffiness + Bilateral grade II pitting pedal oedema + Purpura fulminans +
<b>Systemic examination</b>	CNS – Conscious, disoriented to time, place, person , No signs of meningeal irritation, No focal neurological deficits, Flapping tremors + CVS – NAD RS – B / L NVBS , No added sounds P / A – soft, distended, diffuse tenderness + , No organomegaly or free fluid, BS +

Patient was treated as acute febrile illness with hepatitis in febrile / hepatic encephalopathy. Patient's investigations were as follows.

Patient was treated with empirical third general cephalosporin, anti – malarials , hepatic pre – coma regimen and other supportive measures. However, patient continued to have high grade fever spikes.

### 2.3. Case 3

A 59 year old female from Tumkur presented with history of fever since 10 days and blackish discoloration of the fingers and toes since 5 days associated with a burning sensation. On examination, vitals were stable and all peripheral pulses were well felt. Cardiovascular examination revealed a mid – systolic click with a short systolic murmur in the apex. Patient had marfanoid habitus. Central nervous system examination revealed hyperaesthesia of bilateral lower limbs upto mid – calf with loss of vibration and joint position sense upto the ankle. Other system examination was unremarkable. Investigations were as follows.

Patient was being treated as acute febrile illness with suspected vasculitis. Patient was initiated on empirical antibiotics, steroids in view of possible vasculitis and other supportive measures. However, patient continued to have high grade fever spikes.

## 3. Discussion

All the patients underwent Weil Felix test during the acute phase and the second week of illness in view of persistent symptoms and fever spikes. All three patient's serum was positive for antibodies against OX 2 in significant titres during the second week (of more than 1:320). All other fever

Table 3:

	04/5/21	06/5/21	13/5/21
<b>CBC – Haemoglobin</b>	11.1	11.8	9.4
<b>RBC count</b>	3.79	4.1	3.29
<b>PCV</b>	32.6	35.4	28.68
<b>MCV</b>	86.3	86.7	89.6
<b>WBC</b>	14,740	13,320	11,660
<b>Platelets</b>	2.66	4.40	2.98
<b>ESR</b>	60		
<b>LFT – TB / DB / TP / ALB / AST / ALT / ALP</b>	4/2/19 – 9.03 / 7.77 / 5.6 / 2.3 / 76 / 67 / 34 / 263		
<b>Serum ammonia</b>	62 $\mu$ / L		
<b>Coagulation profile</b>	APTT – 33 sec, INR – 1.10		
<b>RFT – Urea / Creat</b>	15 / 0.8 26 / 1		
<b>Serum Electrolytes – Na / K / Cl</b>	132 / 4.3 / 97 130 / 3.9 / 96		
<b>TSH</b>	1.7 $\mu$ / L		
<b>Urine routine</b>	Pale yellow, pH – 5, Alb + , Pus cells 2 – 3, Ep cells 1 -2 , No casts, RBCs		
<b>Fever profile – Dengue profile</b>	Negative		
<b>PS for MP</b>	Negative		
<b>Widal test</b>	Negative		
<b>IgM leptospira</b>	Negative		
<b>Anti – HAV</b>	Negative		
<b>IgM / IgG</b>			
<b>HIV, HbsAg, HCV</b>	Negative		
<b>Urine C / S , Blood C / S</b>	No growth		
<b>LP – CSF analysis</b>	4 ml, clear, protein and glucose – normal, 16 cells - 100% lymphocytes,		
<b>Radiology – CXR – PA view</b>	WNL		
<b>Ultrasound abdomen and pelvis</b>	Hepatomegaly		
<b>NCCT brain</b>	Normal		
<b>2D – ECHO</b>	Sclerotic aortic valve, Mild TR, Mod PAH, Grade 1 LVDD, LVEF – 57 %		

work up were negative. They were initiated on intravenous doxycycline and gradually improved.

Rickettsial diseases are some of the most covert re-emerging infections of the present times. For India, the reported numbers are an underestimate due to the lack of community based data and non-availability of confirmatory tests. Rickettsial infection in India has been documented from several states including Karnataka, Jammu and Kashmir, Himachal Pradesh, Uttaranchal, Rajasthan, Assam, West Bengal, Maharashtra, Kerala and Tamil Nadu.

Table 4:

	02/9/21	05/9/21
<b>CBC – Haemoglobin</b>	9.60	8.8
<b>RBC count</b>	3.79	3.60
<b>PCV</b>	30	27
<b>MCV</b>	80	76
<b>WBC</b>	10,550	10,000
<b>Platelets</b>	36,000	1.47
<b>ESR</b>	36	
<b>PS</b>	Normocytic anaemia with leucocytosis	hypochromic with neutrophilic
<b>LFT – TB / DB / TP / ALB / AST / ALT / ALP</b>	1.7 / 0.6 / 6.0 / 2.7 / 51 / 69 / 477	
<b>Coagulation Profile</b>	APTT – 46 sec, INR – 1.11	
<b>RFT – Urea / Creat</b>	20 / 0.4 26 / 1	
<b>Serum Electrolytes – Na / K / Cl</b>	127 / 3.3 / 88 129 / 3.1 / 90	
<b>TSH</b>	1.22	
<b>Urine routine</b>	Pale yellow, pH – 5, Alb + , Pus cells 2 – 3, Ep cells 1 -2 , No casts, RBCs	
<b>Fever profile – Dengue profile</b>	Negative	
<b>PS for MP</b>	Negative	
<b>IgM leptospira</b>	Negative	
<b>Widal test</b>	Negative	
<b>HIV, HCV, HbsAg</b>	Negative	
<b>Urine C / S , Blood C / S</b>	Negative	
<b>ANA profile</b>	Negative	
<b>p – ANCA , c -ANCA</b>	Negative	
<b>Radiology – CXR – PA view</b>	WNL	
<b>Ultrasound abdomen and pelvis</b>	Right ovarian simple cyst	
<b>Doppler ultrasound of all 4 limbs</b>	No significant abnormality detected	
<b>NCS</b>	Normal	
<b>2D - ECHO</b>	Degenerative MVP, Mild MR, Grade 1 LVDD, LVEF – 63%	

RMSF is caused by an obligatory intracellular bacteria, *Rickettsia rickettsii*, which spreads to human beings via tick bite,<sup>1</sup> most commonly by the American dog tick (*Dermacentor variabilis*) in eastern US, however, it can also be transmitted by the Rocky Mountain wood tick (*Dermacentor andersoni*) in the Rocky Mountain states.<sup>5</sup> The pathophysiological events leading to the clinical manifestations are due to infection of the endothelial cells lining the small vessels of the organ systems leading to irreversible damage to the endothelium<sup>6</sup>. It initially presents with nonspecific symptoms such as fever, rash, myalgia, headache, nausea and vomiting, which can easily be confused for other illnesses.<sup>7</sup> Uncommon presentations of RMSF are not well categorized, but many neurologic complaints, visual disturbances, myocarditis and generalized weakness.<sup>8</sup> Laboratory investigations are

usually normal during the initial stages of the infection and definitive diagnostic results can take weeks to become positive<sup>9</sup>. Immuno Fluorescence Assay (IFA) of IgG titers during the acute and convalescent phase is considered gold standard. Doxycycline is the recommended treatment in all the age groups and it reduces morbidity and mortality when given within the first five days of symptom onset.<sup>10,11</sup> Current literature shows that tooth staining and enamel hypoplasia do not occur with short duration of therapy with doxycycline, even in those under eight years of age.<sup>12</sup> Chronic sequelae are not completely understood, but, some of the reported complications included neurologic deficits and necrosis of the skin or extremities.<sup>8</sup>

The triad of tick bite, fever and rash is used to identify RMSF.<sup>13,14</sup> Early clinical consideration is critical in RMSF because treatment within the first five days of illness significantly reduces the severity of disease and probability of death

#### 4. Conclusion

Patients can have varied clinical manifestations as presented above. The diagnosis requires a high index of suspicion and can pose a dilemma. Failure of early diagnosis and treatment can lead to significant morbidity, mortality and expensive PUO workup.<sup>15</sup> Because there is no vaccine available against RMSF, avoidance of tick-infested areas is still the best way to prevent the infection.

#### 5. Conflict of Interest

None.

#### 6. Source of Funding

None.

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