

Malignant Mediterranean spotted fever

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ABSTRACT

Fever with rash is one of the most common causes of referral to a dermatologist. A plethora of conditions need to be considered in the differential diagnosis. They may be broadly classified into infectious causes, drug reactions, and autoimmune disorders. Here we present a rare case of rickettsial fever with cardiac involvement in an elderly male patient with no comorbidities.

Key words: Cardiac involvement, doxycycline, LV dysfunction, *Rickettsia conorii*, spotted fever group rickettsia, rockymountain spotted fever

INTRODUCTION

Fever with rash is almost always a diagnostic dilemma for the treating physician. Myriad causes can range from common viral exanthems, bacterial, parasitic, or spirochaete infections to connective tissue disorders and drug reactions. In most cases of fever with rash, the dermatological features provide a clue to the diagnosis and initiation of treatment. Rickettsiosis is one among the causes of fever with rash, and owing to its rarity in the Indian subcontinent, ranks low in the hierarchy of differentials. Rickettsiosis is acute febrile, arthropod-borne disease caused by obligate intracellular bacteria.^[1] The classification of rickettsiosis is given in Table 1. We herein report a rare case of rickettsial spotted fever with severe cardiac involvement in an elderly Tibetan male from India.

CASE REPORT

This patient presented with acute onset of breathlessness along with fever and was admitted in cardiac intensive care unit with an initial diagnosis of pulmonary edema secondary to severe left ventricular dysfunction. Dermatology consult was asked for in view of fever with rash.

A 76-year-old Tibetan male, farmer by occupation, hailing from Mungod in North Karnataka presented fever of nine days and skin rash of four days duration. Fever was intermittent in nature

associated with malaise. He went on to develop a skin rash over his hands, legs, and face, four days prior to admission. Lesions initially appeared as flat reddish lesions, which gradually increased in size and number and later became hemorrhagic with associated swelling of both hands and feet. He denied any history of joint pains or swelling of any specific joint.

He was not a known diabetic or hypertensive individual, and had no significant medical or surgical history. On general examination, he was found to be well built and nourished, also well oriented to time, place, and person. He was febrile, with a pulse rate was 110/min, irregular, and a blood pressure of 100/70 mmHg. On systemic examination, cardio-vascular system—S1 was variable, S2 was normal, there were no murmurs; respiratory system—bilateral basal crepitations were present. There were no significant findings on per abdomen and central nervous system examination. Cutaneous examination revealed multiple petechiae and palpable pupura with hemorrhagic bullae localized to extensor and flexor aspect of both

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hands and feet along with involvement of the tip of nose. The oral and genital mucosa were not affected.

Routine investigations were done. Complete blood count showed neutrophilia and LFT showed mild elevation of liver enzymes. Echocardiography (ECG) showed atrial fibrillation. Echocardiography revealed severe LV dysfunction with ejection fraction (EF) of 25% (Normal: 55%–70%), and LV global hypokinesia. Tests for dengue, malaria, leptospirosis, and typhoid were negative. Weil–Felix test showed OX 2 positive in high titers (1:160) favoring a diagnosis of spotted fever group rickettsia. The rickettsial immunofluorescence assay (IFA) and PCR could not be done due to financial constraints.

He was given oral doxycycline 100 mg twice a day for 15 days along with supportive treatment for LV dysfunction and atrial fibrillation. He showed a remarkable improvement clinically within a week of initiating treatment, with regression of rashes (pretreatment images: Figures 1 and 2 and posttreatment images: Figures 3 and 4).

He was discharged on diuretics, rate limiting and bathmotropic agents, and advised bed rest in view of his LV dysfunction. A follow-up ECG done at 4 weeks post-discharge revealed marked improvement in ejection fraction to 40%. Atrial fibrillation persisted with controlled ventricular rate. Weil–Felix test was repeated and the titers had decreased to 1:40.

Table 1: Classification of rickettsiosis^[1-5]

Disease	Causative organism
Scrub typhus	Orientia/tsutsugamushi
Spotted fever	R. rickettsii, R. conorii, R. africae, R. japonica
Murine/Epidemic typhus	Rickettsia typhi and R. prowazekii



Figure 1: Pretreatment image 1: multiple petechiae and palpable pupurae with hemorrhagic bullae localized to extensors and flexor aspect of both hands

DISCUSSION

Rickettsiae are obligate intracellular gram-negative bacteria causing acute febrile, zoonotic diseases. Rickettsiosis is an endemic condition in many areas of the world, and ticks play an important role as vector, among the various other arthropods.^[2] As each tick species has a preference for certain environmental conditions, tick-borne diseases are habitually restricted to specific geographic areas. The SFG rickettsiae of Southeast Asia are yet to be identified.^[3] Rickettsioses are generally believed to have re-emerged in many parts of India. Various studies indicate endemicity of rickettsiosis in parts of India as well as the existence of Indian tick typhus as a zoonosis.^[4-6] Mungod, a town in northern Karnataka, has been referred to as 'Little Tibet'. The town is surrounded by forests to the northeast and the



Figure 2: Pretreatment image 2: multiple petechial rash localized on nose

primary occupation being farming and the major crop being paddy rice.

Ours is a rare case of malignant Mediterranean spotted fever from southern India with severe cardiac involvement in an elderly male with no prior medical conditions. The prefix malignant is used to signify the co-occurrence of complications, which are usually seen in the elderly and/or immunocompromised patients.^[7,10] A single case of myocarditis as the presenting feature of rickettsia has been reported in a child from India.^[1] Another the case report of rickettsiosis in an adult male with pre-existing diabetes was reported from Uttar Pradesh, India in 2014.^[10]

Most patients with rickettsiosis have a benign and self-limiting course. The presenting features include a clinical triad of fever, headache, and rash.^[7] The differential diagnosis for spotted fever group rash is enumerated in Table 2. In our case, a similar clinical triad was present but the patient also had a severe form of petechial, purpuric eruptions including hemorrhagic bullae involving mainly palms and soles. Along with this severe rash, our patient had cardiac involvement in the form of severe LV dysfunction and atrial fibrillation leading to congestive cardiac failure. According to a review of the literature, cardiac involvement in the spotted fever group is very rarely seen. In 7%–16% of cases it may present as dysrhythmias.^[9] There are few articles regarding cardiac involvement in Rocky Mountain Spotted Fever in the form of myocarditis and LV dysfunction in children. Our elderly male patient had cardiac involvement, which is a rare entity in the spotted fever group.

Serological testing by Weil–Felix test showed OX 2 positivity in 1:160 titers, which goes in favor of spotted group rickettsia. Titers dropped to 1:40 after treatment. Interpretation of Weil–Felix reaction is given in Table 3.

Our patient responded to doxycycline, which is the drug of choice for the spotted fever group.



Figure 3: Posttreatment image 3: resolving petechiae and palpable pupura of both hands and feet

Successful therapeutic drugs for treatment include doxycycline (100 mg bid PO), ciprofloxacin (750 mg bid PO), and chloramphenicol (500 mg qid PO). Pregnant patients should be treated with josamycin (3 g/day PO for 5 days).^[8] The recommended duration of treatment for patients presenting with the benign form is 7 days, whereas the duration for the malignant form is 2 weeks.^[11]

CONCLUSION

To summarize, ours was a rare case of malignant Mediterranean spotted fever with cardiac involvement in an elderly male patient with no prior medical illnesses.

Table 2: Differential diagnosis for spotted fever group of rickettsial rash^[14]

Disease	Causative agent	Clinical features
Rocky mountain spotted fever	Rickettsia rickettsii	Erythematous macules/papules to petechial rash starting on ankles/wrists, spreads centripetally, may involve palms soles
Endemic typhus	Rickettsia typhi	Erythematous macules/papules involving trunk > extremities
Human monocytic ehrlichiosis	Ehrlichia chaffeensis	Erythematous macules/papules, or petechial rash; more common in children
Meningococcal disease	Neisseria meningitidis	Erythematous macules/papules to petechiae usually start on lower extremities & spreads centripetally
Group A streptococcal pharyngitis	Streptococcus pyogenes	May cause petechial rash in children
Erythema infectiosum	Human parvovirus B19	“Slapped cheek” appearing erythematous rash on face and trunk
Roseola infantum	Human herpes virus 6	Morbiliform rash begins on trunk, which spreads & disappears rapidly
Enteroviral infection	Echovirus, coxsackie virus, other enteroviruses	Fine morbilliform rash on face, spreads caudally; occasionally petechial

Table 3: Weil-Felix reaction in rickettsial diseases^[15,16]

Diseases	Agglutination pattern with		
	OX 19	OX 2	OX K
Epidemic typhus	+++	+	–
Endemic typhus	+++	+/-	–
Spotted fever group	+	+++	–
Scrub typhus	–	–	+++

OX are antigens required for weil felix test

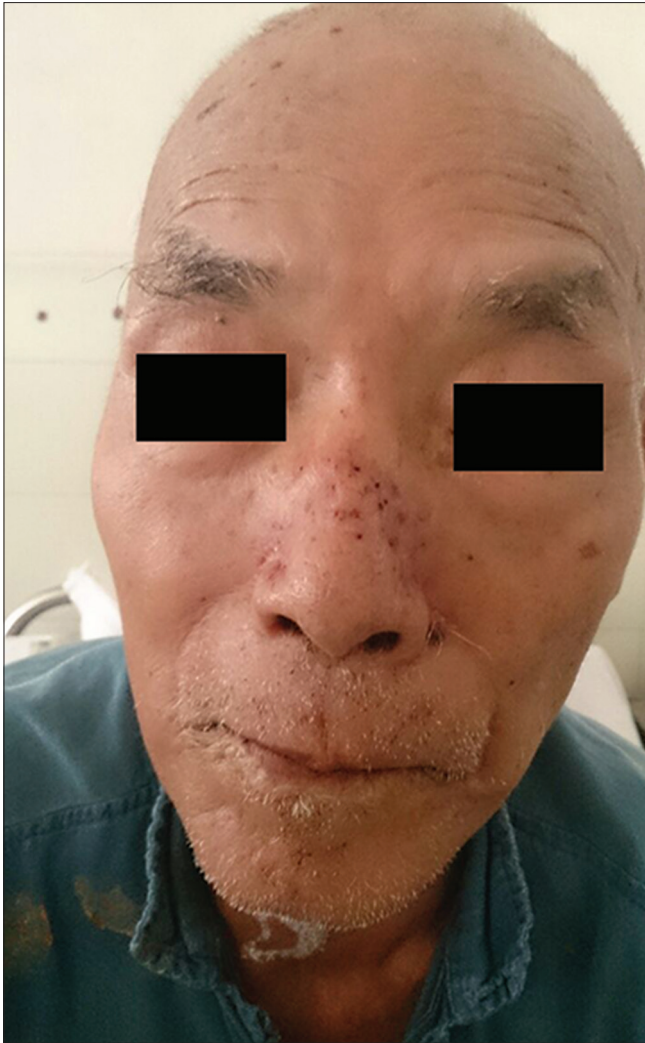


Figure 4: Posttreatment image 4: resolving petechial rash on nose

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published

and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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