HHS Public Access

Author manuscript

Am J Med Sci. Author manuscript; available in PMC 2017 April 18.

Published in final edited form as:

Am J Med Sci. 2013 November ; 346(5): 427–429. doi:10.1097/MAJ.0b013e318295c788.

Atypical Rocky Mountain spotted fever with polyarticular arthritis

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Abstract

Background—Rocky Mountain Spotted Fever (RMSF) is an acute, serious tick borne illness caused by Rickettsia rickettsi. Frequently RMSF is manifested by headache, a typical rash and fever but atypical disease is common, making diagnosis difficult. Inflammatory arthritis as a manifestation is rare

Purpose—Describe a patient with serologically proven RMSF who presented in an atypical manner with inflammatory arthritis of the small joints of the hands, and to review the previously reported patients with rickettsial infection and inflammatory arthritis

Patient—An 18 year old woman presented with a rash that began on the distal extremities and spread centrally, along with hand pain and swelling. She had tenderness and swelling of the metacarpophlangeal joints on exam as well as an erythematosus macular rash, and occasional fever. Acute and convalescent serology demonstrated Rickettsia rickettsi infection. She was successfully treated with doxycycline.

Conclusion—Inflammatory arthritis is a rare manifestation of RMSF or other rickettsial infection with eight previously reported patients, only one of whom had RMSF. Physician must have a high index of suspicion for RMSF because of atypical presentations.

Introduction

Rocky mountain spotted fever (RMSF) is an acute, potentially lethal tick borne illness (1,2). The disease is curable if identified promptly but its diverse presentations make early diagnosis difficult. Even with the classical presentation, sometimes physicians are unable to institute early treatment because the initial diagnosis must be purely clinical (1, 2) and hence it is very commonly missed even in endemic areas (3). But if this disease presents in an atypical fashion it is even harder to recognize and the life of patients involved may be at great risk.

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There are no sources of support.

-There are no disclaimers, or conflicts of interest.

-Informed consent has been obtained.

Here we describe an 18 year old woman who presented with rash and swelling of hands with inflammatory arthritis of the metacarpophalangeal joints, but no classical rash progression or fever. We then review of the epidemiology, clinical features, differential diagnosis, treatment, and prognosis of this interesting disease entity.

Case report

An 18 year old woman was admitted with an itchy rash on both arms since three days (see Table 1 for a summary of her course). She had switched to a new brand of tampons four days ago, two days after which she started having pruritic arms along with mild pain and swelling in both hands. The swelling subsided and pain resolved but the rash, which was blanching, macular and erythematous, spread to her knees, legs, ankles and feet along with worsening of the pruritis. She did have some chills the day of admission along with a single episode of non-bloody vomiting but she had not taken her temperature despite the chilly sensation. There were no complaints of sore throat, odynophagia, oral ulcers, fatigue, cough, diarrhea, dysuria or burning micturition. There was no discharge from the eyes, ears or nose, nor was there history of trauma, sick contacts, travel, pets, insect bites, recent sexual activity, vaginal itch or discharge. There was no allergic history and no smoking, alcohol or drug abuse.

On admission the vital signs were: body temperature: 37.7 F, pulse rate: 108/min, respiratory rate: 20/min, blood pressure: 109/81 mm of Hg, oxygen saturation: 97% on room air. Neck exam was significant for posterior cervical lymphadenopathy. There was a blanching, erythematous, macular, fleeting rash from ankles to thighs bilaterally. There was tenderness of all metacarpophalangeal joints with thickening of the synovium and moderate swelling. No other joints were tender. On admission the laboratory tests showed normal electrolytes, renal function, liver enzymes, hemoglobin and hematocrit. The only abnormality was a mild leukocytosis (11.3/mm^3) with a left shift but no immature forms. Urine analysis was normal. Serologies for Hepatitis A, B and C were negative. Anti-nuclear antibodies were positive with a titer of 1:80 and a homogenous pattern. Rapid streptococcus antigen test and anti-streptolysin O (ASO) titers were negative. Human immunodeficiency virus (HIV) testing was negative as was rheumatoid factor. C-reactive protein was elevated (18.4 mg/L). Other serological testing, including for Epstein-Barr virus, parvovirus, cytomegalovirus, toxoplasma, and coxsackie virus A and B, were negative as well.

During her hospital stay she was initially started on vancomycin and clindamycin for possible toxic shock syndrome. She felt better on the third day and there was resolution of leukocytosis. Cultures of the blood and urine did not grow a pathogenic organism, so the diagnosis of toxic shock syndrome was in doubt. Because she had definite inflammatory arthritis of the small joints of the hands, additional diagnoses were entertained. These included Still's disease as well as rheumatoid arthritis. While the rash was not typical of the former, she did have acute arthritis and fever, the latter after admission. History was obtained that the rash started distally on her upper extremities and spread proximally. Thus, we made a presumptive diagnosis of a RMSF based on the rash and spring season in an endemic region. Antibiotic therapy was changed to doxycycline and the rash almost completely resolved. She was discharged with instructions to take doxycycline for two weeks.

Indeed, three days after discharge IgM antibody for RMSF returned as positive at 1.37 units, considered high positive for the assay. The patient was called about the result. She had not been taking the doxycycline, and had developed extreme fatigue, fever, nausea, vomiting, headache, abdominal pain and the rash had reappeared (Table 1). Doxycycline was re-started at that time and within one week there was a complete resolution of her symptoms. Acute serology for RMSF IgG was negative while the titer after three months was 1:128, a 7-fold rise (Table 1). Hence, the diagnosis was confirmed with seroconversion with a greater than 4-fold rise in the tier.

Discussion

Rocky mountain spotted fever is a life threatening tick borne illness caused by *Rickettsia ricketsii,* which is a fastidious, small (0·2–0·5 μm by 0·3–2·0 μm), pleomorphic Gram-negative, obligate intracellular coccobacillus (1,2). The American dog tick (*Dermacentor variabilis*), is the primary vector of *R rickettsii* in USA (1, 2). RMSF was described at the end of the nineteenth century among residents of the Bitter Root and Snake River valleys of Montana and Idaho (4). The etiologic agent is name after Howard Ricketts, who isolated the pathogen (5).

The highest prevalence of the disease is in south eastern and south central states (most cases in Oklahoma and North Carolina) with 90–93% cases occurring between April and September. In the past, RMSF had a high mortality rate up to 87% but currently it is fatal in 20% of untreated and 5% of treated cases (6).

Patients with RMSF can have a diverse spectrum of presentation with cutaneous, cardiac, pulmonary, gastrointestinal, renal, neurological, ocular, and skeletal muscle manifestations (7), which are highly variable from patient to patient. The mean incubation period of RMSF is 7 days. The classic triad of fever, headache and rash is present in only 3% of patients in first three days (3,8). The typical clinical triad develops in 60–70% of patients within 2 weeks following the tick bite (9). About one-third of patients do not recall a tick bite or tick contact despite the short incubation time. Rash can occur from second day to fourteenth day of illness and initially appears as small (1–5 mm) erythematous macules usually seen first on wrists, forearms, and ankles spreading rapidly and involving the palms and soles, becoming petechial by the end of the first week (10). Fourteen percent of patients can have rash on the first day, while less than 50% have a rash in first 72 hours. The rash of RMSF can also be atypical and can be delayed in onset past five days. In 10% of patients, spotless RMSF occurs (10,11).

Physical findings such neck stiffness, hepatosplenomegaly and lymphadenopathy can be seen. Laboratory abnormalities including anemia, leukocytosis, thrombocytopenia, hyponatremia, deranged coagulation parameters, elevated liver enzymes and bilirubin and elevated creatine kinase can occur. Complications in order of most frequent to least frequent occurrence are encephalopathy, seizures, acute renal failure, acute hepatic dysfunction, myocarditis and death. The differential diagnosis is extensive as listed in the Table 2.

In our patient, Still's disease (or systemic onset idiopathic juvenile arthritis) was considered due to rash and inflammatory arthritis but lack of persistent fevers and limited involvement of only metacarpophalangeal joints made it less likely. Polyarticular inflammatory arthritis as a presentation of RMSF has not been previously reported to our knowledge. Sexton and his colleagues reported monoarticular arthritis in a 30 year man with RMSF, who also presented with fever, headache, declining mental status, and diarrhea. He had a petechial rash from thrombocytopenia but no rash typical of RMSF. White blood cell count in the joint fluid was 378/mm^3. Other rickettsial infections have been reported with acute arthritis on presentation. Mediterranean spotted fever or Boutonneuse fever caused by *Rickettsia conorii* has been reported to cause monoarthritis in Spain (12). In a report from Israel, 3 of 15 patients with a disease similar to Mediterranean fever had arthritis (13). One of these had monoarthritis of the knee, one had olgioarthritis (knee and elbow) and one had a polyarthritis with involvement of the elbows, ankles, and wrists (13). Sri Lankan investigators recently reported three patients presenting with arthritis, erythema nodosum but no fever. A serological diagnosis of acute *Rickettsia conorii* was made, and the arthritis as well as the rash resolved with doxycycline therapy (14). Lastly, endemic typhus, caused by *Rickettsia typhi,* has been reported with bilateral knee arthritis. Again, this patient responded to doxycycline (15). One investigation of arthritis with Mediterranean spotted fever showed immune complexes in both the serum and synovial fluid along with low complement C3 levels in the synovial fluid. These data suggest immune complex deposition in the joint mediated the acute arthritis, at least in this patient (16). The significant features of Rickettsial infections presenting as arthritis are outlined in Table 3.

The treatment of choice for rickettsial illness is doxycycline 100 mg given twice daily for adults, and 2.2 mg/kg body weight per dose given twice daily for children weighing less than 45 kg. These recommended doses may be given orally or intravenously and treatment should be maintained for 5–7 days (17,18). Doxycycline therapy should be continued until the patient is afebrile for at least 2 or 3 days. Our patient and others reported with arthritis have responded to this therapy.

Our patient has a certain diagnosis of acute Rocky Mountain Spotted Fever but also certainly had a highly unusual presentation. She had fever and this was perhaps the only characteristic finding. Along with the polyarthritis, she had an atypical rash, and no laboratory or other features common with consistent with the disease. Thus, our patient is unique because of the unusual presentation without fever (at least on presentation, as she later had fever) and without the typical petechial rash although early on the rash can be classically macular as in our case. Other confounding elements were posterior cervical lymphadenopathy and inflammatory arthritis in metcarpophalangeal joints along with the resolution and then the reappearance of the rash.

Arthritis is a rare manifestation of RMSF and other rickettsial diseases as discussed above. Even with typical features, the diagnosis of RMSF is particularly difficult in the non-specific early stages of the disease. The clinical presentation of our patient made the correct diagnosis extremely challenging. We emphasise the fact that physicians should have a high index of suspicion for RMSF in spring and summer seasons because, if missed, this disease can be fatal even in previously healthy, young people (19).

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Am J Med Sci. Author manuscript; available in PMC 2017 April 18.

Table 1

Course of the patient presented herein with Rocky Mountain Spotted Fever and polyarthritis. Day 1 is the start of the illness. She was hospitalized on Day 4–7.

	Time Course (days)					
Feature	**Days 1–3**	**Day 4**	**Day 5–7**	**Day 8–12**	**Day 13–23**	**Day 90**
Fever	−	+	−	+	−	−
Rash	+	++	−	++	−	−
Headache	−	−	−	+	−	−
Arthritis	+	++	+	++	−	−
Leukocytosis		+	−			
Abdominal pain	−	−	−	−	−	−
Doxycycline *			+	−	+	−
RMSF IgM			positive			
RMSF IgG			negative			1:128

+ This manifestation was present − This manifestation was not present

* She received doxycycline while hospitalized on Days 6–7 and then as an outpatient on Days 13–23.

Table 2

Differential diagnosis of Rocky Mountain Spotted Fever

Infectious	Non-infectious
Typhoid fever	Idiopathic thrombocytopenic purpura
Scarlet fever	
Pharyngitis	
Pneumonia	
Meningococcemia	
Hepatitis	
Leptospirosis	
Rubella	
Parvovirus	
Toxoplasma	
Infectious mononucleosis (Epstein-Barr virus)	
Cytomegalovirus	
Coxsackie virus A, B	

Table 3

Salient features of reported Rickettsial infections presenting as arthritis

Reference	Rickettsia/disease	Type of Arthritis
Present	Rickettsia rickettsi	Polyarticular involving hands
Pascual et al, 1991	Rickettsia typhi	Monoarticular
Sexton et al, 1992	Rickettsia rickettsi	Monoarticular
Cobeta et al, 1993	Rickettsia conorii	Monoarticular
Klein et al, 1995	Israeli spotted fever	Monoarticular oligoarticular polyarticular involving elbows, ankles, wrists
Premaratna et al, 2009	Rickettsia conorii	Monoarticular