Case Reports

Successful Treatment of Rocky Mountain 'Spotless' Fever

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IN THE WESTERN United States, a person with a febrile illness who has been exposed to ticks may be infected with *Rickettsia rickettsii, Borrelia* sps or Colorado tick fever virus. In the early stages of a patient's illness, the clinician may not be able to distinguish among the diseases caused by these infectious agents. If clinical findings suggest the possibility of rickettsial infection the physician should institute treatment while tests to define the etiologic agent are being pursued. A case of a patient who was successfully treated for Rocky Mountain "spotless" fever illustrates the importance of early empiric therapy for *R rickettsii.*

Report of a Case

A previously healthy 35-year-old woman from Seattle, Washington, went hiking in Idaho in early July 1982. She was exposed to numerous ticks, but noted no definite tick bites. Four days after her first tick exposure, a high fever suddenly developed that was associated with a frontal headache, myalgia and general malaise. She was seen by Dr Royal A. McClure at the Mollie Scott Clinic in Sun Valley, Idaho, where results of a physical examination were entirely normal except for an oral temperature of 39.1°C (102.4°F). Initial laboratory findings included a hematocrit of 42%; leukocyte count, 7,400 per μl, with 83% polymorphonuclear leukocytes and 5% band forms. Serum electrolyte, blood sugar and blood urea nitrogen values were normal, but the serum aspartate amino transferase value was elevated to 101 IU per liter. The woman was admitted to hospital and on the second day her temperature rose to 40.2°C (104.4°F) despite aspirin and acetaminophen administration. Eight cultures of blood specimens drawn during the first 48 hours of her hospital course were negative for any pathogens and a chest roentgenogram showed no abnormalities. On the third hospital day, the patient's temperature dropped to 37.3°C (99°F) and her headache and other symptoms resolved. On the following day, however, her fever returned along with headache, nausea and myalgia; she also had one episode of diarrhea. In addition, her urine was "dark" and tested positive for hemoglobin. On the fourth day in hospital, the hematocrit was 30% and the leukocyte count was 5,700 per μl with 60% polymorphonuclear leukocytes and 31% band forms; the platelet count was 140,000 per μl. No abnormalities were found on repeat physical examination and no skin rash was seen. Over the next two days, the patient's temperature remained elevated at 38.3°C (101°F) and the hematocrit values remained stable. A repeat serum aspartate amino transferase test showed a value of 194 IU per liter. At this time, six days after the onset of illness, the patient was started on a regimen of tetracycline (500 mg by mouth four times a day) because of a possibile diagnosis of Rocky Mountain "spotless" fever.

The patient returned to Seattle and three days later was admitted to University Hospital because of continued fever, headache, nausea, myalgia and general malaise. She had been taking tetracycline faithfully for three days. On initial physical examination, vital signs were as follows: blood pressure 114/66 mm of mercury, temperature 38.4°C (101.1°F) and pulse 76 per minute. No skin rash was present and results of physical examination were entirely normal.

Laboratory data included a hematocrit of 32%; leukocyte count of 13,000 per μl, with no band forms in the differential, and normal serum electrolyte, blood urea nitrogen, blood glucose and creatinine values. Tests revealed elevated values for serum aspartate amino transferase (143 IU per liter), serum alanine amino transferase (170 IU per liter) and alkaline phosphatase (234 IU per liter). Analysis of urine and chest x-ray studies showed no abnormalities. There was no evidence of past or present hepatitis A or B infection. Tetracycline therapy was continued at a dose of 500 mg by mouth four times a day for the next five days. The patient's symptoms slowly resolved during this period and, at the time of discharge home, she had no fever.

During the patient's hospital course, a sample of clotted blood was sent to the Vector Borne Diseases Division, Bureau of Laboratories, Center for Disease Control (CDC) in Fort Collins, Colorado, for culture for Colorado tick fever virus. The culture yielded no organisms. Blood specimens for serologic studies were obtained at the time of admission to University Hospital (eight days into the illness) and again three weeks later. The specimens were analyzed by the CDC laboratories at Fort Collins, Colorado, using the neutralization test, and no evidence of Colorado tick fever was found. The specimens were also sent to the Centers for Disease Control laboratories in Atlanta for detec-

(Ramsey PG, Press OW: Successful treatment of Rocky Mountain 'spotless' fever. West J Med 1984 Jan; 140:94-96.)

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Submitted, revised, August 1, 1983.

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TABLE 1.—*Clinical Features of Three Tick-borne Infections Found in the Western United States*

	Rocky Mountain Spotted Fever	*Relapsing Fever*	*Colorado Tick Fever*
Agent	*Rickettsia rickettsii*	*Borrelia* sps	RNA virus
Tick vector	*Dermacentor* sps	*Ornithodoros* sps	*Dermacentor* sps
Incubation period	4 to 8 days	3 to 7 days	4 to 5 days
Onset of symptoms*	Sudden	Sudden	Sudden (50% of cases have biphasic course)
Rash			
At onset of illness	No	No	No
At day 4	Typical rash see in approximately 90% of patients†	Maculopapular rash or petechiae may occur	No (5% to 10% of patients may have a macular rash)
Respiratory tract findings	Possible	Possible	Rare
Splenomegaly	Possible (50%)	Possible (50%)	Rare
Hepatitis	Possible	Possible	Rare
Edema	Possible	No	No
Encephalopathy	Possible	Rare	Rare
Laboratory findings	Hyponatremia, anemia, thrombocytopenia, disseminated intravascular coagulation	Thrombocytopenia	Leukopenia

*Fever, headache, myalgia and malaise occur in most patients. Some patients may also experience abdominal pain, nausea, vomiting or diarrhea.
†Rash may not appear in patients who receive early treatment.

tion of rickettsial antigens by indirect fluorescent antibody and complement fixation techniques. By indirect fluorescent antibody assay, a rise in titer for Rocky Mountain spotted fever from 1:64 in the acute serum to 1:512 in the convalescent specimen was reported. These results were interpreted as indicating acute infection with Rocky Mountain spotted fever. The CDC does not currently use the complement fixation technique in serologic studies to diagnose Rocky Mountain spotted fever. A *Proteus* agglutination test done in our laboratory on a specimen taken during convalescence showed a strong reaction with OX-19 (1:160), a weak reaction with OX-2 (1:20) and no reaction with OX-K.

The patient has been seen in follow-up visits twice since her hospital stay. Liver function test values returned to normal and the patient felt entirely well one month after leaving the hospital. She remained well and had no evidence of relapsing infection when she was examined during a clinic visit five months later.

Discussion

The widely accepted terms for diseases associated with tick-borne infections are misleading. Rocky Mountain spotted fever occurs more frequently in the eastern United States than in the Rocky Mountain area,[1,2] and the typical spotted rash may be absent.[1,3,4] Colorado tick fever has been reported in eight western states in addition to Colorado[5] and relapsing fever does not necessarily relapse.[6] A history of tick bite suggests the possibility of one of these infections, but 50% of patients may not report a tick bite and as many as 10% to 20% of patients may not even report tick exposure.[1,5,6]

Clinical findings may help a clinician distinguish among the tick-borne infections (Table 1). However, these diseases often are clinically similar during the first week of illness. Careful microscopic examination of a blood smear can provide a rapid diagnosis of infection with *Borrelia* sps,[6] but there are no rapid laboratory tests available for promptly diagnosing Colorado tick fever or *Rickettsia rickettsii* infection. Fluorescent antibody staining of erythrocytes may allow detection of Colorado tick fever virus[5] and fluorescent antibody staining of a specimen from a skin lesion can provide a rapid diagnosis of Rocky Mountain spotted fever.[7,8] However, these techniques are only available in a few laboratories. The *Proteus* agglutination test (Weil-Felix reaction) is not a reliable method for early diagnosis of *R rickettsii* infection.[9] Multiple organ system involvement with clinical findings of coagulation abnormalities, hepatitis, lower respiratory tract findings, encephalopathy or renal failure may suggest the diagnosis of Rocky Mountain spotted fever in the later stages of a patient's illness.[10-14]

As many as 86% of patients with Rocky Mountain spotted fever may not have the typical spotted rash within the first four days of the onset of illness[4] and in a few patients a skin rash[1] may never develop. Several investigators have suggested that early antibiotic treatment of Rocky Mountain spotted fever can delay or prevent the rash. When the characteristic rash does not develop in the first few days of a patient's illness, delay in diagnosis and treatment results. Five recent cases of fatal Rocky Mountain "spotless" fever have been reported in patients in whom the diagnosis was missed because of the absence of typical skin findings in the first five to seven days of illness.[3,4]

Fever and systemic symptoms did not resolve in our patient until she had received tetracycline for seven days. The delayed response to tetracycline and the biphasic nature of the initial symptoms suggested the possibility of Colorado tick fever[5] or of another viral infection. However, a slow response to tetracycline has been recognized in patients with *R rickettsii* infection,

though the biphasic nature of the onset of illness is unusual for this infection.

Our patient was successfully treated for Rocky Mountain "spotless" fever, though the diagnosis was not proved until the results of serologic studies became available six weeks after stay in hospital. The eight-day course of tetracycline was administered because of the history of tick exposure and the sudden onset of high fever, headache, myalgia, mild liver function abnormalities and the possibility of a hemolytic episode. In a patient in whom the sudden onset of a severe febrile illness develops within two weeks of possible tick exposure, empiric use of tetracycline may be indicated. Although the presence of the typical rash of Rocky Mountain spotted fever can be helpful in the differential diagnosis of tick-borne fever, the absence of cutaneous findings may be consistent with multiple causes of tick-borne fever, including *R rickettsii.*

REFERENCES

1. Hattwick MAW, O'Brien RJ, Hanson B: Rocky Mountain spotted fever: Epidemiology of an increasing problem. Ann Intern Med 1976 Jun; 84:732-739

2. D'Angelo LJ, Winkler WG, Bregman DJ: Rocky Mountain spotted fever in the United States, 1975-1977. J Infect Dis 1978 Aug; 138:273-275

3. Green WR, Walker DH, Cain BG: Fatal viscerotropic Rocky Mountain spotted fever—Report of a case diagnosed by immunofluorescence. Am J Med 1978 Mar; 64:523-528

4. Westerman EL: Rocky Mountain spotless fever—A dilemma for the clinician. Arch Intern Med 1982 Jun; 142:1106-1107

5. Goodpasture HC, Poland JD, Francy DB, et al: Colorado tick fever: Clinical, epidemiologic, and laboratory aspects of 228 cases in Colorado in 1973-1974. Ann Intern Med 1978 Mar; 88:303-310

6. Fihn S, Larson EB: Tick-borne relapsing fever in the Pacific Northwest: An underdiagnosed illness? West J Med 1980 Sep; 133:203-209

7. Walker DH, Cain BG, Olmstead PM: Laboratory diagnosis of Rocky Mountain spotted fever by immunofluorescent demonstration of *Rickettsia rickettsii* in cutaneous lesions. AJCP 1978; 69:619-623

8. Fleisher G, Lennette ET, Honig P: Diagnosis of Rocky Mountain spotted fever by immunofluorescent identification of *Rickettsia rickettsii* in skin biopsy tissue. J Pediatr 1979 Jul; 95:63-64

9. Woodward WE, Hornick RB: *Rickettsia rickettsii* (Rocky Mountain spotted fever), *In* Mandell GL, Douglas RG, Bennett JE (Eds): Principles and Practice of Infectious Diseases. New York, John Wiley & Sons, 1979, pp 1508-1514

10. Fine D, Mosher D, Yamada T, et al: Coagulation and complement studies in Rocky Mountain spotted fever. Arch Intern Med 1978 May; 138:735-738

11. Adams JS, Walker DH: The liver in Rocky Mountain spotted fever and jaundice. AJCP 1981 Feb; 75:156-161

12. Ramphal R, Kluge R, Cohen V, et al: Rocky Mountain spotted fever and jaundice. Arch Intern Med 1978 Feb; 138:260-263

13. Donohue JF: Lower respiratory tract involvement in Rocky Mountain spotted fever. Arch Intern Med 1980 Feb; 140:223-227

14. Walker DH, Mattern WD: Acute renal failure in Rocky Mountain spotted fever. Arch Intern Med 1979 Apr; 139:443-448

Bordetella bronchiseptica Bacteremia

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Bordetella bronchiseptica, a Gram-negative nonfermentative bacillus, has been extensively studied as a veterinary pathogen and in animal models of bacterial superinfection following viral respiratory tract disease.[1] There are few reports of disease in humans caused by this organism. We describe the case of a patient in whom *B bronchiseptica* bacteremia developed in hospital and persisted for ten days, despite treatment with antimicrobial agents to which the organism was susceptible in vitro. The clinical course and autopsy findings in this patient are described and previously reported cases of *B bronchiseptica* infection in humans are summarized.

Report of a Case

The patient, a 70-year-old black man, was admitted to the Veterans Administration Medical Center because of weight loss, anorexia and intermittent abdominal pain for two months. There was no history of respiratory tract infection, contact with animals or previous illness. On physical examination he was noted to have icterus and an enlarged liver; stool specimens were guaiac positive. A chest roentgenogram showed a subtle density in the right midlung field. Liver function tests showed an aspartate aminotransferase (AST, formerly SGOT) level of 200 IU and an alkaline phosphatase value of 980 IU per liter. The total bilirubin level was 7.7 mg per dl, of which 4.3 mg per dl was direct reacting. The peripheral leukocyte count was 4,500 per μl, the hemoglobin 13.3 grams per dl and the hematocrit 37.9%.

Metastatic cancer was suspected, and the following special studies were done: barium enema, liver-spleen radioisotope scan, abdominal ultrasound, endoscopic retrograde cholangiopancreatography, whole lung tomography and bronchoscopy. None of the above showed abnormalities. Serologic tests for hepatitis A and B viruses, α-fetoprotein, antimitochondrial antibody, cytomegalovirus, Epstein-Barr virus, toxoplasma and Q fever were negative. Results of serum immunoglobulins and a serum protein electrophoresis were normal. Contrast studies of the gastrointestinal tract showed a small duodenal ulcer, and treatment with cimetidine was begun on the 12th hospital day.

An elevated temperature was noted on the 18th hospital day, and one of two blood cultures done grew a Gram-negative bacillus from the aerobic bottle after 24 hours. Three additional blood cultures were taken and, again, one of three aerobic bottles was positive. Therapy that had been initiated with a "third-generation" cephalosporin (cefoperazone sodium) was changed to gentamicin sulfate, 1.5 mg per kg of body weight every eight hours, when antibiotic susceptibility studies showed that the organism was resistant to

(Katzenstein DA, Ciofalo L, Jordan MC: *Bordetella bronchiseptica* bacteremia. West J Med 1984 Jan; 140:96-98.)

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Submitted, revised, March 18, 1983.

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