

Case Report: A Case of Colorado Tick Fever Acquired in Southwestern Saskatchewan

Kamran Kadkhoda,^{1,2,3} Michael Semus,⁴ Tom Jelic,⁵ and Andrew Walkty^{2,4,6*}

¹Cadham Provincial Laboratory, Winnipeg, Manitoba, Canada; ²Department of Medical Microbiology and Infectious Diseases, Max Rady College of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada; ³Department of Immunology, Max Rady College of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada; ⁴Department of Internal Medicine, Max Rady College of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada; ⁵Department of Emergency Medicine, Max Rady College of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada; ⁶Diagnostic Services Manitoba, Winnipeg, Manitoba, Canada

Abstract. Colorado tick fever virus is transmitted by *Dermacentor andersoni* ticks. In Canada, these ticks are found in the southern regions of British Columbia (Rocky Mountains) and Alberta, as well as southwestern Saskatchewan. Colorado tick fever should be clinically suspected in patients presenting with a biphasic febrile illness and leukopenia following tick exposure in the appropriate geographic area.

CASE

A 65-year-old male presented to a tertiary-care hospital emergency department in Winnipeg (Manitoba, Canada) on April 11, 2017, with new onset of fever. The patient had been hiking in southwestern Saskatchewan near Fox Valley from March 31 to April 2. He reported several tick bites at that time. Four days after returning to Winnipeg (April 6), he developed acute onset of fever, chills, and myalgias. He also complained of reduced appetite and watery diarrhea. He received azithromycin empirically as an outpatient and symptomatically improved over the following 48 hours. However, on April 11, he had a recurrence of fever, reduced oral intake, and diarrhea. He also had a syncopal episode while sitting on the toilet at home. He denied chest pain, dyspnea, vomiting, abdominal pain, arthralgias, genitourinary symptoms, and rash. The patient was assessed by his family physician who ordered a complete blood count. This demonstrated significant leukopenia and he was then referred to a local emergency department for further evaluation. There was no other relevant travel history. The patient denied any specific animal contact and had no sick contacts. His past medical history was significant for coronary artery disease, hypertension, elevated cholesterol, and a remote episode of atrial fibrillation.

On physical examination at the time of presentation, the patient was febrile with a documented temperature of 38.4°C but otherwise hemodynamically stable. Cardiac, respiratory, and abdominal examinations were unremarkable. There was no lymphadenopathy or rash. Basic electrolytes were normal and the patient had a serum creatinine of 102 µmol/L (normal range: 44–102 µmol/L). His alanine aminotransferase and aspartate aminotransferase levels were mildly elevated at 36 U/L (normal range < 30 U/L) and 47 U/L (normal < 32 U/L), respectively. His total white blood cell count was strikingly depressed at $0.9 \times 10^9/L$ (normal = $4.5\text{--}11 \times 10^9/L$), with an absolute neutrophil count of $0.32 \times 10^9/L$ (normal = $1.8\text{--}5.4 \times 10^9/L$), an absolute lymphocyte count of $0.38 \times 10^9/L$ (normal range = $1.3\text{--}3.2 \times 10^9/L$), and an absolute monocyte count of $0.20 \times 10^9/L$ (normal range = $0.3\text{--}0.8 \times 10^9/L$). The patient was also thrombocytopenic with a platelet count of $86 \times 10^9/L$ (normal = $140\text{--}440 \times 10^9/L$),

but his hemoglobin remained normal at 141 g/L. The acute onset of constitutional symptoms shortly following several tick bites raised clinical suspicion of a tick-borne infection. The patient was admitted to hospital and empirically treated with doxycycline pending microbiological investigations. He also received piperacillin-tazobactam for the first 24 hours.

Blood cultures obtained at the time of admission remained sterile following 5 days of incubation. Serologic testing results were negative for human immunodeficiency virus-1/2 using a fourth-generation serology test, parvovirus B19 immunoglobulin M (IgM), hepatitis B virus, hepatitis C virus, Epstein-Barr virus IgM, cytomegalovirus IgM, *Borrelia burgdorferi* IgM/immunoglobulin G (IgG), *Francisella tularensis*, *Rickettsia* spotted fever group, *Rickettsia* typhus group, *Leptospira* spp. IgM, *Anaplasma phagocytophilum* IgG, and *Babesia* spp. Blood for molecular detection of *Babesia* spp., *Borrelia* spp., *Ehrlichia* spp., *Rickettsia* spp., and *A. phagocytophilum* was also negative. Given the history of a biphasic febrile illness with associated leukopenia in the setting of a recent tick exposure while hiking in an area with established populations of *Dermacentor andersoni* ticks, the possibility of infection with Colorado tick fever virus (CTFV) was also considered. An ethylenediaminetetraacetic acid-plasma sample obtained from the patient 8 days after the onset of signs and symptoms was subsequently sent to the Centers for Disease Control and Prevention (CDC) Diagnostic and Reference Laboratory, Arbovirus Diseases Branch in Fort Collins, CO, where CTFV RNA was detected by a real-time reverse transcription polymerase chain reaction (RT-PCR) assay.

The patient clinically improved within 2 days of admission to hospital and he was discharged home on oral doxycycline (continued pending final results for all microbiology tests). When seen in follow-up, he reported no ongoing symptoms. His peripheral white blood cell count and platelet count had both normalized on repeat laboratory testing performed approximately 2 weeks after discharge.

DISCUSSION

Colorado tick fever, also referred to as mountain fever and mountain tick fever, is a tick-borne illness caused by CTFV.^{1,2} CTFV is a non-enveloped, double-stranded RNA virus that belongs to *Coltivirus* genus in the *Reoviridae* family of viruses.^{1,2} Colorado tick fever is not a new disease. It was originally described in 1930 by Becker, but possible cases have appeared in the published literature as early as 1855.¹

* Address correspondence to Andrew Walkty, MS673B Microbiology, Health Sciences Centre, 820 Sherbrook St., Winnipeg, Manitoba, R3A 1R9, Canada. E-mail: awalkty@dsm Manitoba.ca

The rocky mountain wood tick, *D. andersoni*, is the principle vector of the CTFV.^{1,2} In nature, the virus is maintained in an enzootic cycle involving transmission between the larval and nymphal stages of the tick and their mammalian hosts, which typically include small mammals, ground squirrels, and rabbits, among others.^{1,2} Transstadial transmission also occurs once a tick acquires the virus.¹ Humans generally become infected from the bite of an adult tick as this is the life stage than most frequently bites people.¹ CTFV has a similar distribution to its main vector, *D. andersoni*.¹ The vector is generally found at an elevation of 1,200–3,300 m above sea level and is particularly prevalent in the Rocky Mountain region.^{1,2} In the U.S., cases have been identified in more than 14 states, but most of the human cases have occurred in residents of Wyoming, Montana, Utah, Oregon, Colorado, and Idaho.³ The average annual incidence of reported cases in the U.S. from 2002 through 2012 was 0.02 per million population.³ In Canada, the distribution of *D. andersoni* includes the southern regions of British Columbia (Rocky Mountains) and Alberta, as well as southwestern Saskatchewan.⁴ Only one clinical case of Colorado tick fever acquired in Canada has been published in the literature.⁵ However, two serosurveys conducted in the 1960s among residents of British Columbia found that a small number of individuals were positive by the complement fixation serology test, suggesting possible previous exposure.^{6,7} Human cases of Colorado tick fever may occur between March and October, but most cases have been documented between May and July.^{3,8,9} Approximately 50% of cases occur in individuals 20–49 years of age.^{1,8,10} The male to female ratio for cases is roughly 2:1, likely related to differences in risk of exposure to the vector.^{2,3}

The average incubation period of Colorado tick fever is 3–5 days, with a range of 0–14 days.^{1,8} Patients typically present with an abrupt onset of fever, chills, headache, myalgias, generalized weakness, and lethargy.^{1,2,8} A biphasic (saddleback) pattern of 2–3 days of fever, followed by defervescence for 2–3 days, and then recurrence of fever is reported in approximately half of the patients.^{2,8,9} Symptoms of photophobia, retro-orbital pain, and conjunctival injection may occur during the acute febrile phase.² Gastrointestinal symptoms are reported in 20–25% of patients, and a rash (macular, maculopapular, or petechial) has been documented in 5–12% of patients.^{2,8,9} In terms of laboratory abnormalities, leukopenia is common and thrombocytopenia may also occur.^{1,8} Treatment is supportive. Resolution of clinical illness generally occurs within 1 week, although in individuals above the age of 30 symptoms of weakness, lethargy, and malaise may last longer than 3 weeks.^{1,8} Reported complications include aseptic meningitis, meningoencephalitis, encephalitis, pneumonitis, hepatitis, pericarditis, and epididymo-orchitis.^{1,2} Neurologic complications are more common among pediatric patients.¹ Mortality is rare. Because CTFV infects erythrocyte progenitor cells in the bone marrow, erythrocytes remain infected for their life span. Transmission via blood transfusion has been documented; therefore, patients are advised not to donate blood for 6 months after the onset of Colorado tick fever.¹¹

Laboratory confirmation of infection with the CTFV may be done by serology and/or with molecular techniques.^{1,2} Antibody production can be delayed for 14–21 days, so serology may not be helpful in the acute setting.^{1,2,11} RT-PCR can be performed on a

blood specimen in the acute phase of illness (i.e., ideally within the first 5 days of symptoms). Given the persistence of CTFV in erythrocytes, whole blood is a preferred sample to serum or plasma for RT-PCR.^{1,2,11} At present, specific diagnostic testing for CTFV is not offered by the National Microbiology Laboratory (Winnipeg, Manitoba) in Canada; however, testing can be performed by the CDC Arbovirus Diagnostic Laboratory in Fort Collins, CO.¹¹

The patient described here presented with the classic biphasic fever pattern and leukopenia, starting approximately 4 days after exposure to ticks in an area of Canada where populations of *D. andersoni* ticks are known to be established. These features all served as diagnostic clues pointing to Colorado tick fever. Based on a review of the published literature, acquisition of Colorado tick fever in Canada seems to be a rare event; however, the paucity of Canadian cases reported to date may simply reflect the mild or self-limited nature of the illness, lack of diagnostic testing available in Canada at the current time, and lack of awareness among healthcare providers. Repeating a serosurvey among residents in the southern parts of British Columbia (Rocky Mountains), Alberta, and southwestern Saskatchewan may be useful to assess whether the occurrence of human cases in these provinces is on the rise. Enhanced surveillance of *D. andersoni* tick populations in Canada for CTFV may also be helpful in assessing the risk for human exposure. Given the frequency of travel to the Canadian Rockies as a tourist destination, physicians in North America should be familiar with the clinical characteristics of Colorado tick fever such that appropriate and timely diagnostic testing can be obtained for patients presenting with the typical clinical features.

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Authors' addresses: Kamran Kadkhoda, Cadham Provincial Laboratory, Winnipeg, Manitoba, Canada, E-mail: kamran.kadkhoda@gov.mb.ca. Michael Semus, Department of Internal Medicine, Max Rady College of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada, E-mail: msemus1@exchange.hsc.mb.ca. Tom Jelic, Department of Emergency Medicine, Max Rady College of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada, E-mail: tjelic@gmail.com. Andrew Walkty, MS673B Microbiology, Health Sciences Centre, Winnipeg, Manitoba, Canada, E-mail: awalkty@dsmanitoba.ca.

REFERENCES

- Romero JR, Simonsen KA, 2008. Powassan encephalitis and Colorado tick fever. *Infect Dis Clin North Am* 22: 545–559.
- Klasco R, 2002. Colorado tick fever. *Med Clin North Am* 86: 435–440.
- Yendell SJ, Fischer M, Staples JE, 2015. Colorado tick fever in the United States, 2002–2012. *Vector Borne Zoonotic Dis* 15: 311–316.
- Eklund CM, Kohls GM, Brennan JM, 1955. Distribution of Colorado tick fever and virus-carrying ticks. *J Am Med Assoc* 157: 335–337.
- Cimolai N, Anand CM, Gish GJ, Calisher CH, Fishbein DB, 1988. Human Colorado tick fever in southern Alberta. *CMAJ* 139: 45–46.
- Kettyls GD, Verrall VM, Wilton LD, Clapp JB, Clarke DA, Rublee JD, 1972. Arbovirus infections in man in British Columbia. *Can Med Assoc J* 106: 1175–1179.
- Kettyls GD, Verrall VM, Hopper JMH, Kokan P, Schmitt N, 1968. Serological survey of human arbovirus infections

- in southeastern British Columbia. *Can Med Assoc J* 99: 600–603.
8. Goodpasture HC, Poland JD, Francy DB, Bowen GS, Horn KA, 1978. Colorado tick fever: clinical, epidemiologic, and laboratory aspects of 228 cases in Colorado in 1973–1974. *Ann Intern Med* 88: 303–310.
 9. Spruance SL, Bailey A, 1973. Colorado tick fever. A review of 115 laboratory confirmed cases. *Arch Intern Med* 131: 288–293.
 10. Lindquist EE, Galloway TD, Artsob H, Lindsay LR, Drebot M, Wood H, Robbins RG, 2016. *A Handbook to the Ticks of Canada*. Available at: <http://biologicalsurvey.ca/public/Bsc/Controller/Page/AGR-001-Ticks-Monogram.pdf>. Accessed July 17, 2017.
 11. Centers for Disease Control and Prevention, 2015. *Colorado Tick Fever*. Available at: <https://www.cdc.gov/coloradotickfever/healthcareproviders.html>. Accessed July 17, 2017.