

Rats! Hantavirus: A Case Report of a Suspected Case in Eastern Tennessee

Lindsey C Shipley, MD; S Trevor Taylor; Christina Grimsley; Kevin Stoffer; Jack Goldstein, MD

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ABSTRACT

Introduction: Hantavirus is an RNA virus that is transmitted to humans by inhalation of aerosolized excrement from infected rodents. This case report demonstrates the value of taking a thorough social history and highlights the challenges associated with early diagnosis of this viral infection.

Case Presentation: We highlight a case of suspected hantavirus infection with subtle gastrointestinal and pulmonary symptoms that challenged the initial diagnosis.

Discussion: Efforts are needed to improve clinical recognition and rapid detection of hantavirus infections, to reduce associated mortality. In a patient presenting with gastrointestinal prodromal symptoms followed by cardiopulmonary findings, physicians should pay special attention to that patient's living conditions and maintain a high index of suspicion for hantavirus infection. Early diagnosis is critical to prevent rapid deterioration to hantavirus pulmonary syndrome in some patients.

INTRODUCTION

Hantavirus is a negative-sense, single-stranded RNA virus of the Bunyaviridae family. It is transmitted to humans by inhalation of aerosolized infected rodent feces.¹ Although rodent reservoirs are widespread throughout the US, less than 3% of cases have occurred in the Eastern US.² The onset typically begins with a 4- to 7-day prodromal stage of myalgia (most common), fever, headache, nausea, and vomiting,^{2,3} often followed by dyspnea and cough.⁴ On rare occasions, severe pulmonary manifestations

of disease can quickly become life-threatening with pulmonary edema and hemorrhage.²

Hantavirus infection affects 30,000 individuals annually⁵ and tends to occur among people living in lower socioeconomic housing environments and those enjoying the outdoors.¹ In the US from 1993 to January 2017, a total of 728 cases of hantavirus pulmonary syndrome (HPS) infections were reported, with a 36% case fatality rate.⁶ Morbidity associated with hantavirus infection is exacerbated by preexisting medical conditions such as chronic obstructive pulmonary disease (COPD), malignancy, trauma, burns, or surgery.^{4,6} Hantavirus occurrence in Tennessee has not been reported to the Centers for Disease Control and Prevention⁴ as of January 2017.

The following case report describes a patient presenting with subtle gastrointestinal and pulmonary symptoms with suspected Hantavirus infection.

CASE PRESENTATION

Presenting Concerns

A 61-year-old white woman presented to the Emergency Department with complaints of shortness of breath and subjective fever. Shortly after admission, she began experiencing positional midchest pain (worse when lying flat) and dyspnea with audible wheezing.

Her medical history included COPD, for which she received 2.5 L of oxygen at home, as well as hypertension, chronic heart failure, and tobacco use. She lived with her significant other in a trailer without water or power. Her significant other was male and reported testing positive for inactive tuberculosis in the past.

On physical examination, the patient was afebrile at 36.3°C (97.3°F) with a blood pressure of 104/69 mmHg. Her oxygen saturation was more than 90% on room air, with diffuse wheezing on expiration. Initial laboratory values were remarkable for the following: Leukocyte count, $6 \times 10^9/L$ (52% neutrophils, 36% lymphocytes, 11% monocytes, and 1% basophils); hematocrit, 44.2%; arterial pH, 7.4; partial pressure of carbon dioxide, 48 mmHg; and partial pressure of oxygen, 74 mmHg.

Initially, pulmonary symptoms were suspected to be associated with an acute exacerbation of COPD. Oxygen, corticosteroids, ceftriaxone, and azithromycin treatments were initiated in the hospital and the patient symptomatically improved. Continuous home oxygen therapy was recommended, and she was discharged home with prescriptions for a methylprednisolone dose pack, azithromycin 500 mg orally for 1 day, and oral cefuroxime, 500 mg twice a day, for 1 additional day.

The patient was unable to fill any prescriptions because of a lack of transportation and returned to the Emergency Department 4 days later complaining of shortness of breath and chest pain again. She now had a temperature of 39.5°C (103.1°F), a pulse of 130/min, blood pressure of 108/70 mmHg, respirations of 20/min, and a pulse oximetry reading of 80%. On physical examination, she had labored breathing with use of accessory muscles, inspiratory stridor, difficulty speaking fluent sentences, diffusely diminished lung sounds, and diffuse moderate wheezing on inspiration and expiration. Additionally, an erythematous macular rash without vesicles was noted

Lindsey C Shipley, MD, is an Internal Medicine Resident at the University of Alabama in Birmingham. E-mail: crosnoe@goldmail.etsu.edu. S Trevor Taylor is a Medical Student at the East Tennessee State University James H Quillen College of Medicine in Johnson City. E-mail: taylorst1@etsu.edu. Christina Grimsley is a Medical Student at the East Tennessee State University James H Quillen College of Medicine in Johnson City. E-mail: grimsley@etsu.edu. Kevin Stoffer is a Medical Student at the East Tennessee State University James H Quillen College of Medicine in Johnson City. E-mail: stoffer@goldmail.etsu.edu. Jack Goldstein, MD, is a Professor of Internal Medicine at the East Tennessee State University James H Quillen College of Medicine in Johnson City. E-mail: goldsteinj@mail.etsu.edu.

around the upper extremities. The patient reported that the lesions had been present for 2 weeks, causing mild pruritis. The remainder of the physical findings were normal. Laboratory values were as follows: Lymphocyte-predominate leukocyte count, $11.4 \times 10^9/L$ (24% neutrophils, 66% lymphocytes, and 7% monocytes); hematocrit, 44.0%; platelet count, $113 \times 10^9/L$; arterial pH, 7.35; partial pressure of carbon dioxide, 61 mmHg; partial pressure of oxygen, 66 mmHg; serum bicarbonate, 33.7 mEq/L; international normalized ratio, 1.2; partial thromboplastin time, 29.0 seconds; fibrinogen, 153 mg/dL; and d-dimer 920 ng/mL.

Results of a cardiology workup revealed a Type 2 non-ST-elevation myocardial infarction, maximum troponin level of 0.17 mg/mL, and mild respiratory acidosis. The myocardial infarction was managed according to protocol, and the patient was readmitted to the hospital unit. A coronary angiogram showed no coronary artery disease and a left ventricular end-diastolic pressure of 33 mmHg. Additionally, a computed tomography scan of the chest

revealed interstitial markings in upper lung fields as well as enlarged right hilar and prevascular lymph nodes (Figure 1), prompting a consultation with an infectious disease specialist. The infectious disease workup included a respiratory viral panel, for which all results were negative. Testing for *Legionella*, *Cryptococcus*, *Blastomyces*, and *Histoplasma* organisms showed negative results. Results for a tuberculosis workup were also negative. Sputum cultures and blood cultures yielded no growth. Results of a peripheral blood film showed normocytic anemia and thrombocytopenia. Neutrophils showed a mild left shift, and lymphocytes showed normal morphology and absolute count, without atypia.

Therapeutic Intervention and Treatment

Intravenous regimens of cefepime, vancomycin, and methylprednisolone were started in the hospital.

During the second hospital stay, the patient's living conditions were further explored, eliciting details from the patient of her exposure to rat feces while living in and vacuuming her trailer. The patient reported



Figure 1. Computed tomography scan with lung views demonstrating interstitial markings in upper lung fields, enlarged right hilar and prevascular lymph nodes, and small bilateral pleural effusions.

having nausea and diarrhea two weeks before her initial admission but denied any changes in her pulmonary status until the first admission. The timeline of preceding gastrointestinal symptoms, repeated admissions for respiratory failure, history of exposure to rats, chest computed tomography findings, and relative lymphocytosis suggested a viral cause and led the medical team to pursue serologic testing for hantaviruses during the second hospital admission.

Table 1. Timeline of the case

Date	Visit summary	Diagnostic testing	Interventions
8/5/17	Patient presented to ED with shortness of breath; respiratory rate, 18; pulse oximetry, 92. Physical examination showed diffuse expiratory wheezing. Patient reported history of cigarette smoking, hypertension, and COPD requiring 2.5L home oxygen.	Laboratory revealed leukocyte count, $6 \times 10^9/L$ (52% neutrophils, 36% lymphocytes, 11% monocytes, and 1% basophils); hematocrit, 44.2%; arterial pH, 7.4; partial pressure of carbon dioxide, 48 mmHg; and partial pressure of oxygen, 74 mmHg.	Oxygen, steroids, azithromycin, and ceftriaxone were initiated in the hospital.
8/8/17			Patent discharged to home with methylprednisolone, azithromycin, and cefuroxime
8/12/17	Patient returned to the ED with shortness of breath, temperature of 103.1, pulse 130, and respiratory rate of 20. Physical exam revealed diffuse expiratory wheezing. She reported she was unable to make it to the pharmacy to pick up her prescriptions provided at previous admission because of lack of transportation.	ECG revealed NSTEMI, troponin max of 0.17, no valvular abnormalities, and left ventricular ejection fraction was estimated to be 60%-65%. CXR revealed no active heart of lung disease. A left heart catheter showed no coronary artery disease with left ventricular end-diastolic pressure of 33 mmHg.	Intravenous regimens of cefepime, vancomycin, and methylprednisolone were started in the hospital.
8/16/17		Serum samples were submitted for ELISA, and results were returned suggesting recent hantavirus exposure (ie, Hanta IgG < 2.0, Hanta IgM 10.86). A sample was sent to a regional health department and the CDC for further testing and speciation. The results were equivocal with recommendation the patient undergo repeated testing.	
8/18/17			Patient was discharged home with counseling about her cardiopulmonary status and with recommendations for repeat testing and a repeat chest x-ray in 6-8 wks. Patient did not return for follow-up.

CDC = Centers for Disease Control and Prevention; COPD = chronic obstructive pulmonary disease; CXR = chest x-ray; ECG = electrocardiogram; ED = Emergency Department; ELISA = enzyme-linked immunosorbent assay; NSTEMI = non-ST-elevation myocardial infarction.

Follow-up and Outcomes

Serum samples were submitted for enzyme-linked immunosorbent assay, and results were returned the same day, confirming recent hantavirus exposure (*Hantavirus* immunoglobulin G antibody titer < 2.0, *Hantavirus* immunoglobulin M antibody titer = 10.86). The sample was sent to a regional health department and the Centers for Disease Control and Prevention for further testing and speciation. The results were reported as equivocal, and it was recommended the patient undergo repeated testing.

The patient's shortness of breath improved daily with corticosteroids and intravenous antibiotics. The patient was continued on a regimen of cefepime and doxycycline while an inpatient. At discharge, her treatment was switched to oral amoxicillin and clavulanic acid (Augmentin) and doxycycline to finish a 7- to 10-day course. A case manager was recruited to help arrange alternate housing and acquisition of medications. The patient was advised to have another chest radiograph in 6 to 8 weeks to reassess her condition and pulmonary findings. The patient did not return for follow-up testing. A timeline of the case appears in Table 1.

DISCUSSION

The most commonly documented physical findings associated with hantavirus infection are tachycardia and tachypnea. Rash is not a common finding in hantavirus infection and thus was suspected to be a contact dermatitis acquired while cleaning. Laboratory test results may show increased hematocrit and increased leukocytes with thrombocytopenia.^{2,3} The diagnosis of hantavirus is made with polymerase chain reaction, which can be isolated from the patient's urine and/or blood.¹ Chest radiographs commonly show diffuse bilateral infiltrates acutely during presentation.³ Smoking history and viral load may determine severity of illness.² Furthermore, immunohistochemical studies of samples obtained from patients with a diagnosis of HPS fail to exhibit direct cytotoxic harm, which raises suspicion that the disease process is predominantly caused by an immunologic response to viral antigens.⁷ The risk of HPS is low; however, 36% of HPS cases result in death.⁴ In patients with fatal hantavirus infection, death was

caused by cardiac arrhythmias.³ Ribavirin is the current treatment of choice for HPS, but future studies are ongoing to determine the efficacy of other antiviral agents and vaccinations.^{8,9}

In the case presented, a 61-year-old woman was given a diagnosis of hantavirus infection after 2 hospital admissions. During the first hospital course, the patient's shortness of breath improved daily with corticosteroids and antibiotics until she was mostly asymptomatic and was discharged home on an oral regimen of antibiotics. At second admission, she had a lymphocyte-predominate leukocytosis and thrombocytopenia that prompted investigation for viral causes. It is possible the patient truly presented initially with a COPD exacerbation and was then exposed for the first time to the virus after becoming immunocompromised between admissions. It is more plausible, however, that the patient initially presented with early hantavirus infection, the diagnosis was missed, and she was reexposed to the virus in her trailer after the first hospital discharge. This possibility would explain the timeline and exacerbated presentation at second admission. Although the patient was ultimately diagnosed with non-HPS hantavirus infection, she was counseled on her cardiopulmonary status, particularly regarding smoking cessation and the importance of pursuing safe and clean living conditions as well as follow-up care.

CONCLUSION

In a patient presenting with prodromal symptoms followed by cardiopulmonary findings, physicians should pay special attention to the patient's living conditions and should maintain a high index of suspicion for hantavirus infection. An early diagnosis is critical to prevent rapid deterioration to HPS in some patients. This case demonstrates the value of taking a thorough social history and highlights the challenges associated with early diagnosis of hantavirus infection. Efforts are needed to improve clinical recognition and rapid laboratory detection of hantavirus infections to reduce associated mortality. ♦

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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Author Contributions

Lindsey C Shipley, MD, contributed by drafting the manuscript and performed literature search and review; has read and approves this manuscript. S Trevor Taylor contributed to project design, writing, editing, and critical revision of the manuscript; has read and approves this manuscript. Christina Grimsley contributed to project design, writing, editing, and critical revision of the manuscript; has read and approves this manuscript. Kevin Stoffer contributed to project design, writing, editing, and critical revision of the manuscript; has read and approves this manuscript. Jack Goldstein, MD, contributed to the project design; has read and approves this manuscript.

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