
Department of Health

Of Rats, Horses, and Zebras – An Old World Hantavirus Investigation


Angela M. Maxted, DVM, PhD, DACVPM
 Bureau of Communicable Disease Control
 New York State Department of Health, Albany NY

Northeast Epidemiology Conference, October 1, 2015


The Investigation Begins

- **May 15, 2015**
- **Electronic laboratory report received from commercial laboratory**
- **Positive for Hantavirus IgM**
 - 7.44 (Ref: <2.00)
- **Positive Lyme disease IgM serologies**
 - Western Blot, 23KD, 39KD, 41KD bands
- **Initial patient interview**
 - Female, nurse, 58 years
 - Onset May 2, 2015
 - Not hospitalized
 - Fever, mild respiratory illness (cough), myalgia, fatigue, N/V, rash all over body



Hantavirus vs. Lyme Disease




Hantavirus Pulmonary Syndrome (HPS) Cases, by State of Exposure



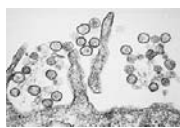
Reported Cases of Lyme Disease - United States, 2013







Hantaviruses

- **Dozens of different viruses**
 - Specific rodent reservoirs for each
- **2 clinical syndromes**
 - Hemorrhagic fever with renal syndrome (HFRS) – Old World viruses
 - Hantavirus pulmonary syndrome (HPS) – New World viruses





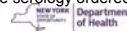
Patient History/Background

- Lives in rural area of central NY with husband
- Home is a basement with a roof, plywood for a door
 - Built 2 years ago, plans to build rest of home delayed for lack of funds
- Have had mouse infestations “off and on”
- Developed a rat infestation over the winter
- Jan 2015 they poisoned the rats, which died in walls and ceilings
 - Soon “dead rats began falling from the bathroom ceiling”
- ~ April 1, insulation and dead rats removed, gloves and dust masks worn
- May 1, swept up storage area without mask
- No history of tick bites

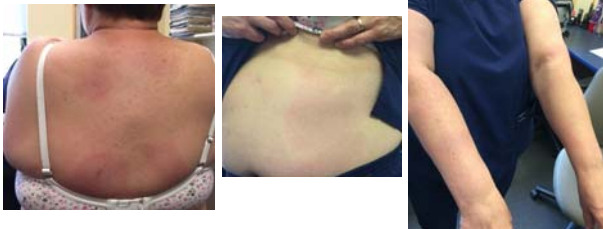


Clinical Presentation

- Illness onset May 2
 - Self-reported fever to 103.5°F, body aches, cough, congestion
- Sought care May 11
 - PMH: Obesity, HTN, hyperglycemia, anxiety, atrial fibrillation
 - Symptoms mostly resolved, but fatigue persisted
 - Rash developed and worsening, now all over body
 - Look like petechiae to patient
 - Described by PCP as multiple, large, non-raised, blanchable, erythematous, irregular in shape but circular. No purpura/petechiae.
 - Patient concerned about hantavirus
 - Bloodwork/UA/hantavirus serology ordered. Lyme disease serology ordered after consult with another provider at practice.



Rash



Laboratory Findings

- CBC → normal, no thrombocytopenia
- UA → normal, no renal dysfunction
- Chem panel → unremarkable, no renal dysfunction
- Coagulation studies → normal
- Elevated CRP, LDH, sedimentation rate
- Lyme disease screen, WB, all 3 bands positive
- Hantavirus serology at a commercial laboratory
 - IgG screen: <2.0 (ref 2.0), Negative
 - IgM screen: 7.44 (ref 2.0), Positive
 - Sin Nombre virus IgM Confirmation test: Positive



3 Days Later – Results Available, More Symptoms Develop (May 14)

- **Right flank pain, worsening cough, rash persists**
- **Further testing**
 - Urine culture – negative
 - Renal ultrasound – no abnormalities found
 - Chest X-ray – no abnormalities found
 - Repeat UA and bloodwork normal (↑CRP)
- **Started on doxycycline**
 - Delayed
- **Referred to ID**



ID Consult – May 21

- **Had been on doxycycline for 1 week**
- **Rash and other symptoms had resolved**
 - Notes rash consistent with disseminated EM from photos
- **Only complaint fatigue**
- **ID physician concludes**
 - Rash and other symptoms consistent with Lyme disease (doxy to 21 d)
 - Hantavirus serology false positive
- **One more PCP visit...May 27**
 - Chief complaint dyspnea, several episodes of shortness of breath
 - Normal enhanced CT scan of chest



Hantavirus Acute Specimen Confirmatory Results (collection date May 11)

- **CDC Special Pathogens branch (prelim results June 11)**
 - Sin Nombre virus
 - IgM and IgG negative
 - **Seoul virus**
 - IgM **Positive**
 - IgG negative
- **Lab information matches epi information**
- **Reminder: commercial laboratory results positive for Sin Nombre IgM 7.44 (IgG neg)**



Hantavirus Pulmonary Syndrome (HPS)

- **Sin Nombre, Monongahela, and New York viruses in NY**
 - *Peromyscus* spp. reservoir
- **Primarily respiratory involvement**
- **Fever, myalgia, GI → cough, pulmonary edema, ARDS**
- **Thrombocytopenia, left shift, hemoconcentration**
- **CFR ~35%**
- **Mild illness possible**
- **Extremely rare in Northeast**
 - 5 cases with exposure in NY

Hemorrhagic Fever with Renal Syndrome (HFRS)

- **Seoul virus (in North America)**
 - *Rattus norvegicus* reservoir
- **Primarily renal involvement**
- **Fever, myalgia, hemorrhage (GI, urinary, brain, conjunctiva)**
- **Acute renal failure with oliguria**
- **Thrombocytopenia, fluid overload**
- **CFR <1% (worldwide)**
- **Extremely rare in North America**
 - Travel-related cases
 - Few locally acquired (~5 total)

Seoul Virus as a Public Health Concern in Rural New York?

- Norway rats have "worldwide" distribution
- Antibodies to Seoul virus can be found in Norway rats
 - Studies in urban areas
- In the US: rare locally-acquired HFRS, demonstrated antibodies to Seoul virus on serosurveys
- This patient
 - Mild symptoms masked by Lyme disease?
 - Evidence of exposure but not pathogenic?
 - Something completely different?
 - A case?
 - "Get a convalescent sample"



Convalescent Serum Specimen Collected June 23

- Sin Nombre Virus final results reported July 10
 - Acute IgG and IgM Negative
 - Convalescent IgG and IgM Negative
- Seoul Virus final results
 - Waiting...
 - More waiting...
 - Still waiting!
- Sept 4: Convalescent was negative, acute was falsely positive

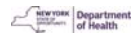


Summary

- Lyme disease – yes, hantavirus infection – no
- Patient's symptoms attributable to lab-confirmed Lyme disease
- Patient's rash not immediately recognized as multiple erythema migrans
- Treatment with doxycycline was delayed
- False positive hantavirus serology results occurred at both commercial and CDC laboratories
- No abnormalities of CBC, blood chemistries, UA, coagulation studies, or imaging of chest or kidneys consistent with HPS/HFRS
- Substantial rodent exposure in basement home

Conclusions

- Providers should exercise caution when ordering tests without correlating clinical and epidemiologic information
- The patient's anxiety and medical training might have contributed to progression of hantavirus "symptoms"
- Convalescent specimen testing was necessary for real answers
 - No good explanation why acute specimen false+



Co-Authors and Acknowledgments

- **Co-Authors**
 - NYSDOH
 - Amy Burns
 - Jenn White
 - Cortland County Health Department
 - Suzanne Osterhoudt
 - Pam Griffith
- **Acknowledgements**
 - CDC
 - Barbara Knust
 - Ute Stroehler
 - NYSDOH Wadsworth Center
 - Karen Kulas
 - NYSDOH
 - Bryon Backenson
 - Andie Newman



Hantavirus in New York – Five Previous Cases with Exposure in NY

Year	Place of Exposure	Place of Residence	Exposure	Virus	Outcome
1994	Shelter Island (Queens?)	RI	Summer home (warehouse?)	New York	Died
1995	South Fork, Long Island	Long Island	Occupational? Landscaper	New York	Died
1999	Catskills	PA	Cabin cleaning, handled rodents	Monongahela	Recovered
2011	South Fork, Long Island	Long Island	Home cleaning	New York or Sin Nombre	Died
2012	Adirondacks	Long Island	Camping in lean-to, mouse bite	Sin Nombre	Mild illness, Recovered

Pathogenic Hantaviruses in the United States

Virus	Disease	Distribution	Rodent Host
Sin Nombre virus	HPS	Mostly West, Midwest	Deer mouse <i>Peromyscus maniculatus</i>
Monongahela virus	HPS	East	Deer mouse <i>Peromyscus maniculatus</i>
New York virus	HPS	East	White-footed mouse <i>Peromyscus leucopus</i>
Bayou virus	HPS	South, Southeast	Rice rat <i>Oligoryzomys palustris</i>
Black Creek Canal virus	HPS	Southeast	Cotton rat <i>Sigmodon hispidus</i>
Seoul virus	HFRS	Worldwide	Norway rat <i>Rattus norvegicus</i>