



A CASE OF ACUTE
RESPIRATORY
FAILURE

Hillary Glick, MD
PGY-3
MMC

Chief Complaint

- 20 year old woman presenting to Redington-Fairview ED with several days of progressive dyspnea associated with a fever and dry cough.

Background

- 10 days prior, dx with e. coli UTI by PCP, prescribed Bactrim
- 5 days prior, seen by PCP for continued dysuria, headache, fever, sore throat
- 3 days prior, seen by PCP for rash ?from Bactrim along with continued sore throat, fever, dysuria

Medical Hx, etc

- Med Hx: None
- Medications: OCP, Bactrim
- Allergies: Penicillin
- Surgical Hx: None
- Family Hx: None
- Social Hx: Non-smoker, no IVDU, No ETOH. Works in an ice cream shop

Physical Exam

- PE: BP 109/73, HR, 82, **RR 18, O2 sat 75% on RA**, Temp 98F
- **O2 sat up to 91% on 5 L**
- General: AOX4, non-toxic, no acute distress
- Cardiovascular: RRR, no murmurs, rubs or gallops
- Respiratory: Prolonged expirations in bilateral bases. Decreased air movement. No accessory muscle use, retractions, wheezes, stridor or rales. No chest wall tenderness or rhonchi.

Data

- UA: trace leuk esterase
- CBC: normal
- CMP: Alk phos 153, AST 101, ALT 167
- CXR: Probable moderately extensive bibasilar pneumonias
- CTA: Pneumomediastinum without clear pneumothorax. Extensive alveolar consolidation in lower lobes probably representing atypical inflammation. Early ARDS can have a similar configuration.

Management

- Supplemental O2
- Cefepime, Vancomycin, Duonebs
- **Transfer to MMC**

Transfer to MMC

- RR 40, SPO2 95% on 6L
- Full sentences, no accessory muscle use; fingers cold
- ABG: pH 7.42, pCO2 43, HCO3 28, pO2 47 on 6L NC
- Put onto 100% non-rebreather, then transferred to ICU for High Flow
- Vancomycin, Cefepime, Doxycycline/Azithromycin, Prednisone
- Thoracic surgery consulted for pneumomediastinum, no intervention

Ddx

Ddx

- CAP
- Atypicals
- Fungal
- Viral
- Opportunistic
- Rheumatologic
- Drug Rxn

Clinical Course

- Day 5: intubated for worsening respiratory distress on BiPAP. Put on lung-protective protocol. Bronchoscopy performed.
- Vanc/Cefepime/Azithromycin/Doxycycline – 14 day course completed
- Prednisone, Methylprednisolone
- Day 16: extubated
- Day 19: dx with superficial thrombus, brief heparin ggt
- Day 24: discharged from MMC to New England Rehab

Work-up

- Legionella Ag Ur: neg x2
- HIV, Hep Chronic panel: neg
- C3 + C4: normal
- ANCA, ANA, proteinase 3 Ab, myeloperoxidase Ab: neg
- RF, CCP: neg
- EBV Early Ag Ab IgG: neg
- **CRP: 41.9 (ULN 8)**
- **ESR: 96 (ULN 96)**
- HSV 1+2: neg
- **LDH: 374 (ULN 250)**
- IgG, IgA, IgM: normal; **IgE: 127 (ULN 100)**
- Fungitell, Aspergillus Ag: normal
- Myoplasma pneumoniae Ab: IgG, IgM normal
- Fungal Blood cultures: no growth
- BAL cytology: atypical cells, likely reactive 2nd to inflammatory/infectious process
- BAL cell count: 1% eos
- BAL fungal, bacterial, acid fast, legionella testing: no growth
- BAL viral testing: neg for adenovirus, influenza A & B, RSV, Parainfluenza 1,2 3
- Tick panel: lyme, anaplasma, Babesia neg
- CMV Ab: IgG, IgM neg
- CK: 17
- RNP Ab IgG: normal
- Sjogren's Ab SSA + SSB: normal
- SCL 70 Auto Ab IgG: normal
- Myomarker Panel 2: Mi-2, PL-12, PL-7, EJ, OJ, SRP, Ku, U2 snRNP, Anti-PM/Sci-100 Ab, Anti-Jo-A Ab –

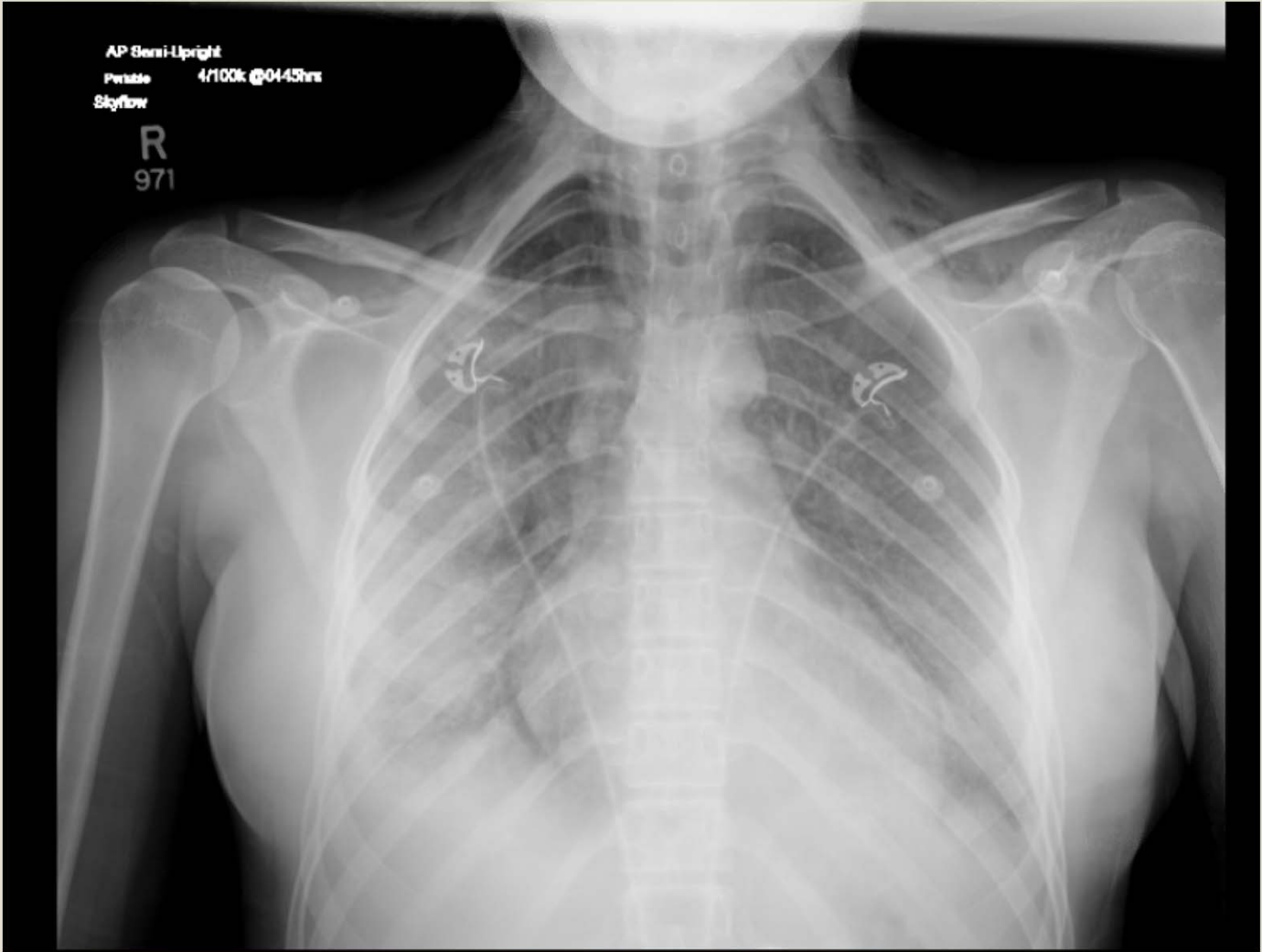
Additional Patient History

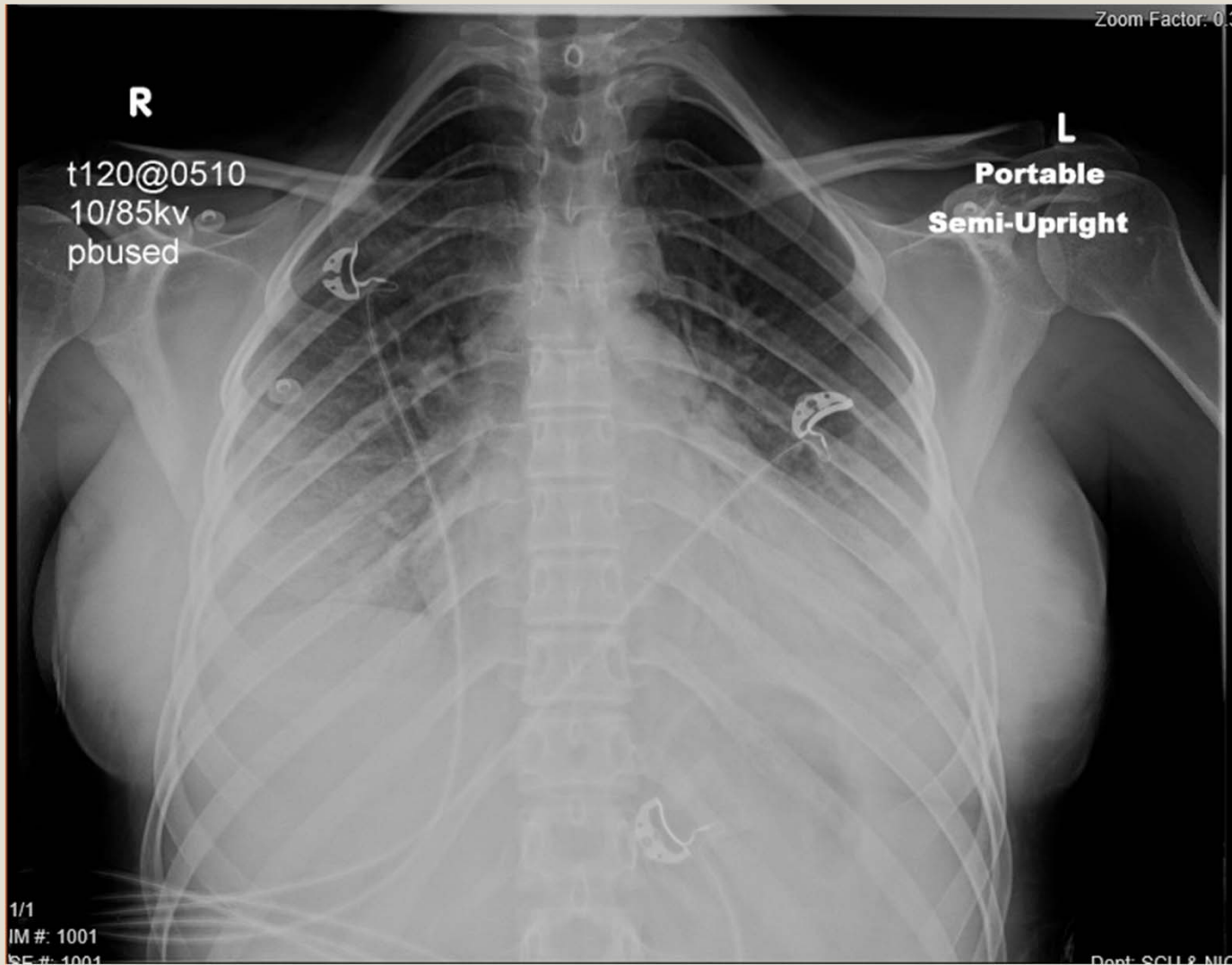
- Travel to Yosemite 3 months prior
- Camping in rural Maine <1 month prior

Work-up

- Hantivirus IgG - <2.00
- *Hantavirus IgM – 3.35; 3.49 on repeat*
- No evidence of recent or current infection with Sin Nombre virus

Imaging





Zoom Factor: 0.3

R

t120@0510
10/85kv
pbused

L

**Portable
Semi-Upright**

1/1
IM #: 1001
SF #: 1001

Dept. SCH & NIC



Desc

L
410

Hantavirus – Overview

- Genus of >20 enveloped negative-sense ssRNA virus in the Bunyaviridae family
- Transmitted to humans via inhalation of aerosolized infected rodent feces, urine, saliva
- Disease process likely predominantly caused by immunologic response to viral antigens
- Most people who are seropositive for hantavirus are asymptomatic

Hantavirus – Overview

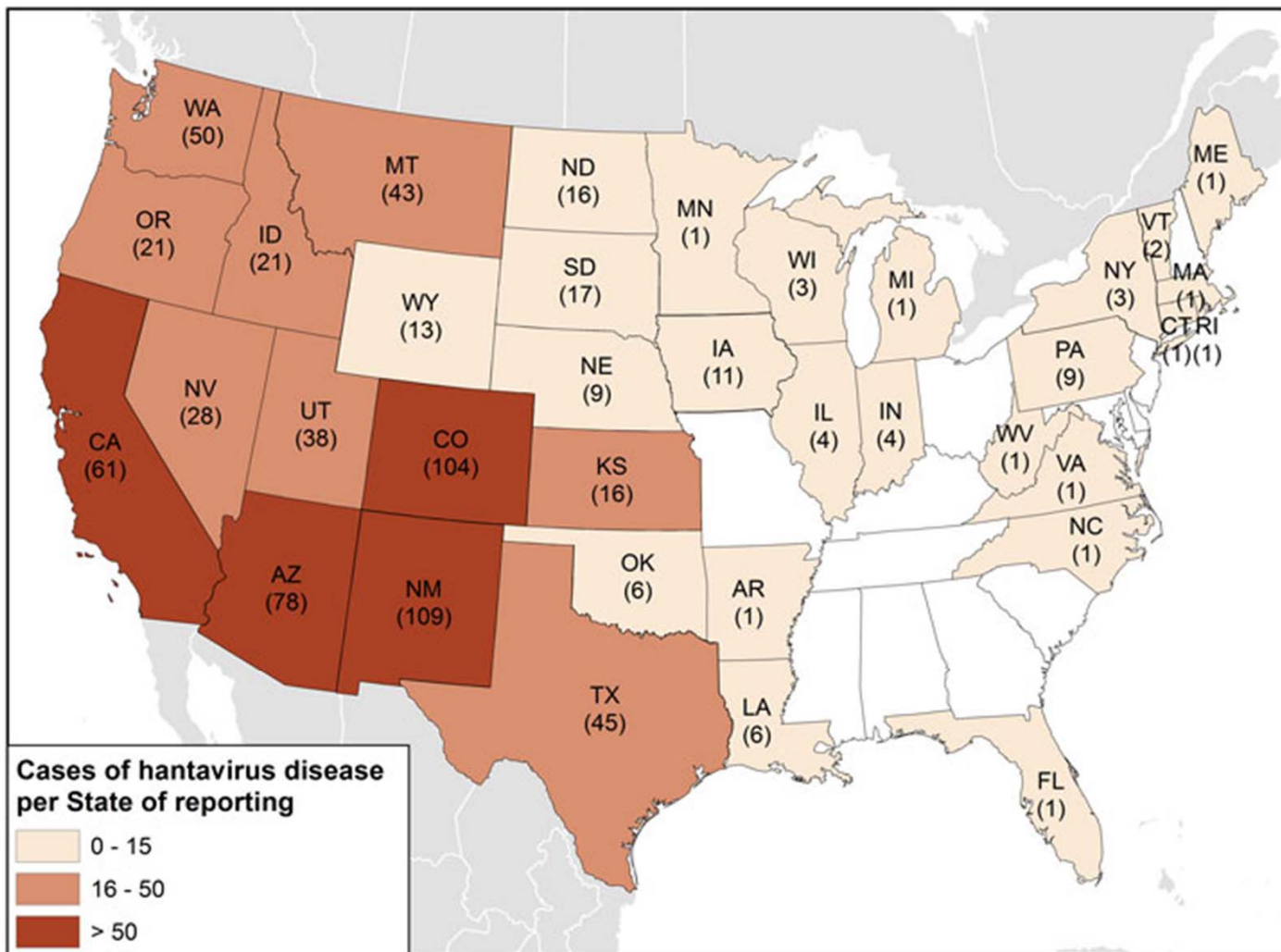
- Mean incubation period 18 days, but can range from 1-6 weeks
- Causes 2 different febrile illnesses
 - HCPS – Hantavirus cardiopulmonary syndrome
 - HFRS – Hemorrhagic fever with renal syndrome

Hemorrhagic fever with renal syndrome (HFRS)

- Caused by the Old World Viruses - Seoul, Hantaan, Dobrava and Puumala viruses
- Seen mainly in Asia and Europe
- Begins with fever, headache
- Patients can rapidly develop hypotension, renal failure
- Mortality rate of 12%
- First diagnosed during the Korean War

Hantavirus cardiopulmonary syndrome (HCPS)

- Caused by the New World Viruses – Sin Nombre
- Seen mainly in North and South America
- Begins with a nonspecific viral prodrome, can rapidly progress to respiratory failure
- Mortality rate of 40-60%
- Approx 2000 cases to date
- More common in the Southwestern US
- Rural predominance
- Most cases seen in the late spring, early summer



Hantavirus cardiopulmonary syndrome (HCPS)

- Lung is the main site of infection
- Inflammatory response then facilitates dissemination to vascular endothelium
- Vascular permeability increases, capillary leak occurs
- SVR increases, cardiac output decreases, lactic acidosis develops
- Cardiogenic shock develops, caused by either a functional cardiac depression or a typical myocarditis

HCPS – Diagnosis & Clinical Course

- Symptoms begin with a 4-7 day flu-like prodrome w/myalgias, headache, N/V, fever, chills, cough, dyspnea
- Pts commonly have tachycardia, tachypnea
- Can rapidly progress to respiratory distress w/hemodynamic compromise, hemorrhage and noncardiogenic pulmonary edema
- Pts often only require intubation for 1-4 days before diuresing
- May be weakened w/abnormal diffusion capacity for months afterwards
- Death occurs from cardiogenic shock, arrhythmias

HCPS – Data

- CXR will show pulmonary edema - resembles ARDS
 - Pleural effusions, extensive bibasilar/perihilar airspace disease often seen
 - Presence of interstitial edema helps distinguish HCPS from ARDS
- Thrombocytopenia in 80% pts
- Leukocytosis w/neutrophilia, a left shift and atypical lymphocytes
- Metabolic acidosis, elevated lactate
- Hemoconcentration



Figure 6 – Chest radiograph of an HCPS patient, showing the initial interstitial infiltrate

HCPS - Management

- ICU admission for intubation & mechanical ventilation, inotropic and vasopressor support
- Noninvasive ventilation contraindicated due to pulmonary edema
- ECMO can be utilized in younger patients
- Should avoid aggressive fluid resuscitation due to the risk of pulmonary edema
- Tx is mainly supportive care
- Broad-spectrum abx often utilized as the dx of hantavirus takes time to confirm
- Some evidence that Ribavirin reduces mortality

HCPS – Diagnosis

- CDC definition:
 - *A febrile illness (temp >101) characterized by bilateral diffuse interstitial edema that may radiographically resemble ARDS, with respiratory compromise requiring supplemental oxygen, developing within 72 hours of hospitalization, and occurring in a previously healthy person*
- Only recommended to test previously healthy patients
- Formal testing should occur at a reference laboratory
- Lab criteria:
 - Detection of hantavirus-specific IgM
 - Rising titer of hantavirus-specific IgG
 - Detection of hantavirus RNA via PCR
 - Detection of hantavirus Ag via IHC

Hantavirus – Future Directions

- Vandetanib, a drug that blocks VEGF-R has shown some benefit in animal models
- Plasma from HCPS survivors contains significant amounts of antihantavirus Abs and can improve survival when injected into pts
- Concern for the use of Hantavirus as a bioterrorism agent
- Vaccine for HFRS is used in China and South Korea
- No current vaccine for the New World Hantavirus; investigating the use of viral antigens.
- Avoiding inactivated virus vaccines for HCPS due to concerns about mass production of a high-containment virus

References

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- Guardado-Calvo P, Rey F. Chapter Three – The Envelope Proteins of Bunyavirales. *Advances in Virus Research* 2017; 98: 83-118
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