MRSA pneumonia during the H1N1 Influenza Pandemic - A Case Series

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Goals for the Talk

• Describe H1N1-associated MRSA pneumonia
  • Clinical course
  • Microbiology data
  • Post-mortem data

• QA: change in practice

FIRST WAVE OF PANDEMIC

SPRING 2009

Patient 1

9 year-old previously healthy girl

• 4 days PTA presented CHOB ED
  • History
    • Sore throat
    • Rhinorrhea
    • Temperature = 103 F
  • PE:
    • Tachycardia (HR = 127)
    • Other VS WNL
    • RA saturation = 98%
    • No respiratory distress
    • Labs:
      • NP swab influenza A positive
        • (Next day - confirmed H1N1)
    • Discharged home

• Day of Admission presented CHOB ED via ambulance
  • History
    • Worsening severe cough
    • Fatigue
    • Difficulty breathing
  • PE:
    • HR = 159
    • RR = 66
    • BP = 101/57
    • RA saturation = 87%
    • Lungs
      • Respiratory distress
      • Severe retractions
      • Very poor aeration bilaterally
      • Crackles
  • Rx:
    • Intubated
    • Admitted to PICU

• 2 days PTA returned to CHOB ED
  • History
    • Rapidly worsening cough
    • Difficulty breathing
    • Persistent fatigue
    • Low grade fever
  • PE:
    • Tachycardic
    • Other VS WNL
    • RA saturation = 95%
  • Imaging
    • PA and lateral CXR - normal
  • Discharged home
  • Discharge diagnosis
    • Upper airway irritation due to influenza A
    • Cough

Patient 1

PICU Day 1

• On admission
  • Lab
    • Adequate oxygenation and ventilation, normal pH
    • Profound neutropenia, absent segmented forms
    • Na+ = 130
    • Glucose = 227
    • PT = 23.9
    • PTT = 108
    • INR = 2.05
  • CXR - bilateral patchy infiltrates
Patient 1

- PICU Day 1
  - Within 1 hour
    - Hypoxemic, hypercarbic
    - Lactic acidosis
    - Coagulopathic
    - Renal failure
  - Diagnosis
    - Septic shock from Influenza A pneumonia
  - Treatment
    - Fluids, DA, NE, vasopressin
    - Vancomycin, meropenem, Tamiflu
    - HFOV
    - ECMO
    - Prior to & during ECMO cannulation
    - 3 cardiac arrests
    - Lung sounds absent
    - CXR
    - bilateral complete lung opacification

- PICU Day 1 - 3
  - BC and tracheal aspirate culture - MRSA
  - Course
    - Multiple organ dysfunction syndrome (MODS)
      - Lung
      - Heart
      - Kidney
      - Liver
    - Cardiac tamponade from bilateral pleural effusions
      - Decreased ECMO flows
      - Hemodynamic instability
      - Treated with chest tube drainage (> 1 Liter)

- PICU Day 4 - 7
  - Renal failure requiring dialysis
  - Complete opacification of lungs
    - Bronchoscopy and BAL
      - Glistening, chalky secretions occluding distal trachea, main bronchi
      - Old fibrinous clot removed from intermediate bronchi
    - Distal airways patent
    - Airway mucosa
      - Ragged and severely edematous
    - Adherent fibrinous debris
    - BAL
      - Many WBCs, NOS
      - Culture negative
    - CXR remained unchanged

- PICU Day 9 - 11
  - Complete opacification of lungs
    - Bronchoscopy and BAL
      - Blood, packed blood clots completely occluding airway above carina
      - Suctioned, clot removed
    - Distal airways completely filled with clot
    - Consultation with other ECMO Centers and Lung Center
    - Intratracheal TPA
    - Risks/benefits discussed with family
    - Consent signed
    - Massive pulmonary hemorrhage
      - Hemodynamically unstable
      - Anemia requiring transfusion
    - Left CT
      - Increased output
      - Bloody, black drainage- ? Necrotic lung

- PICU Day 12
  - Continued deterioration
    - Pulmonary hemorrhage
    - Lung necrosis
    - Ongoing MODS
    - Further therapy futile
    - Discussed with family
    - ECMO support withdrawn
    - Patient died
Eureka Moment

- High mortality with combination of
  - Refractory hypoxemia
  - Refractory shock

- Resolution
  - Consider ECMO early

Patient 2
15 year-old previously healthy boy

- 6 days PTA presented to another ED
  - Fever, cough, vomiting
  - Diagnosed with Influenza A
  - Discharged home
  - Did not take Tamiflu

- Day of Admission returned to other ED
  - History
    - Unable to take po
    - Vomiting
    - High fever
    - 20 h/ diarrhea
    - Decreased UO
    - Myalgias, LE pain
    - Difficulty breathing
    - Collapsed at home
  - Diagnosis
    - Shock - treated with fluids, NE
    - Hypoxemia - treated with FiO2 = 1.0 via NRB mask
    - Ceftriaxone
    - STAT team requested & dispatched

Patient 2

On STAT team arrival
- Received 6 Liters IVF, on NE
- PE
  - HR = 155, RR = 60, BP=Unable
  - Restless, pale, grunting, fair aeration, difficulty speaking but normal IM, poorly perfused
  - Intubated
  - Given Vancomycin
  - Direct admission to PICU

Patient 2

- PICU Day 1 - ECMO team in room prior to arrival
  - Profound septic shock with hypotension
    - VR = 160s
    - Delayed cap refill
    - Unresponsive to fluids, epi, NE, vasopressin, milrinone, DA
  - Lactic acidosis (~12)
  - Neutropenia, coagulopathy
  - Multiple organ dysfunction syndrome (MODS)
    - Heart
    - Lungs (ARDS)
    - Kidney (BUN = 50, Cr = 5.6), anuric
  - Rx:
    - ECMO (flows 6 - 6.5 Lpm)
    - Antimicrobials - vancomycin, meropenem
    - Fluids, pressors, inotropes
    - Blood products

Patient 2

- PICU Day 2:
  - Persistent shock, despite high ECMO flows (4.9 - 5.9 Lpm)
  - DA, epi, milrinone, vasopressin
  - Lactic acidosis (~10)
  - MODS
    - Heart
      - Lungs (complete white out of lungs)
      - Kidney (BUN = 50, Cr = 5.6), anuric
      - Treated with continuous hemofiltration, hemodialysis
    - Liver - coagulopathic, elevated transaminases
    - Bone marrow - neutropenia, thrombocytopenia
    - Rigid muscles LE (? tetany) with CPK >100,000
    - treated with dantrolene (without effect)
    - Sloughed gut

Patient 2

- PICU Day 3:
  - MRSA in trach asp
  - Persistent shock and MODS
    - Rising lactate (>12)
  - Acute neurologic deterioration
    - Pupils fixed, dilated
    - No spontaneous movements
    - Off sedation and paralysis
    - EEG - flat
  - Withdrawal of care - death
MRSA coverage

- Before July 2009
  - Vancomycin
    - Goal - trough to 8-10x MIC
    - MIC 1 - goal trough ~10 mcg/mL
    - MIC 2 - goal trough ~20 mcg/mL
- July - December 2009
  - Vancomycin + aminoglycoside (synergy)
  - Vancomycin:
    - Same goal
    - Achieved quickly due to renal failure
  - Gentamicin or tobramycin
    - Goal - peak 4-5 mcg/mL
    - Dose - 1 mg/kg IV q8
    - Adjust for renal dysfunction

QA: review of literature suggests delayed clearing of MRSA bacteremia with single drug therapy

SECOND WAVE OF PANDEMIC

FALL 2009

Patient 3

15 year-old previously healthy girl

- Day of admission presented CHOB ED
  - History
    - 7 days of cough
    - fever
    - fatigue
    - <1 day of difficulty breathing
  - PE
    - VS
      - Afebrile
      - HR = 131
      - RR = 30
      - Normal BP
    - RA saturation = 74%
    - Unable to speak - severe distress
    - Lungs - Decreased aeration on right
  - Rx
    - Rx
      - FiO2 = 1.0 NRB mask
      - Intubation
      - Ceftriaxone, Vancomycin
      - CXR:
        - Right-sided pneumonia
        - Pleural effusion

Patient 3

PICU day 1:

- VS
  - T = 38.8ax
  - HR =160
  - BP = 60/30
  - sat = 79% on FiO2 = 1.0
- Placed on HFOV
  - Fluid resuscitation
  - EPi, NE, DA
  - Stress dose steroids
  - Respiratory
    - Desaturation despite NO and HFOV
    - Changed back to CMV with high pressure

Patient 3

PICU day 2

- CV
  - Hemodynamic instability
  - Fluid resuscitation
  - Epi, NE, DA
  - Stress dose steroids
- Respiratory
  - Desaturation despite NO and HFOV
  - Changed back to CMV with high pressure
- Placed on ECMO
  - Cardiac ECHO - severe LV dysfunction

Patient 3

PICU day 3 - 6

- CV
  - Severe LV dysfunction with minimal improvement
  - DA, milrinone, NE, Epi
  - Treated for influenza myocarditis with IV Ig and steroids
  - Episodic hypotension
  - Nitroprusside, esmolol, hydralazine
- Respiratory
  - Persistent pneumonia with consolidation
  - Influenza A - treated with tamiflu
  - Trach aspirate, blood culture - MRSA
  - Vancomycin, Ceftriaxone, Meropenem
- ECMO
  - Bleeding
    - Treated with pRBCs, IVFs, FFP, plts, vitamin K
  - Technical complication
    - Coded, unable to be resuscitated
Patient 3 - CXR

Before ECMO

After ECMO

Patient 4

15 year-old previously healthy boy

Day of admission presented CHOB ED
- History:
  • Cough, fever for 4 days
  • Decreased intake, chest pain for 1 day
- PE:
  • VS:
    • T = 39.3°C
    • HR = 152
    • RR = 32
    • BP = 120/59
  • Labs:
    • Neutropenia
- CXR:
  • Bilateral infiltrates, focal opacities
- Diagnosis:
  • Severe bilateral pneumonia
  • Respiratory distress
- Workup:
  • PPD with ID consult
  • Chest CT scan with contrast
- Treatment:
  • Ceftriaxone, Azithromycin
  • Tylenol, Motrin

On Floor
- CXR
- Nodular infiltrates
- Diagnosis:
  • Severe bilateral pneumonia
  • Respiratory distress

Patient 4

PICU Day 1
- Respiratory Failure
  • BiPAP
  • Intubated within 2 hours
- CT scan
  • Severe bilateral pneumonia
  • Possible subsegmental pulmonary embolus
- Septic Shock
  • Fluids
  • Epi, DA, CaCl
  • Ceftriaxone, Oxacillin, Vancomycin, Gentamicin, Tamiflu
- Coagulopathy
  • PT > 25, plt = 94

CXR - Patient 4

Before intubation

After intubation

Patient 4

PICU Day 2 - 3
- ECMO
  • Worsening respiratory status
  • Ongoing shock despite
    • Fluids - CVP in mid-teens
    • DA, NE, vasopressin, Epi
  • ID
    • Negative respiratory screen
      • novel H1N1 screening - positive (day 12)

CXR - Patient 4

Before ECMO

After ECMO

Patient 4

On Floor
- CXR
- Nodular infiltrates
- Diagnosis:
  • Severe bilateral pneumonia
  • Respiratory distress

Workup:
- PPD with ID consult
- Chest CT scan with contrast
- Line, arterial catheter
- Respiratory screen for sars
- Repeat CBC
- PICU consult

Treatment:
- Ceftriaxone, Oxacillin, Vancomycin, Gentamicin, Tamiflu
- Coagulopathy
  • PT > 20, plt = 94

Course - deterioration
- Respiratory distress
- Hypoxemia
- Impending respiratory failure
- Transferred to PICU ~ 4 hours after admission
Patient 4

- PICU Day 4 - 7
  - MODS
    - CV deterioration
    - Second venous line placed to augment ECMO flows
      - Milrinone, Epi, DA, NE
  - Respiratory
    - Tension Pneumothorax - multiple
    - Chest tube
    - Pleural effusions
  - Renal
    - CVVHD
  - Coagulopathy
    - FFP and platelet replacements
    - Severe epistaxis - packing
  - ID
    - Trach aspirate culture positive for MRSA

Patient 4

- PICU Day 8 - 18
  - Encephalopathy
  - Sedation and/or uremia
  - Cardiac failure
    - EF 35%
    - SvO2 = 65 - 70%
    - Milrione, NE, DA
  - Respiratory failure
  - Renal
    - CVVHD
  - Hepatic Failure
    - Hyperbilirubinemia
    - Rising Transaminases
  - Coagulopathy
    - Epistaxis
    - UGI
  - ID
    - Trach aspirate culture positive for MRSA

Patient 4 - MRSA Cultures

<table>
<thead>
<tr>
<th>Day</th>
<th>Tracheal Aspirate</th>
<th>Blood</th>
<th>Throat</th>
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<tbody>
<tr>
<td>1</td>
<td>Negative</td>
<td>CTX</td>
<td>Vanc</td>
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<td>2</td>
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<td>CTX</td>
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<td>Negative</td>
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<td>Vanc</td>
</tr>
<tr>
<td>4</td>
<td>Positive</td>
<td>CTX</td>
<td>Vanc</td>
</tr>
<tr>
<td>5</td>
<td>Negative</td>
<td>Vanc</td>
<td>Gent</td>
</tr>
<tr>
<td>6</td>
<td>Negative</td>
<td>Vanc</td>
<td>Gent</td>
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<tr>
<td>7</td>
<td>Negative</td>
<td>Vanc</td>
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<td>Negative</td>
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<td>15</td>
<td>Positive</td>
<td>Vanc</td>
<td>Gent</td>
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<td>16</td>
<td>Positive</td>
<td>Vanc</td>
<td>Gent</td>
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<tr>
<td>17</td>
<td>Positive</td>
<td>Vanc</td>
<td>Gent</td>
</tr>
</tbody>
</table>

SUMMARY OF CASES

- Ill for 4 - 7 days prior to admission
- Presented in shock and/or respiratory failure
- Profound neutropenia
- Appropriately covered for MRSA coverage from admission
- Refractory shock and MODS requiring ECMO
- Death

LABORATORY AND AUTOPSY DATA

- Day 18
  - Continued care futile
  - Worsening MODS
  - Inability to eradicate MRSA
  - ECMO withdrawn
  - Patient died
### Day of Admission

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC (Differential)</td>
<td>0.7</td>
<td>0.6</td>
<td>3.3</td>
<td>0.5</td>
</tr>
<tr>
<td>ANC</td>
<td>133</td>
<td>192</td>
<td>815</td>
<td>295</td>
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<tr>
<td>Serum creatinine</td>
<td>1.0</td>
<td>5.6</td>
<td>1.0</td>
<td>1.1</td>
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<tr>
<td>Total bilirubin</td>
<td>1.0</td>
<td>2.2</td>
<td>0.9</td>
<td>0.7</td>
</tr>
<tr>
<td>Vancomycin trough</td>
<td>12.7</td>
<td>12.4</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Blood culture</td>
<td>MRSA</td>
<td>MRSA</td>
<td>Negative</td>
<td>Negative</td>
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### Hospital Day 2

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC (Differential)</td>
<td>3.8</td>
<td>1.5</td>
<td>1.9</td>
<td>0.5</td>
</tr>
<tr>
<td>ANC</td>
<td>2,964</td>
<td>195</td>
<td>684</td>
<td>115</td>
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<tr>
<td>Serum creatinine</td>
<td>3.6</td>
<td>5.0</td>
<td>1.1</td>
<td>1.4</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>6.0</td>
<td>7.8</td>
<td>1.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Vancomycin trough</td>
<td>13.8</td>
<td>8.2</td>
<td>5.7</td>
<td>5.2</td>
</tr>
<tr>
<td>Blood culture</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
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### Day of Death

<table>
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<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
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<tr>
<td>Hospital Day</td>
<td>11</td>
<td>3</td>
<td>7</td>
<td>18</td>
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<tr>
<td>WBC (Differential)</td>
<td>45</td>
<td>2.0</td>
<td>46.0</td>
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<tr>
<td>Serum creatinine</td>
<td>0.2</td>
<td>3.6</td>
<td>1.4*</td>
<td>0.3*</td>
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<tr>
<td>Total bilirubin</td>
<td>57.1</td>
<td>11.7</td>
<td>38.2</td>
<td>65.9</td>
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<tr>
<td>Vancomycin trough</td>
<td>11.2</td>
<td>16.9</td>
<td>21.1</td>
<td>19.9</td>
</tr>
<tr>
<td>Blood culture</td>
<td>negative</td>
<td>negative</td>
<td>negative</td>
<td>negative</td>
</tr>
</tbody>
</table>

### Postmortem

- **Patient 1** - Necrotizing pneumonia
- **Patient 2** - Necrotizing pneumonia
- **Patient 3** - Necrotizing pneumonia

<table>
<thead>
<tr>
<th>Culture for H1N1</th>
<th>Negative</th>
<th>Negative</th>
<th>Negative</th>
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</thead>
<tbody>
<tr>
<td>Blood Culture</td>
<td>MRSA</td>
<td>MRSA</td>
<td>MRSA</td>
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</tbody>
</table>

**Patient 4 - no autopsy**

### Microbiology Lab Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
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</thead>
<tbody>
<tr>
<td>Lowest Vancomycin MIC</td>
<td>1</td>
<td>1</td>
<td>≤ 0.5</td>
<td>≤ 0.5</td>
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<tr>
<td>Pulse field Type</td>
<td>USA300</td>
<td>USA300</td>
<td>USA300</td>
<td>USA300</td>
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<tr>
<td>PVL - associated with</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>leukocyte destruction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>and tissue necrosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PVL: cytotoxin associated with leukocyte destruction and tissue necrosis.

- Associated with necrotizing pneumonia.

### MRSA at CHOB PICU

- 2008: 52
- 2009: 53

- **MRSA**
- **MSSA**

---

* on dialysis

* on ultrafiltration
**PICU: Influenza A and Staphylococcus aureus**

**January - December 2009**

<table>
<thead>
<tr>
<th>Influenza A +</th>
<th>#</th>
<th>Ventilated</th>
<th>ECMO</th>
<th>Died</th>
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</thead>
<tbody>
<tr>
<td>MRSA</td>
<td>4</td>
<td>4 (100%)</td>
<td>4 (100%)</td>
<td>4 (100%)</td>
</tr>
<tr>
<td>MSSA</td>
<td>4</td>
<td>3 (75%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Staph Aureus, no sensitivities</td>
<td>2</td>
<td>1 (50%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>10</td>
<td>8 (80%)</td>
<td>4 (40%)</td>
<td>4 (40%)</td>
</tr>
</tbody>
</table>

**Influenza A+ Ventilated ECMO Died**

- **All MRSA**: 13, 4 (31%)
- **MRSA + H1N1**: 4, 4 (100%)
- **MRSA without H1N1**: 9, 0

**2009 Fun Facts**

- **January**: 1 RSV, 2 Flu A
- **February**: 2 RSV, 11 Flu A
- **December**: 26 RSV, 26 Flu A

**Conclusion**

- **Combination of MRSA and H1N1 is lethal**
  - Despite timely initiation of antimicrobial therapy
  - Despite aggressive resuscitation & use of ECMO
  - Death
    - Necrotic lung
    - Refractory shock
    - Persistent MODS