Cross Canada Rounds – Short Cases

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• No disclosures

• Consent obtained for presentation of both cases
Case 1
Case Presentation

- 9 year old female
  - Refugee from Syria, living in Turkey prior to arrival

- Upon arrival in Canada, she was asymptomatic
  - History of small volume hemoptysis 1 month prior to arrival
DDx of Cystic Chest Lesion?
DDx of Cystic Chest Lesion -- BROAD

- Infectious
  - Pneumonia
  - Abscess
  - Tuberculosis
  - Aspergillus
  - Hydatid Cysts

- Vascular lesion
  - Pulmonary Embolus
  - AVM

- Malignancy
  - Pleuropulmonary Blastoma
  - Carcinoma
  - Leiomyosarcoma
  - Neuroblastoma

- Congenital
  - CPAM
  - Bronchogenic Cyst
Past Medical History

• Small volume hemoptysis
  • Initially 3 years ago → “conservative management”
  • Re-occurred 1 month prior to admission
    • Intermittent, sputum streaked with blood
    • Occasional cough, clear sputum with “membrane” within

• Previous liver surgery
  • Resection of 2 “cysts” followed by “6 months of medication”
  • Complete resolution noted on imaging
Physical Examination

- Afebrile, RR: 18, O₂ Sats: 99% on RA
- HR: 90’s, BP 90’s/60’s
- CVS:
  - Normal S₁/S₂, no murmurs. Well perfused.
- Resp:
  - Equal breath sounds bilaterally. No crackles or wheeze. No clubbing. No increased WOB.
- Abdo:
  - Soft, non tender, no HSM. Scar noted over RUQ.
<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hgb</td>
<td>115</td>
</tr>
<tr>
<td>WBC</td>
<td>8.8</td>
</tr>
<tr>
<td>Eo</td>
<td>0.2</td>
</tr>
<tr>
<td>Neut</td>
<td>4.9</td>
</tr>
<tr>
<td>Lymph</td>
<td>3.1</td>
</tr>
<tr>
<td>CRP</td>
<td>5.4</td>
</tr>
<tr>
<td>ESR</td>
<td>33 (0-10)</td>
</tr>
<tr>
<td>Lytes</td>
<td>normal</td>
</tr>
<tr>
<td>BUN/Cr</td>
<td>normal</td>
</tr>
<tr>
<td>LDH</td>
<td>224</td>
</tr>
<tr>
<td>Liver Enzymes</td>
<td>Normal</td>
</tr>
<tr>
<td>Liver Function</td>
<td>Normal</td>
</tr>
</tbody>
</table>
Initial Work Up: Infectious

- Sputum Culture for Mycobacterium:
  - No AFB seen

- Mantoux
  - Negative
Work Up: Abdominal Imaging

• U/S & CT:
  • 2 complex cystic lesions
    • Bi-lobed appearance
  • No rim enhancement
  • No blood flow noted within lesions
  • Cyst density consistent with fluid
Updated DDx?
Disease Confirmation

• *Echinococcus* Serology:
  • Highly Positive
Echinococcosis
Echinococcosis Etiology

- Caused by 4 species of the *Echinococcus* family

  - **E. granulosus**
    - Cystic echinococcosis
    - Worldwide distribution

  - **E. multilocularis**
    - Alveolar echinococcosis
    - Colder climates
Echinococcus Life Cycle

Image from CDC: https://www.cdc.gov/parasites/echinococcosis/biology.html
E. granulosis: Worldwide Distribution
Cyst Growth

- Hydatid cyst slowly grows over time
  - Common in liver and lung
  - Rate of growth is dependent on surrounding tissue distensibility
    - Typically quoted rate of 1-5cm/yr

- Cysts layers
  - Endocyst
  - Ectocyst
  - Adventitia/Pericyst

Pedrosa et al, Radiographics, 2000
Symptoms

• Younger children are more commonly affected
  • Most are asymptomatic

• Tend to occur following cyst rupture
  • Contained
  • Communicating

• Leak of cystic fluid may cause anaphylaxis

• Symptoms:
  • Chest pressure/pain
  • Cough
    • May expectorate cystic elements
      • “Grape skins”
  • Wheeze
  • Hemoptysis
  • Fever
  • Malaise

Diagnosis

• Diagnosis depends on:
  • High clinical suspicion
  • History of travel to endemic area
  • Radiographic evidence
  • +/- Presence of cysts elsewhere
  • +/- Special tests
  • +/- Pathology
Radiographic Findings

• Most common finding are cysts
  • Typically occur in lower lobes (60%)
  • Calcification is rare

• Over time:
  • Multiple cysts can form
  • Surrounding lung tissue affected
  • Erosion into surrounding airways
  • Variable degree of rupture/leakage

Influences radiographic findings
Crescent Sign

Garget al, World J Radiol, 2016
Cumbo Sign

Pedrosa et al, Radiographics, 2000
Serpent Sign

Pedrosa et al, Radiographics, 2000
Water Lily Sign

Monod’s Sign
(Mass within a Cavity)

Pedrosa et al, Radiographics, 2000
Special tests

- Serologic testing
  - Enzyme immunoassay
    - Specificity = 91.6%
    - Sensitivity = 97.8%

- Other tests
  - Latex agglutination
  - Indirect hemagglutination
  - Complement fixation
  - Casoni skin test

- Pathology
  - 3 layer cyst
  - Protoscolices
Treatment

- Medical
- Aspiration
- Surgical Resection
Surgical Management

• Mainstay of treatment

• Eradication of parasite and cystic layers
  • Enucleation, wedge resection, lobectomy, pneumonectomy

• Risks/Complications:
  • Anaphylactic reactions
  • Infection: Cyst recurrence, abscess, empyema, sepsis
  • Leaks: Hydro/Pneumothorax

Mirza et al. Kendig’s, 2012
Medical Management

• Indications:
  - Asymptomatic patient
  - Increased surgical morbidity/mortality risk
  - Multiple cysts
  - Disease recurrence not amenable to surgery
  - With intraoperative spillage from cyst
  - Pre-operatively to aid in removal

Mirza et al. Kendig’s, 2012
Benzimidazoles

- Albendazole > Mebendazole
  - Albendazole: 10-15mg/kg/day
  - Mebendazole: 40-60mg/kg/day

- Treat for > 3-6 months
- +/- Addition of Praziquantel

- Contraindications
  - Pregnancy (first Trimester)
  - Large cysts at risk of rupture
  - Chronic liver disease or Bone Marrow suppression

Mirza et al. Kendig’s, 2012
Percutaneous Aspiration

- Typically reserved for hepatic cysts
- Can confirm diagnosis
  - Evidence of protoscolices, hooklets and hydatid membranes
- Increases the risk of anaphylaxis, cysts fluid spillage
- Generally not considered first line for therapy

Mirza et al. Kendig’s, 2012
E. granulosus var. canadensis

• Similar life cycle

• More benign disease
  • Less frequently symptomatic
  • Smaller, delicate cysts
  • Potential for spontaneous cure

• Diagnostic approach similar to “typical” variant

• Treatment can consist of observation, medical therapy, or surgical management

Mirza et al. Kendig’s, 2012
Back to our case...
• Initiated treatment with Albendazole and Praziquantel x 3 months

• Chest and Abdominal imaging:
  • Improvement in cyst size

• Given that lesions persist, continues on albendazole monotherapy
  • Plan to re-image in 3 months
Questions?
Case 2
Initial History

• 3 year, 8 month old female
  • Chromosomal deletion (9p23)
  • Global developmental delay
  • High Risk B Cell ALL
    • Maintenance phase chemotherapy
• History of febrile x 4 days, with cough and rhinorrhea
  • Not neutropenic
Deterioration

- Developed increased WOB

- Initial vitals:
  - Temp: 38°C  HR: 167  BP: 95/52  RR: 60  O2 Sats: 80% on RA

- Exam:
  - Appeared unwell, dusky, tired
  - Increased WOB, grunting and suprasternal indrawing
  - Normal cardiac sounds, no murmur. Brisk capillary response
  - No organomegaly
Work-up

- Hgb: 87  WBC: 0.8  PLT: 198
  - Neut: 0.5, Lymph: 0, Mono: 0, Eo: 0

- CRP: 368

- VBG: 7.42/36/23, Lactate: 1.8

- Lytes: Na: 130, K: 3.6

- Mild increase in Liver enzymes

- Normal Renal function
Respiratory Intervention

- Oxygen applied, (3L) with initial improved saturation
  - WOB persisted despite BiPAP trial

- Ongoing tachypnea and WOB → intubated
  - FiO₂ = 1.0, Pressure of 32/10 to maintain oxygen saturation
  - Transitioned to HFO

- Anti-infectives were broadened to Vancomycin, Meropenem, Azithromycin, TMP-SMX, and oseltamivir (Tamiflu)
ECLS Activation

• Our patient continued to deteriorate
  • Escalating inotropic/chronotropic agents
  • Ongoing difficulty with oxygenation and ventilation
    • ABG: 6.83/139/23

• After discussion with family, cannulated for ECLS and transferred to regional ECLS center
DDx of Rapidly Progressing Respiratory Failure?
DDx of Rapidly Progressing Respiratory Failure?

- Given speed of deterioration:
  - Infectious etiology most likely

- Viral
  - Influenza
  - Entero/Rhinovirus
  - RSV
  - CMV
  - ....

- Bacterial
  - S. pneumonia, S. aureas, Haemophilus, Morexella
  - Mycoplasma
  - PJP, Legionella

- Fungal less likely given rapid progression, but remains possible
Infectious Workup

- Enterovirus/Rhinovirus positive

- ETT suction:
  - No organisms, no growth on culture
  - Pneumocystis not seen
Bronchoscopy

- Day # 4 of ECLS
  - Galactomannan negative
  - Pneumocystis negative
  - Bacterial and Fungal Culture negative
  - No AFB seen
  - Adenovirus NAT positive

- *Legionella pneumophila* (serogroup 6)
Legionnaires Disease
(Legionellosis)
**Microbiology & Environment**

- *Legionella pneumophila* is a Gram-negative coccobacilli
  - 58 species
  - Multiple serogroups
    - Serogroup 1 (Lp1):
      - Most common subtype (~80%)
      - Most virulent subtype
  - Ubiquitous in aqueous environments
  - Survives as intracellular parasites in environment

Stout et al. NEJM, 1997
RedBook, 2015
Pathogenesis

- Transmission:
  - Inhalation, aspiration, or direct contact
  - Increased risk with cumulative exposure

- Infection of host cells
  - Flagellum, pili, and surface proteins to enter cells
  - Inhibition of phagocyte bactericidal function
    - Growth and replication occurs within host cells
  - Disruption of host cell membrane $\rightarrow$ *Legionella* expulsion

Stout et al. NEJM, 1997
The incidence of legionellosis decreased slightly from 2011 to 2012, but a general increasing trend in disease began in 2003. Factors contributing to this increase include a true increase in disease transmission, greater use of diagnostic testing, and increased reporting.

* Per 100,000 population.
Risk Factors

- Cigarette smoking
- Chronic Lung disease
- Malignancy/chemotherapy
- Surgery
- Neonates/premature infants
- Immunosuppression
  - Chronic steroid treatment
  - TNF-α treatment
  - Post transplant patients at high risk
- Neutropenia has NOT been identified as a risk factor

Greenberg et al. Lancet, 2006
Stout et al. NEJM, 1997
Clinical Manifestations

- Often resembles pneumococcal pneumonia and Community Acquired Pneumonia (CAP)
- Wide spectrum in disease from mild symptoms to severe pneumonia

Asymptomatic  Pontiac Fever  ARDS

Symptoms

• Fever tends to occur in nearly all individuals (67-100%)
  • May not manifest with immunosuppression

Symptoms

• Cough (41-92%)
• Chills (15-77%)
• Dyspnea (36-56%)
• Neurologic (38-53%)
• Myalgia/arthralgia (20-43%)
• Chest pain (14-50%)
• Gastrointestinal (9-47%)

Greenberg et al. Lancet, 2006
# Investigations

<table>
<thead>
<tr>
<th>Radiographic</th>
<th>Laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>• No consistent/pathognomonic for <em>Legionella</em></td>
<td>• Hyponatremia</td>
</tr>
<tr>
<td>• Patchy, unilobular infiltrate is most common</td>
<td>• Elevated inflammatory markers</td>
</tr>
<tr>
<td>• Pleural effusion (15-50%)</td>
<td>• Leukocytosis/Leukopenia</td>
</tr>
<tr>
<td>• Cavitation can occur (18%)</td>
<td>• Elevated Creatine Kinase</td>
</tr>
<tr>
<td>• Nodular opacities (8%)</td>
<td>• Myoglobinuria</td>
</tr>
<tr>
<td></td>
<td>• Watery sputum with few neutrophils</td>
</tr>
</tbody>
</table>

Greenberg et al. Lancet, 2006
Non-culture Diagnosis

- Urinary Antigen
  - Fast
  - Specificity of 99%
  - Detects only Lp1 subgroup
  - Sensitivity 56-99%
    - Lower in immunocompromised patients
  - Ideal to combine with respiratory culture

- Immunofluorescence
  - Low sensitivity

Culture Diagnosis

- **Gold standard**
  - Detects all Legionella species and antibiotic susceptibilities

- Requires special culture media and environment for growth
  - Appropriate identification on requisition

- Samples should be obtained from suspected sites of infection
Who to test?

- ATS and IDSA Adult Guidelines:
  - Severe Community Acquired Pneumonia (CAP)
  - Failure of outpatient therapy
  - Recent Travel
  - Pleural Effusion
  - Known *Legionella* outbreak
Treatment

- B-lactams and aminoglycosides are ineffective

- First line:
  - Levofloxacain (Fluoroquinolone)
  - Azithromycin (Macrolide)
  - Doxycycline (Tetracycline)

- Extended course in high risk individuals

- Reporting to public health
Mortality

- Early identification and treatment initiation is key
- Overall pediatric mortality = 33%

- Increased mortality in:
  - < 1 year of age (50% vs 25%)
  - Immunosuppressed (42% vs 15%)
  - Inappropriate therapy (76% vs 24%)

Greenberg et al. Lancet, 2006
Stout et al. NEJM, 1997
Back to our Case...
• Levofloxacin was added following identification of *Legionella*

• Hemodynamics improved, decanulated from ECLS on day 10

• Extubated to BiPAP on day 20
  • Quick transition to oxygen
  • On room air at time of discharge

• Completed a 6 week course of Levofloxacin
Source Identification?

• Public Health notified…

• Parents have a hot tub at home
  • Medical grade filters

• Legionella identified from hot tub water
Questions?
References – Echinococcosis


References – Legionnaires Disease


