Pleural Disease

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Disclosure

• None
• Special thank you to Dr Scott Schissel
  – Significant contribution to the development of
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Outline

• Normal pleural anatomy and function
• Mechanisms of pleural fluid accumulation
  – Transudates vs. Exudates
• Evaluating pleural effusions
  – Imaging
  – Thoracentesis
  – Pleural fluid analysis
• Diagnosis and management of common exudative effusions
• Evaluating the exudative effusion of unknown etiology
• Diagnosis and management of Pneumothorax

Normal Pleural Anatomy

• Basal pleural fluid volume: ~2.0 ml/hr
  – Daily production: ~25 ml/day
• Drainage capacity: ~15 ml/hour
  – Daily absorption ~350 ml/day

Pleural Fluid Origins: Transudates

Parietal

Visceral

Pleural Space

Serous Fluid

\[ P_{\text{pleural}} = -3 \text{ cmH}_2\text{O} \]

\[ P_{\text{hydrostatic}} \]

Lymphatics

Peritoneal Fluid

Pleural Fluid Origins: Exudates

Parietal

Visceral

Pleural Space

Cellular Fluid

\[ P_{\text{pleural}} = -3 \text{ cmH}_2\text{O} \]

\[ \uparrow \text{Vascular Permeability} \]
Pleural Fluid Origins: *Trapped Lung*

- Parietal
- Visceral

\[ \text{Pleural Fluid Origins:} \quad \text{Trapped Lung} \]

\[ \text{Parietal} \quad \text{Visceral} \]

\[ \text{P}_{\text{hydrostatic}} \quad \text{P}_{\text{pleural}} \]

\[ \text{Fluid} \quad \text{Serous} \]

\[ -25 \text{ cmH}_2\text{O} \]

\[ \text{NL} \quad \text{NL} \]

Diagnostic Evaluation of Pleural Effusions

- Identifying the etiology of a pleural effusion requires:
  - CLINICAL information
    - To suggest an underlying diagnosis
  - Radiographic findings
    - Infiltrate, mass, lymphadenopathy
  - Pleural fluid analysis
    - Transudate v. Exudate ->
      - Cell count and differential, cytology, culture, etc....

Causes of TRANSUDATIVE Pleural Effusions

- **Congestive Heart Failure (40%)**
- Cirrhosis
- Nephrotic Syndrome
- Trapped Lung (also can be exudative)
- Pulmonary Embolism (also can be exudative)
- Myxedema
- Urinothorax
- CSF leak

Causes of EXUDATIVE Pleural Effusions

- **Parapneumonic / empyema (25%)**
- Malignancy (12%)
- PE (10%)
- Tuberculosis
- Pancreatitis
- RA, SLE
- Uremia
- Post-cardiac injury / surgery
- Asbestos
- Chylothorax
- Intra-abdominal Abscess
- Meig’s Syndrome

Dasatinib (TKI for CML) up to 35% of patients develop exudative (78%) effusions

Evaluation of Pleural Effusions: is a thoracentesis always necessary?

- 68 yo man with:
  - Severe HTN and LVH
    - Presents 5 days after misplacing his antihypertensive medications with DOE and orthopnea x 1 day
  - Exam
    - BP 188/99
    - JVD 12 cm H\text{2}O
    - + dullness in the lower lung fields with inspiratory rales
    - 1/2 up the both lungs
    - + L-sided S\text{4}

Quick Quiz I

In addition to beginning anti-hypertensive and diuretic therapy, the next step in managing the patient’s pleural effusions is:

A. Perform a unilateral thoracentesis to analyze the fluid
B. Repeat a CXR in 24 hours and perform a thoracentesis if a significant effusion remains
C. Repeat a CXR in 72 hours and perform a thoracentesis if a significant effusion remains
D. No follow-up for the pleural effusions needed
Pleural Effusions: When to Tap

- Pleural effusion
- Lateral film
  - >10 mm thick on lateral decubitus CXR

<table>
<thead>
<tr>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Thoraentesis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thoraentesis (Asymmetry, chest pain, fever)</td>
<td></td>
</tr>
</tbody>
</table>

  | Effusion <10 mm |
  | Observation |

  | Effusion >3 days |
  | Thoraentesis |

Imaging Pleural Effusions

- AP film
- Lateral film

- Up to 500 ml can be “hidden” on an AP film

The Value of the Lateral Film

- Thickness of effusion <10 mm likely too small to tap

Value of the Lateral Decubitus CXR

- AP film
- Lat Decubitus film

Chest Ultrasound for Thoracentesis?

- RCT comparing the complication rate (e.g. pneumothorax) of sampling method: needle, needle with catheter, and needle with direct TUS
  - 0/19 serious complications with TUS guided
  - 14/33 serious complications (included inadequate tap) with blind aspiration

- Retrospective cohort over 30-month period
  - (N= 342 thoracenteses; 154 conventional techniques by the clinical services, vs.188 were with TUS)
  - PTX 18% in absence of TUS
  - PTX 3% with TUS

Grogan DR et al Arch Intern Med 1990 150:873-7
Raptopoulous V AJR 1991;156:917-20
Chest Ultrasound for Thoracentesis?

- Diacon et al. 2003 Chest 123: 436
  - CXR and Exam versus US to identify an optimal thoracentesis site
  - US proved more accurate in 25% of cases
  - US identified potential sites of organ puncture in 10% of cases
  - TUS located a suitable site in 54% of cases where the clinician was unable to locate a site
- Other studies have demonstrated low pneumothorax rates (0-1.5%) for US-guided thoracenteses performed on mechanically ventilated patients

Recommendations

- The safety of a thoracentesis is dictated by operator experience, regardless of whether US-guidance is used
- US-guidance for a thoracentesis is reasonable if:
  - the effusion is small
  - there is difficulty in obtaining fluid without guidance

Imaging Pleural Effusions

Chest CT Scan

Effusion

Large Volume Thoracentesis: OK to remove > 1 liter ??

185 pts with 1L -> 3.5L removed
- 1 pt (0.5%) had symptomatic re-expansion pulmonary edema (RPE) [1.4L removed]
- 4 pts (2.2%) had radiographic RPE only
- RPE did not correlate with pleural fluid volume, end-expiratory pleural pressure, or symptoms during the procedure
- No clear guidelines, but RPE is rare and strict adherence to limiting thoracenteses to 1L is not supported by data

Pleural Fluid Analyses

- Appearance (bloody, pus, turbid)
  - Malignancy is the most common cause of bloody pleural effusion
  - Non milky appearance doesn’t r/o chylothorax especially if fasting
- Odor (putrid = anaerobic infection)
- Chemical analysis
- Cellular analysis
- Microbiologic analysis
- Cytology
  - samples > 50ml do not seem to increase yield
Appearance: Bloody

<table>
<thead>
<tr>
<th>Fluid Hematocrit</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1%</td>
<td>Not significant</td>
</tr>
<tr>
<td>1-20%</td>
<td>Cancer &gt;&gt; PE &gt; Trauma &gt; Pneumonia</td>
</tr>
<tr>
<td>&gt;50% circulating HCT</td>
<td>Hemothorax</td>
</tr>
</tbody>
</table>

Appearance: Turbid

<table>
<thead>
<tr>
<th>Supernatant</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear</td>
<td>Cellular debris</td>
</tr>
<tr>
<td>Turbid</td>
<td>Increased lipid</td>
</tr>
</tbody>
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Chylothorax?

Chylothorax v pseudochylothorax

Pleural Fluid Studies to Send

- Total protein, and LDH
  - Distinguish transudate from exudate
    - Pleural fluid (PF) and serum samples simultaneously
    - Consider PF and serum albumin
  - Total and differential cell counts
  - pH
  - Glucose, amylase
  - Smears/cultures
    - Cytology: diagnostic ~ 70% of cases
    - Probable increased yield with 1 repeat sample
  - Other:
    - Adenosine deaminase (ADA), Interferon-gamma, RF, ANA, LE cells, triglycerides, HCT

Transudate or Exudate?: Light’s criteria

- One or more of the following defines an exudate:
  - Pleural fluid (PF) protein : Serum protein > 0.5
  - PF LDH : Serum LDH > 0.6
  - PF LDH > 2/3 upper limit normal serum LDH

Transudate or Exudate?: Light’s criteria

- If still suspect a transudate (e.g. a “diuresed” CHF-related pleural effusion), measure albumin gradient
  - Serum albumin - PF albumin > 1.2 g/dl = transudate
  - Pleural Fluid N-terminal – pro BNP (NT-proBNP)*:
    - Value > 1500 pg / mL is > 90% sensitive and specific for CHF, similar to the albumin gradient

*Janda S and Swiston J BMC Pulmonary Medicine 2010;10:58
**Transudate or Exudate?**

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity*</th>
<th>Specificity*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PF: serum protein &gt;0.5</td>
<td>98%</td>
<td>83%</td>
</tr>
<tr>
<td>PF: serum LDH &gt;0.6</td>
<td>86%</td>
<td>84%</td>
</tr>
<tr>
<td>PF LDH &gt;2/3 nl serum</td>
<td>90%</td>
<td>82%</td>
</tr>
<tr>
<td>Serum-PF alb &lt; 1.2</td>
<td>87%</td>
<td>92%</td>
</tr>
</tbody>
</table>

For determining cardiac origin

| PF NT-pro-BNP >1500 | 94%    | 94% |

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**Cell Counts**

- **Total WBC:** Not particularly discriminative

- **Differential**
  - **Neutrophils (>50%):** acute inflammation
    - Parapneumonic, PE, pancreatitis
  - **Lymphocytes (>50%):** cancer, TB, post-CABG
    - Flow-cytometry (lymphoma)
    - TB: Cultures, ADA, IFN-γ, PCR
  - **Eosinophils (>10%):** blood, air most common
    - Drugs, asbestos, paragonimiasis, Churg-Strauss

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**Pleural Fluid GLUCOSE < 60**

- Tuberculosis
- Rheumatoid arthritis
- Malignancy
- Parapneumonic
- Rare:
  - Paragonimiasis
  - Churg-Strauss
  - Hemothorax
  - Lupus

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**HIGH Pleural Fluid AMYLASE**

- Pancreatitis
  - Acute (10% of cases)
  - Chronic (Implies sinus tract)
- Esophageal Rupture
  - Life-threatening if not treated
- Malignancy
  - Mild elevation

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**LOW Pleural Fluid pH**

- Complicated parapneumonic effusion/empyema
- Esophageal rupture
- Rheumatoid pleuritis
- Tuberculous pleuritis
- Malignant pleural disease
  - Poor prognosticator
- Hemothorax
- Systemic acidosis
- Lupus pleuritis
- Urinothorax

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**Parapneumonic Effusions**

- 72 yo man with 3 days of
  - Cough, Sputum, Fever, and DOE
- **Exam**
  - T 100.9, Decreased B/S right base
- **Labs**
  - Serum WBC 15K (80 poly’s, 10% bands)
- **Lateral Decubitus CXR** revealed a free-flowing moderate-sized effusion
- Blood cultures were obtained and antibiotics started
Quick Quiz II

- Thoracentesis???
- Pleural Fluid Analysis
  - Sero-sanguinous
  - PF protein 3
    - Serum 4
    - PF LDH 800
    - Serum 300
    - PF pH 7.18
    - Gram stain and cultures NEG

The next step in managing this effusion is:
A. Antibiotics and close observation, including daily CXRs
B. Thoracentesis to drain the pleural space, repeat procedure as necessary
C. Chest tube drainage
D. Chest tube drainage + fibrinolytic to the pleural space

E. B or C

COMPLICATIONS of Parapneumonic Effusions (Why Drain it??)

- Chronic Pleural Infection
- Secondary Lung Abscess
- Bronchopleural Fistula
- Empyema Necessitans
  - Pleuro-cutaneous fistula
- Pleural Fibrosis
  - Lung entrapment →
  - Impaired lung function →
  - Surgical decortication

Who to Drain ??

<table>
<thead>
<tr>
<th>Pleural Anatomy</th>
<th>Fluid Micro</th>
<th>Fluid pH</th>
<th>Risk of Poor outcome</th>
<th>Drain?</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10 mm on Lat decub CXR</td>
<td>N/A</td>
<td>N/A</td>
<td>LOW</td>
<td>No</td>
</tr>
<tr>
<td>&lt;½ hemithorax AND -&gt;</td>
<td>GS and Cx NEG AND -&gt;</td>
<td>pH &gt; 7.20</td>
<td>LOW</td>
<td>No, BUT need to follow</td>
</tr>
<tr>
<td>&gt; ½ hemithorax, loculated, thick pleura Or -&gt;</td>
<td>GS or Or -&gt;</td>
<td>pH &lt; 7.20</td>
<td>Moderate / High</td>
<td>YES</td>
</tr>
</tbody>
</table>

Complex Parapneumonic Effusions and Empyema: Treatment

- Definitive Pleural Drainage
  - Commonly via chest tube
  - Serial thoracenteses an alternative, but not well-studied
- Appropriate Antibiotics
  - Duration uncertain….3 weeks minimum, but up to 4 – 6 weeks
  - Sometimes longer courses required for atypical pathogens or in cases of prolonged pleural drainage

Malignant Pleural Effusions

- 73 yo man with stage IIIB non-small cell lung Ca
- Presents with 3 weeks of progressive DOE
- CXR reveals a new large R pleural effusion
- A large volume thoracentesis is performed removing 1.8L of sero-sanguinous fluid
- Pleural fluid analysis reveals malignant cells
- The patient reports marked improvement in his dyspnea

Complex Parapneumonic Effusions and Empyema: Treatment

- Pleural Fibrinolytics
  - Variously used
  - Multicenter Intrapleural Sepsis Trial (MIST-1)
    - Pleural saline v. streptokinase
      - Streptokinase did NOT improve survival, need for surgical intervention, Chest CT appearance, or lung function
- Surgical Decortication
  - Considered if there is little clinical or radiographic improvement after 1 week of antibiotics and chest tube drainage
  - Required in 30% of cases
  - However, VATS adequate in 60% of these cases
Malignant Pleural Effusions

- Most commonly associated tumors:
  - Non-small cell Lung Ca
  - Breast Ca
  - Mesothelioma
  - Ovarian Ca
  - Lymphoma
- Dyspnea present in > 50% of cases
- Mean life expectancy with a malignant pleural effusion:
  - 7 months!
  - Can be longer in lymphoma and chemo-responsive solid tumors:
    - Breast Ca, small-cell lung Ca

Quick Quiz III

He presents 3 weeks later with recurrent dyspnea and a large pleural effusion. His family is very involved in his care and reports a declining functional status (ECOG 2-3).

The next step in managing his effusion is:
A. Place an indwelling pleural catheter
B. Radiation therapy to the R hemithorax
C. Systemic chemotherapy alone
D. Thoracoscopy (VATS) + Pleurodesis
E. Thoracotomy with pleurectomy

Therapeutic Approach to Malignant Effusions

Exudative Effusion of Unclear Etiology

- 78 yo man with dyspnea x 8 weeks, ROS otherwise NEG
- Exam with decreased BS L base, otherwise NL

Pleural Fluid Analysis:
- PF protein 5.7 (serum 8.3)
- LDH 1220 (serum 221)
- 620 WBC (19P, 67L)
- Glucose 98
- pH 7.46
- GS, Cultures AFB smear NEG
- Cytology NEG

Quick Quiz IV

The next step in managing his effusion is:
A. Place an indwelling pleural catheter
B. Thoracoscopy with pleural biopsy and pleurodesis
C. Measure a serum D-DIMER
D. Measure pleural fluid adenosine deaminase and interferon-gamma levels
E. C and D

Exudative Effusion of Unclear Etiology

- Up to 15% of exudative pleural effusions have no clear etiology, even after:
  - Pleural fluid analysis from thoracentesis and thoracoscopy and pleural biopsy
- Most undiagnosed exudates are from:
  - Malignancy (including mesothelioma)
  - Chronic empyema
  - Tuberculosis
  - Rheumatoid Arthritis
  - Pulmonary Embolus
  - "Diuresed" CHF
Exudative Effusion of Unclear Etiology

Pneumothorax

- Spontaneous
  - Primary spontaneous pneumothorax (PSP)
  - Secondary spontaneous pneumothorax (SSP)
- Trauma
- Iatrogenic
  - Procedural/Post operative
  - Barotrauma

Pneumothorax

- Primary spontaneous pneumothorax (PSP)
  - Pneumothorax that occurs without a precipitating event in a person who does not have known lung disease
  - Risk Factors: smoking, FHx, Marfan’s, homocystinuria, thoracic endometriosis
    - Incidence is substantially less in women
- Secondary spontaneous pneumothorax (SSP)
  - Pneumothorax that occurs as a complication of underlying lung disease
    - Chronic obstructive pulmonary disease (COPD) is the most common cause of SSP
      - Nearly 70 percent of SSP attributed to COPD and rupture of apical blebs
      - Can be seen in virtually every lung disease

Pneumothorax: Presentation

- Patients may complain of dyspnea or chest pain
- Physical findings
  - Tachycardia, tachypnea, hypertension, or oxyhemoglobin desaturation
  - Decreased excursion, diminished breath sounds and hyperresonance to percussion, SQ emphysema
  - Hypotension and tracheal deviation may occur if tension pneumothorax develops

Pneumothorax

- Intervention
  - Observation, rather than chest tube insertion, if clinically stable and the pneumothorax is small
    - Guideline - the distance between the lung and the chest wall is ≤2 cm on a chest radiograph
- Pleurodesis
  - Consider for recurrent PSP
  - Consider for an initial SSP to prevent recurrence
    - Once the air leak has resolved, the lung re-expanded, and pleural air removed
      - Persistent air leaks are more common and tend to persist longer with SSP compared with PSP
    - High rate of recurrence and increased risk secondary to diminished reserve secondary to underlying lung disease
Summary

• Normal pleural anatomy and function
• Mechanisms of pleural fluid accumulation
  – Transudates vs. Exudates
• Evaluating pleural effusions
  – Imaging
  – Thoracentesis
  – Pleural fluid analysis
• Diagnosis and management of common exudative effusions
• Evaluating the exudative effusion of unknown etiology
• Diagnosis and management of Pneumothorax

Further Reading


Disclosure

• None

Bonus Case I

• 67 yo man with dyspnea, cough and scant hemoptysis x 2 months
• Exam with poor chest excursion on the R with absent BS
• US of the R chest: small – moderate pleural effusion
• Pleural Fluid Analysis:
  – PF protein 3.9 (serum 7.9)
  – LDH 200 (serum 250)
  – Glucose 98
  – pH 7.48
  – GS, Cultures AFB smear NEG
  – Cytology NEG

Bonus Quiz I

The next step in managing this patient is:
A. Perform a large volume thoracentesis
B. Place an indwelling pleural catheter
C. Thoracoscopy with pleural biopsy
D. Perform a bronchoscopy
E. B and D

Bonus Quiz I Answer

• **Answer: D, perform a bronchoscopy**
• The CXR revealed near complete opacification of the R hemithorax with shift of the heart and mediastinum to the RIGHT, indicating volume loss and collapse of the R lung.....
• Moreover, the chest US revealed only a small – moderate effusion, resulting from probable lung entrapment due to endobronchial obstruction
• Thus, a reasonable next step would be to perform a bronchoscopy to rule out a proximal R-sided endobronchial lesion (which he had!)