A REVIEW OF PLEURAL EFFUSIONS AND UPDATES

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Pleura
TRANSUDATIVE

- ONCOTIC
  - LIVER FAILURE
  - RENAL FAILURE
- HYDROSTATIC
  - HEART FAILURE
  - RENAL FAILURE
  - MALIGNANCY

EXUDATIVE

- INFLAMMATION
  - PNEUMONIA
  - MALIGNANCY
  - TRAUMA
  - INFLAMMATORY DISEASE
  - PE
INTRODUCTION

• Pleural space normally maintains a small volume (10-15mL)
• Most common clinical presentations are dyspnea, chest pain, and symptoms associated with individual underlying disease
• Dyspnea usually develops with greater than 500-1000mL of pleural fluid
• Physical exam may demonstrate dullness to percussion, decreased breath sounds, or decreased tactile fremitus
• Percussion requires at least 300-400mL of fluid to be present
ETIOLOGY

- 30-40% Cardiac Failure
- 36% Parapneumonic
  - 75% bacterial, 25% viral
- 18% Malignant
  - 50% either breast or lung cancer
- 14% Pulmonary Emboli
- 5% Liver Cirrhosis
- 2% GI diseases (mostly pancreatitis)
- Other
ETIOLOGY

Drugs associated with pleural effusions (normally exudative):

- Amiodarone
- Nitrofurantoin
- Phenytoin
- Methotrexate
- Carbamazepine
PATHOPHYSIOLOGY

• Normal pleural physiology
  • Normally produces and reabsorbs up to 15mL of fluid per day and contains approximately 10mL of fluid at any one time (usually not apparent on imaging)
• Normal pleural chemistries
  • LDH <0.6 serum
  • Protein <0.5 serum
  • Glucose 0.6–0.8 serum
  • pH 7.60
PATHOPHYSIOLOGY

- **Transudate effusion**: due to an increase hydrostatic pressure and/or reduction in tissue oncotic factors
  - CHF: increased venous pressures and lung edema
  - Hepatic Cirrhosis: hypoalbuminemia/oncotic; diaphragmatic defect w/passage of ascitic fluid
  - Nephrotic syndrome: hypoalbuminemia/oncotic
  - Malignancy (10% of malignant effusions are transudate): via infiltration/obstruction of pleural capillaries and/or lymphatics
  - Constrictive pericarditis
• **Exudative effusion**: either direct or cytokine-induced disruption of normal pleural membranes and/or vasculature leading to *increased capillary permeability or impaired absorption*
  
  • Infection/pneumonia
  • Malignancy
  • Inflammatory diseases (i.e. RA, SLE)
  • Trauma/surgery
  • Pulmonary embolus
  • GI diseases: pancreatitis, esophageal rupture
  • Hemothorax
  • Chylothorax
  • Medication
DIAGNOSTIC IMAGING

- CXR
- Thoracic Ultrasonography
- Chest CT with contrast
DIAGNOSTIC IMAGING

• **CXR**: erect PA/lateral chest x-ray (insensitive to small amounts of fluid; only able to detect at least 50mL of fluid)
  • 75-100mL → obscures posterior costophrenic sulcus
  • 175-200mL → obscures lateral costophrenic sulcus
  • 500mL → obscures entire diaphragmatic contour
  • 1000mL → reaches level of the anterior 4^{th} rib
Pleural effusion (lateral view)

- Approx 100 mL of pleural fluid will cause appreciable blunting of the posterior costophrenic angle on the lateral view.
Pleural effusion (PA view)

- 200 mL will cause blunting of the lateral costophrenic angle on the PA projection in an upright patient
• **Lateral decubitus radiograph**
  • Can demonstrate fluidity; i.e. if fluid is moving freely or loculated
  • Usually amenable for thoracentesis if fluid layers >1cm
Thoracic Ultrasonography

- Can identify fluid amounts as small as 3-5mL
- Better differentiates loculation or pleural thickening than CXR
- Provides real-time guidance for thoracentesis or thoracostomy tube placement reducing complication rates
DIAGNOSTIC IMAGING
• Chest CT with contrast
  • Helpful in distinguishing fluid from lung mass, atelectasis, pneumonia, or hemothorax
  • Can define/characterize pleural loculation, thickening, nodularity, or other abnormalities
CT Image with Loculated Pleural Effusion on the Left

Fluid is here, but if not loculated (stuck in a pocket) would be here.
Thoracentesis:

Indications:
- All parapneumonic effusions
- New undiagnosed effusions

(However, consider risk versus benefit) Usually not required if:
- Small amount of pleural fluid (<1CM on lateral decubitus CXR)
- Diagnosis is secured or clinically obvious (CHF, viral pleurisy)

Also consider thoracentesis if CHF patient has atypical clinical features:
- Bilateral pleural effusions are markedly different sizes
- Does not resolve with adequate diuresis
- Fever or other clinical features of infection
DIAGNOSTIC PROCEDURES

• **Thoracentesis:**
  • No absolute contraindications
  • Have increased caution with:
    • Mechanical ventilation carries 1-7% risk of PTX
      • PEEP does not increase risk of PTX (JAMA 2014)
    • Active skin infection at needle insertion
    • PT/PTT 2X normal
    • Platelets >25K
    • Creatine >6.0
Thoracentesis:

Complications:

- Pneumothorax (most common clinically important complication)
  - With US guidance occurs <2% (without US occurs 12-33%)
- Infection/Empyema (very rare) (<2%)
- Liver or spleen puncture (if patient not sitting absolutely upright)
- Bleeding (hematoma, hemothorax)
LABS TO ORDER AFTER THORO

- Culture
- Cytology
- Cell count
- LDH
- Protein

- pH
- Albumin
- Glucose
- Amylase
- Triglycerides
DIAGNOSTIC CRITERIA

Light’s Criteria:

- **Transudate:**
  - Fluid:Serum protein ratio <0.5
  - Fluid:Serum LDH ratio <0.6
  - Pleural LDH >0.6 of upper limit of normal serum LDH

- **Exudative:** (presence of ANY of Light’s criteria as above)

- Consider pseudo-exudate (meet one or more of Light’s, but actually transudate)
  - Usually due to diuretic-treated CHF, cirrhosis, or nephrotic disease
**DIAGNOSTIC CRITERIA**

- **Simple parapneumonic effusion:**
  - Sterile, small (less than ½ hemithorax)
  - Free flowing pleural effusion in setting of pneumonia
  - pH >7.20, glucose >60mg/dL

- **Complicated parapneumonic effusion (ANY of the following)**
  - Encompassing more than one-half of the hemithorax
  - Effusion of any size with loculation
  - Thickened parietal pleura on chest CT
  - Positive gram-stain or culture
  - pH <7.20 or glucose <60mg/dL

- **Empyema** (gross pus in pleural space or positive gram stain)
  - Positive culture not required for diagnosis
DIAGNOSTIC CRITERIA
Diagnostic Criteria

- Gross appearance
  - Clear/Serous/Light yellow - transudate of any etiology, urinothorax
  - Bloody/serosanguinous - PE, TB, Malignancy, Trauma, Aortic Aneurysm, Parapneumonic, Thoracic endometriosis
  - Purulent/turbid/brown - empyema
- Nucleated Cells
  - Total >50,000, neutrophilia - empyema
  - Lymphocytosis (>85%) - TB, lymphoma, chronic rheumatoid, sarcoid, pseudoexudates
  - Eosinophilia (>10%) - pneumothorax, fungal, parasitic, medications, asbestos effusion
  - Mesothelial cells (>5%) - normal, transudate
Diagnostic Criteria

- Chemical analysis
  - Protein
    - >3 g/dL - most exudates
    - >4 g/dL - Tuberculosis
    - >7-8 g/dL - Blood cell dyscrasias
  - LDH >1000 IU/L - empyema, rheumatoid, malignant
  - Creatinine PE/Serum >1 - Urinothorax
  - Glucose <60 mg/dL - empyema, rheumatoid, lupus, TB, esophageal rupture
  - pH <6.7 - esophageal rupture
  - Amylase - Pancreatitis, esophageal rupture, pancreatic cancer
  - Adenosine deaminase >50 U/L - TB
  - Triglycerides >100 mg/dL - Chylothorax
If pleural effusion remains undiagnosed after fluid analysis via thoracentesis and/or malignancy suspected can also consider:

- **Closed pleural biopsy**: performed via transthoracic needle approach
- **Thoracoscopic pleural biopsy**: performed under direct pleural visualization
- Diagnostic yield is 70–90%
TREATMENT

• **Transudate**: usually resolve with treatment (diuresis) of the underlying cause (CHF, hepatic disease, nephrotic syndrome)
  
  • Therapeutic thoracentesis indicated for persistent large effusions
  
  • Uncommonly, can consider pleurodesis or chronic indwelling catheter for comfort or palliation
TREATMENT

- Simple/uncomplicated parapneumonic effusion → antibiotics and close observation (chest tube not indicated)
- Broad spectrum antibiotics should include anaerobic coverage until sensitivity available (examples of antibiotics with anaerobic coverage include):
  - Clindamycin, Augmentin, Unasyn, Zosyn, Carbapenems
TREATMENT

• Complicated parapneumonic effusion, empyema →
  • Antibiotics (broad spectrum including anaerobic coverage until sensitivity)
  • **Early thoracostomy tube drainage** to avoid inflammatory adhesion and organization
    • Chest tube can be remove when adequate drainage is accomplished: <50-100mL output per day AND resolution documented on follow-up imaging
  • Intrapleural fibrinolysis for empyema (controversial)
    • May improve drainage and decrease need for surgical intervention
    • Increases risk of intra-pleural hemorrhage
  • Surgical decortication (thoracoscopic vs open) may be required for effusions exhibiting complicated anatomy or those unresponsive to tube drainage
    • Extensive pleural thickening
    • Fibrous organization
    • Multiple loculations
• Malignant pleural effusion:
  • Recur in approximately 90% of cases (usually within one week)
  • Observation is appropriate in cases of small, asymptomatic, stable effusions
  • Consider Therapeutic (large volume) thoracentesis (LVT) for comfort/palliative measures
TREATMENT

• Note on LVT (large volume thoracentesis)
  • Reexpansion pulmonary edema is very rare and is unlikely related to rate or volume of fluid removed (Ann Thorac Surg 2007:84)
  • Removal of 1.5L at time is considered safe
  • LVT should be discontinued with development of chest discomfort
  • Can represent surrogate marker for unsafe drop in pleural pressures
TREATMENT

• Note if pleural effusion accumulates rapidly (commonly seen in malignant effusions)
  • Consider chemical pleurodesis: instillation of pleural sclerosing agent
    • Talc→ instilled through thoracostomy tube or through insufflation during thorascopy (more comfortable than alternative→ doxycycline)
    • Not very effective if lung reexpansion is incomplete after drainage (‘trapped’ lung)
  • Consider chronic indwelling pleural catheter
    • Preferred if there is ‘trapped’ lung
New ATS Guidelines for Malignant Pleural Effusion

- American Journal of Respiratory and Critical Care Medicine (Oct 2018):
  - In patients with known or suspected malignant pleural effusion (MPE), we suggest that ultrasound imaging be used to guide pleural interventions.
  - In patients with known or suspected MPE who are asymptomatic, we suggest that therapeutic pleural interventions should not be performed.
  - In patients with symptomatic MPE, we suggest large-volume thoracentesis if it is uncertain whether the patient's symptoms are related to the effusion and/or if the lung is expandable (the latter if pleurodesis is contemplated), to assess lung expansion.
New ATS Guidelines for Malignant Pleural Effusion

• In patients with symptomatic MPE with known (or likely) suspected expandable lung, and no prior definitive therapy, we suggest that either an indwelling pleural catheter (IPC) or chemical pleurodesis be used as first-line definitive pleural intervention for management of dyspnea.

• In patients with symptomatic MPE and expandable lung undergoing talc pleurodesis, we suggest the use of either talc poudrage or talc slurry.

• In patients with symptomatic malignant pleural effusions with nonexpandable lung, failed pleurodesis, or loculated effusion, we suggest the use of IPCs over chemical pleurodesis.

• In patients with IPC-associated infections, treating through the infection without catheter removal is usually adequate. We suggest catheter removal if the infection fails to improve.
References

- MKSAP 17
- UpToDate
- Medscape
- Management of Malignant Pleural Effusions. An Official ATS/STS/STR Clinical Practice Guideline
- Louisville lectures
QUESTIONS?