Approach to Internal Medicine

A Resource Book for Clinical Practice

David Hui · Alexander A. Leung · Christopher Ma *Editors*

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Editors
David Hui
The University of Texas MD
Anderson Cancer Center
Houston, TX
USA

Christopher Ma
University of Calgary
Calgary, AB
Canada

Alexander A. Leung
University of Calgary
Calgary, AB
Canada

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Pleural Effusion

DIFFERENTIAL DIAGNOSIS

EXUDATIVE—malignancy, infection, connective tissue disease, hypothyroidism, pulmonary embolism, hemothorax, pancreatitis, chylothorax, trapped lung

TRANSUDATIVE—HF, hypoalbuminemia (GI losing enteropathy, cirrhosis, nephrotic syndrome, malnutrition), SVC obstruction, hepatic hydrothorax, urinothorax, atelectasis, trapped lung, peritoneal dialysis, hypothyroidism, pulmonary embolism

NOTE—pulmonary embolism, malignancy, hypothyroidism, trapped lung, SVC obstruction, and sarcoidosis are usually exudative, but can occasionally be transudative. HF following diuresis may become "pseudo-exudative"

CLINICAL FEATURES

HISTORY—dyspnea, cough, hemoptysis, chest pain, weight loss, fever, trauma, occupational exposures, past medical history (pneumonia, liver disease, kidney disease, thyroid disease, cancer, HF, thromboembolic disease, connective tissue disease, smoking), medications

CLINICAL FEATURES (CONT'D)

PHYSICAL—vitals, cyanosis, clubbing, tracheal deviation away from side of effusion (if no collapse or trapped lung), peripheral lymphadenopathy, Horner syndrome, respiratory examination (decreased breath sounds and tactile fremitus, stony dullness to percussion), cardiac examination, leg swelling (HF or DVT); chest US is the most sensitive and specific test and should be done at point-of-care

RATIONAL CLINICAL EXAMINATION SERIES: DOES THIS PATIENT HAVE AN EXUDATIVE PLEURAL EFFUSION?

	Sens	Spc	LR+	LR–
Pleural cholesterol >55 mg/dL	85–94%	95–99%	7.1–250	0.07–0.16
Pleural LDH >200 U/L	70%	98%	18	0.32
Pleural: serum cholesterol ratio >0.3	93%	94%	14	0.08

CLINICAL FEATURES (CONT'D)

	Sens	Spc	LR+	LR–
Pleural: serum LDH ratio >0.6	88%	91%	9.2	0.14
Pleural: serum protein ratio >0.5	90%	90%	7.0	0.12
Combined ≥1 of the Light criteria	97%	85%	5.2	0.04
Pleural protein >3 g/dL	88%	86%	5.1	0.14
Pleural LDH >2/3 upper limit of normal	88–89%	93–100%	1.7–13	0.23–0.26
Serum: pleural albumin gradient <1.2 mg/dL	86–95%	42–100%	1.5–36	0.06–0.32

APPROACH—pleural effusions meeting none of the Light criteria are most likely transudative. However, if the effusion meets the Light criteria or if the effusion has a pleural cholesterol >55 mg/dL, pleural LDH >200 U/L, or ratio of pleural cholesterol to serum cholesterol >0.3, the effusion is likely exudative

Wilcox et al. *JAMA* 2014;311(23)

INVESTIGATIONS

BASIC

- **LABS**—CBC, lytes, urea, Cr, LDH, total protein, AST, ALT, ALP, bilirubin, INR, PTT, albumin
- **IMAGING**—bedside US necessary to examine pleural effusion for size, presence of loculations, CXR (PA, lateral), consider CT chest
- **THORACENTESIS**—send pleural fluid for cell count and differential, Gram stain, C&S, AFB and fungal cultures, LDH, total protein, pH, and cytology. Under special circumstances, also consider amylase, glucose, cholesterol, adenosine deaminase (for TB), albumin

SPECIAL

- **BIOPSY**—closed pleural biopsy (useful in diffuse pleural disease such as tuberculosis), medical thoracoscopy, surgical biopsy (video-assisted thoracic surgery); referral to Pulmonary Medicine or Thoracic Surgery necessary

DIAGNOSTIC ISSUES

OVERALL APPROACH—generally, if the effusion is >1/4 of hemithorax, enough fluid is present for diagnostic thoracentesis. US-guided thoracentesis is standard of care. If only a small amount of fluid is present (<10 mm [<0.4 in.]) and/or HF suspected, start with diuresis or continue to monitor with bedside ultrasound. If no improvement, perform thoracentesis to distinguish between transudative and exudative causes

THE LIGHT CRITERIA FOR EXUDATIVE EFFUSION—any one of the following criteria would suggest exudative effusion: fluid/serum total protein ratio >0.5, fluid/serum LDH ratio >0.6, fluid LDH >2/3 upper limit of normal serum level

PLEURAL FLUID ANALYSIS

- **FLUID ACIDOSIS** (pH <7.2)—complicated parapneumonic, TB, malignancy, rheumatoid arthritis, SLE, hemothorax, esophageal rupture, paragonimiasis
- **LOW FLUID GLUCOSE** (<3.3 mmol/L [<60 mg/dL])—parapneumonic, TB, malignancy, rheumatoid arthritis, eosinophilic granulomatosis with polyangiitis, hemothorax, paragonimiasis
- **FLUID EOSINOPHILIA** (>10%)—paragonimiasis, malignancy, eosinophilic granulomatosis with polyangiitis, asbestos, drug reaction, pulmonary embolism, hemothorax, pneumothorax, idiopathic (20%)
- **CYTOLOGY FOR MALIGNANCY**—yield for diagnosis with single attempt is 60%, two attempts is 85%, three attempts is 90–95%; obtain as much fluid as possible to increase diagnostic yield
- **FLUID FOR AFB**—obtain as much fluid as possible and ask laboratory to centrifuge collection and to culture sediment to increase diagnostic yield; if high positive predictive value for TB, consider referral to Pulmonary Medicine for closed pleural biopsy

MANAGEMENT

SYMPTOM CONTROL—**O_2**, **diuresis** (furosemide), **drainage** (thoracentesis, pigtail catheter, indwelling pleural catheter, chest tube), **pleurodesis** (talc slurry or poudrage), **surgery** (talc slurry, pleuroperitoneal shunt, pleural abrasion, pleurectomy)

TREAT UNDERLYING CAUSE

SPECIFIC ENTITIES

PARAPNEUMONIC EFFUSION

- **UNCOMPLICATED**—exudative effusion that resolves with resolution of pneumonia. Generally disappears with antibiotics alone

SPECIFIC ENTITIES (CONT'D)

- **COMPLICATED**—persistent bacterial invasion and fluid collection. Characterized by pleural fluid acidosis but sterile fluid. Pleural loculation may occur as fibrin gets deposited from inflammation. Treated the same as empyema
- **EMPYEMA**—presence of bacteria in Gram stain or pus in drainage (culture not necessary). pH often <7.2. For unloculated fluid, chest tube/small-bore catheter drainage usually adequate. Consider referral to Pulmonary/Thoracic Surgery early. Regardless of degree of loculations, consider use of thrombolytics TPA 10 mg with DNase 5mg instillation into chest tube BID × 3 days. If patient still unwell after several days of antibiotic treatment, consider referral to Thoracic Surgery for consideration of VATS/decortication

Rahman NM et al. *N Engl J Med* 2011; 365:518–526

SPECIFIC ENTITIES (CONT'D)

TRAPPED LUNG—stable chronic effusion, especially with history of pneumonia, pneumothorax, thoracic surgery or hemothorax. Diagnosis is established by measuring negative change in intrapleural pressure during thoracentesis. Depending on chronicity, treat by lung re-expansion. Thoracotomy with decortication sometimes required in infectious cases

HEPATOHYDROTHORAX—suspect if cirrhosis and portal hypertension, even in the absence of ascites. Pleural effusion results from passage of peritoneal fluid into pleura because of negative intrathoracic pressures and diaphragmatic defects. Do not insert chest tube. Treat with diuresis, salt restriction, and consider liver transplantation/TIPS procedure