MINISTRY OF PUBLIC HEALTH OF UKRAINE

Vinnitsa National Pirogov Memorial Medical University

"Approved"
by Methodical Council
Department of Tuberculosis, Clinical Immunology
and Allergy
Chair of Department
Ass Prof of HEI L.Kulyk

30.08.2024

A self-study module for medical students

Learning discipline	Phthisiology (Tuberculosis)
Module №1	Curation of patients with respiratory diseases
Topic of seminar #3	Management of patients with pleural effusion. Pathogenesis, clinical presentation, indications for thoracentesis, treatment outcomes.
Course	6th
Faculty	General medicine

1. Background

Pleural effusion is defined as accumulation of fluid in the pleural space that exceeds the physiological amounts of 10–20 mL. Pleural effusion develops either when the formation of pleural fluid is excessive or when fluid resorption is disturbed. Pleural effusions may represent a primary manifestation of many diseases, but most often they are observed as secondary manifestations or complications of other diseases.

Pleural effusions are a common medical problem with greater than 50 recognised causes. The pathophysiology of fluid accumulation depends on the underlying aetiology but is grossly due to an imbalance in pleural fluid formation and resorption. The distinction between transudative and exudative effusions, according to Light's criteria, is crucial to narrowing the differential diagnosis.

Pleural effusion is found in almost 10% of patients who have internal diseases and the main cause in 30–40% of these is cardiac failure. Among the noncardiac effusions, parapneumonic effusions are the most common at 36%, of which 75% are of bacterial and 25% of viral origin. Malignant pleural effusions follow in 18% of cases, half of which are caused by lung or breast cancer. Pleural effusion is secondary to pulmonary embolism in 14% of cases, to liver cirrhosis in 5%, and to gastrointestinal diseases, mainly pancreatitis, in 2% of cases. Many other possible causes, e.g. collagen vascular diseases like rheumatoid arthritis and systemic lupus erythematosus as well as several drugs, play an important role in differential diagnosis. Often, pleural effusions are observed after abdominal surgery, liver transplantation or coronary artery bypass surgery/pericardiectomy.

Pleural effusion may result from a number of pathophysiological mechanisms, all of which disturb the physiological balance between the formation and removal of pleural fluid (normal production estimated at 15 mL/day-1 in a 60-kg person). Most effusions develop from both an increase in the entry rate of liquid into the pleural space and a decrease in the maximal exit rate of liquid from the pleural space. Transudative effusions are caused either by increased hydrostatic pressure (e.g. in cardiac failure), or by reduced plasma oncotic pressure because of protein

Key points

- Pleural effusions may present as primary manifestations of many diseases. However, most often they are observed as secondary manifestations or complications of other diseases.
- Cardiac failure is the main cause of pleural effusions.
- Of noncardiac causes, parapneumonic effusions are commonest, followed by malignant pleural effusions.
- Small pleural effusions can be detected best by ultrasound (or CT).
- Pleural effusion can in the majority of cases be diagnosed by case history, clinical presentation, imaging techniques and examination of pleural fluid.
- The most important laboratory parameter of pleural fluid is total protein, distinguishing trans- and exudates.
- Biopsy procedures such as closed-needle biopsy or medical thoracoscopy/ pleuroscopy may be necessary to confirm or exclude malignant or tuberculous causes.
- Treatment depends upon the underlying disease.
- Local treatment options include therapeutic thoracentesis, chest-tube drainage, chemical pleurodesis and, rarely, surgical interventions.

deficiency (e.g. liver cirrhosis, nephritic syndrome). The pleura itself remains intact. Rarely, transudates may arise from the entry of liquids with low protein concentrations (e.g. urine, cerebrospinal fluid or iatrogenic intrapleural infusion of fluids). In contrast, pathological changes in the pleura result in exudation caused by diffuse increase of capillary permeability, due to localized ruptures (e.g. blood vessels, lymphatic vessels, lung abscess, oesophagus) or to disturbed absorption (e.g. lymphatic blockage).

Pleural effusion may be demonstrated by a number of techniques with different sensitivities. The demonstration by percussion requires at least 300–400 mL of fluid, whereas at least 200–300 mL is necessary for standard chest radiography.

Smaller amounts can be recognised by lateral decubitus radiography, which also demonstrates whether the fluid is moving freely. Ultrasound is able to demonstrate small effusions, and the sensitivity is almost 100% for volumes of 100 mL. Computed tomography (CT) and magnetic resonance imaging have very similar sensitivities, but require a more advanced technology and are therefore much more expensive. However, if pulmonary embolism is suspected, CT angiography is the preferred test. In the majority of cases, the aetiology is based on the case history, clinical presentation, imaging techniques and examination of the pleural fluid. The presence of a pleural effusion is established only by thoracentesis. The site should be selected according to the results of the diagnostic procedures. If the effusion is small, thoracentesis can be performed under ultrasound guidance. Thoracentesis is indicated in all cases of pleural effusion of unknown origin and in effusions that do not resolve after appropriate treatment. Additional biopsy procedures, such as closed needle biopsy or medical thoracoscopy/pleuroscopy, may be necessary to confirm or exclude malignant or tuberculous causes.

In many cases, evaluation of the pleural fluid yields valuable diagnostic information or even permits a clear diagnosis. The most important criteria are appearance, protein content and cellular components. In case of more specific diagnostic questions, routine measurement of the glucose content is supplemented by determination of further laboratory parameters and search for infecting organisms

Indications for diagnostic thoracentesis

- Effusion >10mm thick on ultrasound or lateral decubitus x-ray with no known cause
- Ultrasound indicated if difficulty in obtaining fluid or if effusion is small
- CXR not necessary after procedure unless air is obtained; cough, chest pain or dyspnea develops; or tactile fremitus is lost over the superior part of the aspirated hemithorax

Tests indicated according to appearance of fluid

- Bloody hematocrit <1% nonsignificant

  1-20% cancer, pulmonary embolism, or trauma

  >50% of peripheral hematocrit hemothorax

- Cloudy or turbid centrifuge turbid supernatant triglyceride level

  >110 mg/dl chylothorax

>50mg/dl, but <110mg/dl ipoprotein analysis

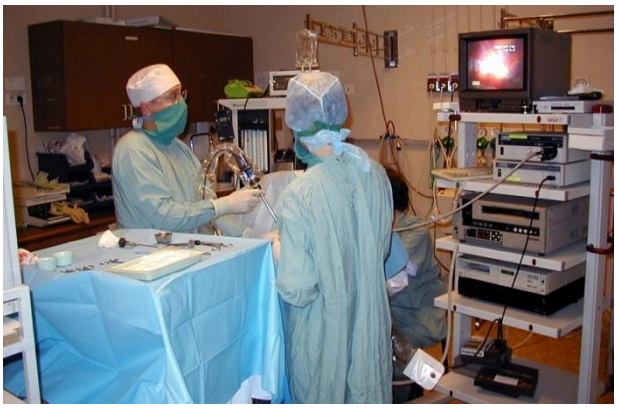
Presence of chylomicrons pseudochylothorax

• Putrid odor 📫 stain and culture 📫 possible anaerobic infection

Differentiate of Exudates and Transudates

• Light's criteria: measurement of levels of protein and LDH in pleural fluid and serum.
  o Pleural fluid protein/serum protein >0.5 = exudate
  o Pleural fluid LDH/serum LDH>0.6 = exudate
  o Or, pleural fluid LDH >2/3 upper limit of normal for serum = exudates

Clinical, radiological and gross pathological features including pleural pain, pleural thickening and pleural effusions are commonplace to both neoplastic and non-neoplastic pleural disease. Furthermore, characteristic imaging features may not be easily appreciated and are not always specific to a particular pleural disease entity. The multidisciplinary approach and comprehensive correlation between clinical presentation, pathological and radiological findings help to overcome these difficulties and achieve a definitive diagnosis.



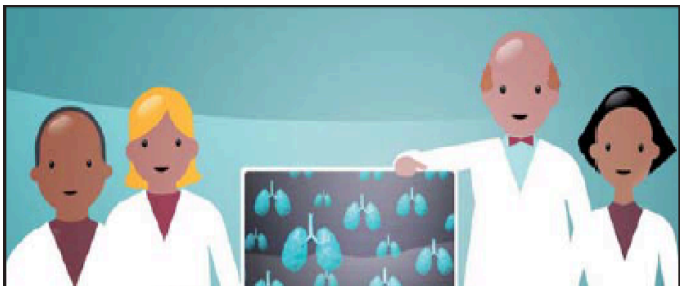
Ultrasound guided thoracocentesis is a safe and effective way to obtain pleural aspirate for analysis. Characteristic plain chest radiograph features of pleural effusion are blunting of the costophrenic angles and the presence of a meniscus.

Pleural Infection

Pleural infection imposes significant morbidity and a mortality rate of 20%. The majority of pleural sepsis is secondary to pneumonia, with up to 57% of pneumonia cases developing an associated pleural effusion. Up to 10% of these effusions progress to empyema.

There are no specific plain radiograph signs to differentiate between empyema, parapneumonic effusion and other non-infective causes of pleural effusion. However, the presence of a loculated pleural collection is suggestive of fibropurulent or organizational stage of disease. Transthoracic

Parenchymal change associated with complicated parapneumonic effusion and empyema is highly variable, ranging for entirely normal adjacent parenchyma to dense consolidation and abscess formation. Occasionally, the distinction between a peripheral pulmonary abscess and loculated empyema can prove challenging. A number of CT features have been described to help differentiate between the two entities. Complicated parapneumonic effusion and empyema tend to have thin walls, make obtuse rather than acute angles with the chest wall, to be lenticular rather than round in shape and cause passive atelectasis of the adjacent lung. The "split pleura" sign was reported to be highly specific for empyema, apparent in 68% of empyema cases but none of the lung abscesses. This sign comprises visualization of the thickened visceral and parietal pleura separated by pleural fluid.



Pleural tuberculosis

This is the most common form of extrapulmonary TB, and can either result from the rupture of a primary sub-pleural lung focus (evident or not on conventional chest X-ray) or be secondary to lymphohematogenic dissemination.

The presence of a pleural TB effusion has also been related to hypersensitivity (Light 1990).

Most cases occur several months after the primary infection, and frequently the patient relates having contact with an active pulmonary TB case in the two years preceding the current episode. The simultaneous presence of active pulmonary TB may be related to recent infection followed by disease. The onset of the disease may be insidious or abrupt, with fever, systemic complaints, dyspnea, dry coughs, and pleuritic thoracic pain. The physical examination shows signs characteristic of pleural effusion. With regard to diagnosis, the result of the TST may be negative at the diagnosis of the disease and become positive during anti-tuberculosis treatment. The pleural effusion is generally unilateral and moderate, and can easily be detected by conventional chest X-ray examination (Figure 1-2). In one third of cases, an underlying lung infiltrate can be observed.

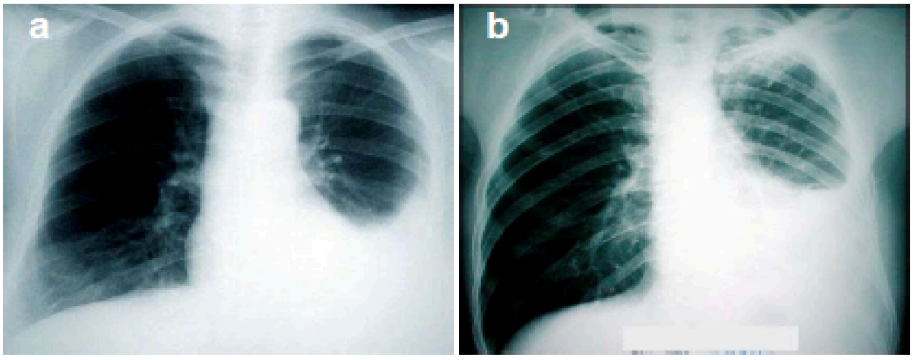


Figure 1-2: Pleural involvement with no parenchymal lesion (**a**) and with upper lobe lung infiltrate (**b**).

Thoracocentesis and puncture pleural biopsy should be indicated. The pleural liquid has a typically citrine yellow aspect and sometimes may be sero-hemorrhagic. It is generally an exudate with a predominance of lymphomononuclear cells, often negative for acid-fast bacilli (AFB) on microscopic examination. The etiological diagnosis is confirmed by the isolation of *M. tuberculosis* by culture of the fluid. The histopathological finding of granulomatous lesions in the pleural biopsy also confirms diagnosis, especially in countries with a high TB prevalence (Light 1990,Uehara 1993). An important auxiliary method in the diagnosis of pleural TB is the determination of adenosine deaminase (ADA), an enzyme liberated by activated lymphocytes.

This examination has a sensitivity and specificity above 90 %. Thus, ADA activity above the cut-off level in the pleural liquid is highly suggestive of pleural TB. If the patient is below 45 years of age and the pleural liquid shows predominance of lymphomonocytic cells, the specificity and positive predictive value of ADA may approach 100 %.

Adenosine desaminase activity

Adenosine desaminase, also known as ADA, is an enzyme involved in the metabolism of purines. Its presence is needed for the breakdown of adenosine from food and for the turnover of nucleic acids in tissues. The specificity is very high in fluids with a lymphocyte-to-neutrophil ratio higher than 0.75 (Burgess 1996, Diacon 2003). The suggested laboratory cut-off of ADA activity is 40 U/L for pleural, peritoneal and

pericardial fluids and 10 U/L for cerebrospinal fluid. However different laboratories have established different cut-offs varying between 33 and 50 U/L. As the description of the ADA assay is not readily available in the literature, it is detailed here. ADA is determined colorimetrically (Giusti 1974).

The differential diagnosis for pleural effusions includes para-pneumonic pleural effusions, mycoses, malignant diseases, and, especially in young women, collagen vascular diseases. Most of the time, the effusion is resolved, even if not treated, leaving minimal or no radiological sequelae (Light 1990, Uehara 1993).

Benign Pleural Thickening

Pleural plaques are the most commonly encountered pleural lesions, occurring in 20-60% of asbestos exposed individuals. Delineating pleural plaques from the normal muscle and fat companion shadows on plain chest radiographs can sometimes prove difficult. Extra-pleural fat tends to have a bilateral, symmetrical distribution whereas pleural plaques are typically asymmetrical. Although most often bilateral, approximately 25% of pleural plaques are unilateral, occurring more frequently on the left.

Computed tomography is more sensitive for pleural plaque identification than plain chest radiography. There is no significant difference between HRCT and low-dose mutlislice spiral CT in the detection of asbestos-related pleural and parenchymal changes. On CT, pleural plaques are characteristically smooth, flat, pleural-based lesions with coarse calcification. A thin layer of fat may be demonstrated separating the plaque from the underlying rib and extra-pleural fat. Visceral plaques may be named ‘hairy plaques’ when associated with adjacent parenchymal changes, such as short interstitial lines radiating from the plaque.

Benign asbestos related pleural thickening occurs much less commonly than pleural plaques in asbestos-exposed individuals. However, unlike pleural plaques, which are largely asymptomatic, benign asbestos related pleural thickening is associated with dyspneoa, chest pain and a restrictive pulmonary defect.

The plain chest radiograph appearance of benign asbestos related pleural thickening was initially defined by McLoud et al. as a smooth uninterrupted pleural opacity extending over at least 25% of the chest wall, with possible blunting of the costophrenic angles. The posterior and postero-medial pleura over the lower lobes are commonly involved.

The American Thoracic Society deem obliteration of the costophrenic angle a requirement for diagnosis of benign asbestos related pleural thickening. Lynch et al. described the following criteria for diffuse pleural thickening which correlate well with functional impairment: greater than 3mm pleural thickness, at least 5cm in transverse diameter, and at least 8cm in cranio-caudal length.

Rounded atelectasis. Plain chest radiography appearances are non-specific, usually comprising a peripheral mass involving the lower lobes. CT appearances are more characteristic; round atelectasis has been described as a round or oval mass abutting a peripheral pleural surface, vessels and bronchi curving into the mass and blurring the central margin (the Comet’s tail) and associated pleural thickening with or without calcification. Parenchymal bands often co-exist and are a sign of visceral pleural thickening. Evidence of characteristic imaging features eliminates the need for further investigation but atypical cases of round atelectasis may still require biopsy. In rare cases where round atelectasis cannot be differentiated from a peripheral pulmonary neoplasm, PET imaging demonstrates a metabolically inactive lesion. Round atelectasis shows similar morphological features on MRI and is typically isointense on T1W images and hyperintense on T2W images.

Solitary Fibrous Tumour of the Pleura accounts for less than 5% of all pleural masses; it is the most frequently occurring benign primary neoplasm of the pleura. There is no

association between SFTP and prior asbestos exposure. Approximately 80% of SFTPs arise from the visceral pleural surface, appearing as a pedunculated or sessile mass projecting into the pleural cavity. Occasionally they may be located within a fissure.

On plain chest radiographs, SFTPs appear as solid, well-circumscribed masses at the lung field periphery adjacent to the chest wall. Altered position of the mass on successive chest radiographs is consistent with a mobile, pedunculated STFP attached to a pleural stalk. Characteristic CT findings of SFTP comprise a solitary, well-demarcated, homogeneous mass involving the inferior hemithorax. Heterogeneity within the mass may indicate calcification, haemorrhage or necrosis. Although postcontrast homogeneous enhancement is common, heterogeneous enhancement is observed in up to 40% of cases. The majority (96%) of SFTPs studied show an acute angle with the pleura, which is unlike most other pleural pathology.

Malignant Pleural Thickening

Metastases to the pleura occur much more frequently than primary pleural neoplasms. The characteristic features exhibited by pleural metastases are similar to those found with a primary pleural neoplasm or inflammatory pleural process e.g. pleural effusions, pleural thickening and pleural-based masses. Positive cytological evidence of malignancy from pleural aspirates varies between 40%-87%.

Metastatic pleural carcinomas, melanomas and lymphomas are more often shed into pleural effusions than primary pleural neoplasms. Certain histological types of malignant mesothelioma, particularly epithelioid type, are more likely to be detected from pleural aspirate whereas purely sarcomatoid types are more elusive. Image-guided cutting needle pleural biopsy has a high diagnostic yield; thoracic ultrasound (TUS)-guided biopsies correctly diagnose in 70% and computed tomography (CT)-guided cutting-needle biopsy yields a sensitivity and specificity of 83% and 100%, respectively.

The features of contrast-enhanced CT (CECT) that favour malignant pleural disease from a benign process were initially described by Leung et al. The overall sensitivity and specificity of TUS is comparable to CECT for malignant pleural disease. Circumferential pleural thickening was reported to be less specific for malignancy in the presence of a pleural effusion. In addition to recognized CECT criteria, TUS demonstrated further morphological features associated with malignant pleural disease including visceral pleural thickening, poor resolution of all five diaphragmatic layers, diaphragmatic nodularity and thickening >7mm.

Although not routinely performed, magnetic resonance imaging may be useful in distinguishing malignant from benign pleural disease. Low signal intensity, on long time-to-repetition MR sequences was reported to reliably predict benign disease with a sensitivity and specificity of 100% and 87%.

Fluorodeoxyglucose positron-emission-tomography (FDG-PET) is another non-invasive imaging technique used to differentiate malignant and benign pleural effusions. Increased FDG uptake was shown in relation to pleural metastases. Malignant and benign inflammatory processes are indiscriminate on FDG-PET. Images should therefore be interpreted with caution as benign changes, for example, inflammation following talc pleurodesis may be mistaken for malignancy on FDG-PET.

Typical plain radiography findings in malignant mesothelioma are unilateral pleural effusion with associated nodular pleural thickening, although 25% of patients have pleural masses without an effusion. Prior asbestos exposure may be evident from co-existent pleural plaques or pleural calcifications. The pleural lesion may be focal or represent more diffuse thickening, encasing the entire lung surface, known as ‘hemithorax en-cuirasse’. There may be associated volume loss on the affected side. Volume loss is a non-specific finding that may present with other benign or malignant

pleural processes. The CT and MRI features of malignant mesothelioma are analogous to those of other causes of malignant pleural thickening. FDG-PET may provide prognostic imaging, with reports of significant correlation between SUV and patient survival. In addition, metabolically active areas within malignant mesothelioma pleural thickening may be identified with FDG-PET enabling targeted biopsies.

Thoracentesis

Except for patients with obvious heart failure, thoracentesis should be performed in all patients with more than a minimal pleural effusion (i.e., larger than 1 cm height on lateral decubitus radiograph, ultrasound, or CT) of unknown origin. In the context of heart failure, diagnostic thoracentesis is only indicated if any of the following atypical circumstances is present: the patient is febrile or has pleuritic chest pain; the patient has a unilateral effusion or effusions of markedly disparate size; the effusion is not associated with cardiomegaly, or the effusion fails to respond to management of the heart failure.

Thoracentesis is urgent when it is suspected that blood (i.e., hemothorax) or pus (i.e., empyema) is in the pleural space, because immediate tube thoracostomy is indicated in these situations. If difficulty in obtaining pleural fluid is encountered because the effusion is small or loculated, ultrasound-guided thoracentesis minimizes the risk for iatrogenic pneumothorax. In most instances, analysis of the pleural fluid yields valuable diagnostic information or definitively establishes the cause of the pleural effusion. This is the case when malignant cells, microorganisms, or chyle are found, or when a transudative effusion is found in the setting of heart failure or cirrhosis.

Observing the gross appearance of the pleural fluid may suggest a particular cause. For example, turbidity of the pleural fluid can be caused either by cells and debris (i.e., empyema) or by a high lipid level (i.e., chylothorax). A uniformly blood-stained fluid (i.e., hematocrit greater than 1 percent) narrows the differential diagnosis of the pleural effusion to malignancy, trauma (including recent cardiac surgery), pulmonary embolism, and pneumonia. If the hematocrit of the pleural fluid exceeds half the simultaneous peripheral blood hematocrit, the patient has hemothorax.

Although common, chest radiography is not necessary after thoracentesis unless air is obtained during the procedure; the patient develops symptoms such as dyspnea, cough, or chest pain; or tactile fremitus is lost over the upper part of the aspirated hemithorax.

PLEURAL EFFUSION

Pathophysiology

- **Systemic factors** (eg, ↑ PCWP, ↓ oncotic pressure) → *transudative* effusion
- **Local factors** (ie, Δ pleural surface permeability) → *exudative* effusion

Transudates

- **Congestive heart failure** (40%): 80% bilateral, ± cardiomegaly on CXR
  occasionally exudative (esp. after aggressive diuresis or if chronic), but ~75% of exudative effusions in CHF Pts found to have non-CHF cause (*Chest* 2002;122:1518)
- **Constrictive pericarditis** (knock on exam, calcification or thickening on imaging)
- **Cirrhosis** ("hepatic hydrothorax"): diaphragmatic defect w/ passage of ascitic fluid often right-sided (2/3) & massive (even w/o marked ascites)
- Nephrotic syndrome: usually small, bilateral, asymptomatic (r/o PE b/c hypercoag)
- Other: PE (usually exudate), malignancy (lymphatic obstruction), myxedema, CAPD

Exudates

- **Lung parenchymal infection** (25%)
  bacterial (parapneumonic): can evolve along spectrum of *exudative* (but sterile) → *fibropurulent* (infected fluid) → *organization* (fibrosis & formation of rigid pleural peel). Common causes: *Strep pneumo, Staph aureus, Strep milleri, Klebsiella, Pseudomonas, Haemophilus, Bacteroides, Peptostreptococcus*, mixed flora in aspiration pneumonia.
  mycobacterial: >50% lymphs 80% of the time, ADA >40, pleural bx ~70% Se
  fungal, viral (usually small), parasitic (eg, amebiasis, echinococcosis, paragonimiasis)
- **Malignancy** (15%): primary lung cancer most common, metastases (esp. breast, lymphoma, etc.), mesothelioma (✓ serum osteopontin levels; *NEJM* 2005;353:15)
- **Pulmonary embolism** (10%): effusions in ~40% of PEs; exudate (75%) > transudate (25%); hemorrhagic—*must have high suspicion b/c presentation highly variable*
- **Collagen vascular disease**: RA (large), SLE (small), Wegener's, Churg-Strauss
- **Gastrointestinal diseases**: pancreatitis, esophageal rupture, abdominal abscess
- Hemothorax (Hct_{eff}/Hct_{blood} >50%): trauma, PE, malignancy, coagulopathy, leaking aortic aneurysm, aortic dissection, pulmonary vascular malformation
- Chylothorax (triglycerides >110): thoracic duct damage due to trauma, malignancy, LAM
- Other:
  post-CABG: left-sided; initially bloody, clears after several wks
  Dressler's syndrome (pericarditis & pleuritis post-MI), uremia, postradiation therapy
  Asbestos exposure: benign; ⊕ eosinophils
  Drug-induced (eg, nitrofurantoin, methysergide, bromocriptine, amiodarone): ⊕ eos
  Uremia; post-XRT; sarcoidosis
  Meigs' syndrome = benign ovarian tumor → ascites & pleural effusion
  Yellow-nail syndrome: yellow nails, lymphedema, pleural effusion, bronchiectasis

Diagnostic studies

- **Thoracentesis** (*NEJM* 2006;355:e16)
  - *Indications:* **all effusions >1 cm in decubitus view**
    if suspect due to CHF, can diurese and see if effusions resolve (75% do so in 48 h)
    asymmetry, fever, chest pain or failure to resolve → thoracentesis
    parapneumonics should be tapped ASAP (*cannot* exclude infxn clinically)
  - *Diagnostic studies:* ✓ total protein, LDH, glucose, cell count w/ differential, Gram stain & culture, pH; remaining fluid for additional studies as dictated by clinical scenario
  - *Complications:* PTX (5–10%), hemothorax (~1%), re-expansion pulm edema (if >1.5 L removed), spleen/liver lac.; post-tap CXR not routinely needed (*Annals* 1996;124:816)
  - ↓PTX w/ U/S and experienced supervisor (*Chest* 2009;135:1315; *Archives* 2010;170:332)
- **Transudate vs. exudate** (*Annals* 1972;77:507)
  - **Light's criteria**: exudate = TP_{eff}/TP_{serum} >0.5 *or* LDH_{eff}/LDH_{serum} >0.6 *or* LDH_{eff} >⅔ ULN of LDH_{serum}; 98% Se, 83% Sp; best Se of all methods (*Chest* 1995;107:1604); however, will misidentify 25% of transudates as exudates; ∴ if clinically suspect transudate but meets criterion for exudate, confirm w/ test w/ higher Sp
  - exudative criteria w/ better Sp: serum-effusion alb gradient ≤1.2, Se 87%, Sp 92%; serum-effusion TP gradient ≤3.1, Se 84%, Sp 91%; $chol_{eff}$ >45 mg/dL *and* LDH_{eff} >200, 90% Se, 98% Sp (no serum required)
  - CHF effusions: *TP may ↑ with diuresis or chronicity* → "pseudoexudate"; alb gradient ≤1.2, $chol_{eff}$ >60 mg/dL (Se 54%, Sp 92%) or clin judgment to distinguish (*Chest* 2002;122:1524)
- **Complicated vs. uncomplicated parapneumonic** (*Chest* 1995;108:299)
  - complicated = ⊕ Gram stain or culture *or* pH <7.2 *or* glucose <60
  - complicated parapneumonic effusions usually require *drainage* to achieve resolution
  - empyema = frank pus, also needs drainage to achieve resolution

- Additional pleural fluid studies (*NEJM* 2002;346:1971)
  - NT-proBNP ≥1,500 pg/mL has 91% Se & 93% Sp for CHF (*Am J Med* 2004;116:417)
  - WBC & diff.: exudates tend to have ↑WBC vs. transudates but nonspecific
    - neutrophils → parapneumonic, PE, pancreatitis
    - lymphocytes (>50%) → cancer, TB, rheumatologic
    - eos (>10%) → blood, air, drug rxn, asbestos, paragonimiasis, Churg-Strauss, PE
  - RBC: Hct_{eff} 1–20% → cancer, PE, trauma; Hct_{eff}/Hct_{blood} >50% → hemothorax
  - AFB: yield in TB 0–10% w/ stain, 11–50% w/ culture, ~70% w/ pleural bx
  - adenosine deaminase (ADA): seen w/ granulomas, >70 suggests TB, <40 excludes TB
  - cytology: ideally ≥150 mL and at least 60 mL should be obtained (*Chest* 2010;137:68)
  - glucose: <60 mg/dL → malignancy, infection, RA
  - amylase: seen in pancreatic disease and esophageal rupture (salivary amylase)
  - rheumatoid factor, C_H50, ANA: *limited utility* in dx collagen vascular disease
  - triglycerides: >110 → chylothorax, 50–110 → ✓ lipoprotein analysis for chylomicrons
  - cholesterol: >60; seen in chronic effusions (eg, CHF, RA, old TB)
  - creatinine: effusion/serum ratio >1 → urinothorax
  - fibulin-3: ↑ plasma and/or effusion levels → mesothelioma (*NEJM* 2012;367:1417)
- Chest CT; pleural biopsy; VATS
- Undiagnosed persistent pleural effusions (*Clin Chest Med* 2006;27:309)
  - *Transudative*: most commonly CHF or hepatic hydrothorax. ✓ s/s CHF or cirrhosis, $NT\text{-}proBNP_{eff}$; consider intraperitoneal injection of technetium-99m sulfur colloid
  - *Exudative* (ensure using Sp test listed above): most commonly malig, empyema, TB, PE. ✓ s/s malig, chest CT (I^+), ADA or IFN-γ release assay; consider thoracoscopy.

Characteristics of Pleural Fluid (*not* diagnostic criteria)						
Etiology	**Appear**	**WBC *diff***	**RBC**	**pH**	**Glc**	**Comments**
CHF	clear, straw	<1000 *lymphs*	<5000	normal	= serum	bilateral, cardiomegaly
Cirrhosis	clear, straw	<1000	<5000	normal	= serum	right-sided
Uncomplicated parapneumonic	turbid	5–40,000 *polys*	<5000	normal to ↓	= serum (>40)	
Complicated parapneumonic	turbid to purulent	5–40,000 *polys*	<5000	↓↓	↓↓ (<40)	need drainage
Empyema	purulent	25–100,000 *polys*	<5000	↓↓↓	↓↓	need drainage
Tuberculosis	serosang.	5–10,000 *lymphs*	<10,000	normal to ↓	normal to ↓	⊕ AFB ⊕ ADA
Malignancy	turbid to bloody	1–100,000 *lymphs*	<100,000	normal to ↓	normal to ↓	⊕ cytology
Pulmonary embolism	*sometimes* bloody	1–50,000 *polys*	<100,000	normal	= serum	no infarct → transudate
Rheumatoid arthritis/SLE	turbid	1–20,000 *variable*	<1000	↓	RA ↓↓↓ SLE nl	↑ RF, ↓ C_H50 ↑ imm. complex
Pancreatitis	serosang. to turbid	1–50,000 *polys*	<10,000	normal	= serum	left-sided, ↑ amylase
Esophageal rupture	turbid to purulent	<5000 >50,000	<10,000	↓↓↓	↓↓	left-sided, ↑ amylase

Treatment

- Symptomatic effusion: therapeutic thoracentesis, treat underlying disease process
- Parapneumonic effusion (*Chest* 2000;118:1158)
  - uncomplicated → antibiotics for pneumonia
  - >1/2 **hemithorax or complicated or empyema → tube thoracostomy** (otherwise risk of organization and subsequent need for surgical decortication)
  - loculated→ tube thoracostomy or VATS; intrapleural t-PA + DNase ↓ need for surgical referral (*NEJM* 2011;365:518)
- Malignant effusion: serial thoracenteses vs. tube thoracostomy + pleurodesis (success rate ~80–90%) vs. indwelling pleural catheter (*JAMA* 2012;307:2383); choice of pleurodesis agent (talc, bleo, doxy) controversial; systemic steroids & pH <7.2 a/w ↑ pleurodesis failure rate
- TB effusions: effusion will often resolve spontaneously; however, treat Pt for active TB
- Hepatic hydrothorax
  - Rx: Δ pressure gradient (ie, ↓ ascitic fluid volume, NIPPV)
  - avoid chest tubes; prn thoracenteses, pleurodesis, TIPS or VATS closure of diaphragmatic defects if medical Rx fails; NIPPV for acute short-term management
  - spontaneous bacterial empyema (SBEM) can occur (even w/o SBP being present), ∴ thoracentesis if suspect infection
  - transplant is definitive treatment and workup should begin immediately

PLEURAL EFFUSION

Pathophysiology

• Systemic factors (eg, ↑ PCWP, ↓ oncotic pressure) → transudative effusion

• Local factors (ie, D pleural surface permeability) → exudative effusion **Transudates**

• Congestive heart failure (40%): 80% bilateral, ± cardiomegaly on CXR

occasionally exudative (esp. after aggressive diuresis or if chronic), but ~75% of exudative effusions in CHF Pts found to have non-CHF cause (Chest 2002;122:1518)

• Constrictive pericarditis (knock on exam, calcification or thickening on imaging)

• Cirrhosis ("hepatic hydrothorax"): diaphragmatic defect w/ passage of ascitic fluid

often right-sided (2/3) & massive (even w/o marked ascites)

• Nephrotic syndrome: usually small, bilateral, asymptomatic (r/o PE b/c hypercoag)

• Other: PE (usually exudate), malignancy (lymphatic obstruction), myxedema, CAPD

Exudates

• Lung parenchymal infection (25%)

bacterial (parapneumonic): can evolve along spectrum of exudative (but sterile) → fibropurulent (infected fluid) → organization (fibrosis & formation of rigid pleural peel).

Common causes: Strep pneumo, Staph aureus, Strep milleri, Klebsiella, Pseudomonas,Haemophilus, Bacteroides, Peptostreptococcus, mixed flora in aspiration pneumonia.

mycobacterial: >50% lymphs 80% of the time, ADA >40, pleural bx ~70% Se

fungal, viral (usually small), parasitic (eg, amebiasis, echinococcosis, paragonimiasis)

• Malignancy (15%): primary lung cancer most common, metastases (esp. breast, lymphoma, etc.), mesothelioma (✓ serum osteopontin levels; NEJM 2005;353:15)

• Pulmonary embolism (10%): effusions in ~40% of PEs; exudate (75%) > transudate (25%); hemorrhagic—must have high suspicion b/c presentation highly variable

• Collagen vascular disease: RA (large), SLE (small), Wegener's, Churg-Strauss

• Gastrointestinal diseases: pancreatitis, esophageal rupture, abdominal abscess

• Hemothorax (Hcteff/Hctblood >50%): trauma, PE, malignancy, coagulopathy, leaking aortic aneurysm, aortic dissection, pulmonary vascular malformation

• Chylothorax (triglycerides >110): thoracic duct damage due to trauma, malignancy, LAM

• Other:

post-CABG: left-sided; initially bloody, clears after several wks

Dressler's syndrome (pericarditis & pleuritis post-MI), uremia, postradiation therapy

Asbestos exposure: benign; □ eosinophils

Drug-induced (eg, nitrofurantoin, methysergide, bromocriptine, amiodarone): eos

Uremia; post-XRT; sarcoidosis

Meigs' syndrome = benign ovarian tumor → ascites & pleural effusion

Yellow-nail syndrome: yellow nails, lymphedema, pleural effusion, bronchiectasis

Diagnostic studies

• Thoracentesis

Indications: all effusions >1 cm in decubitus view

if suspect due to CHF, can diuresis and see if effusions resolve (75% do so in 48 h)

asymmetry, fever, chest pain or failure to resolve → thoracentesis

parapneumonics should be tapped ASAP (cannot exclude infxn clinically)

• **Transudate vs. exudate** (Annals 1972;77:507)

Light's criteria:

exudate = TPeff/TPserum >0.5

or LDHeff/LDHserum >0.6

or LDHeff>2/3 ULN

of LDHserum; 98% Se, 83% Sp; best Se of all methods (Chest 1995;107:1604);

however, will misidentify 25% of transudates as exudates; \ if clinically suspect

transudate but meets criterion for exudate, confirm w/ test w/ higher

CHF effusions: TP may ↑ with diuresis or chronicity → "pseudoexudate"; alb gradient ≤1.2,choleff >60 mg/dL (Se 54%, Sp 92%) or clin judgment to distinguish (Chest 2002;122:1524)

• Complicated vs. uncomplicated parapneumonic (Chest 1995;108:299)

complicated = □ Gram stain or culture or pH <7.2 or glucose <60

complicated parapneumonic effusions usually require drainage to achieve resolution

empyema = frank pus, also needs drainage to achieve resolution

2. Educational aims

Students require to know:

- Features of pathogenesis and pathomorphology of pleural effusion.
- The mechanism of pleural exudation.
- Causes of Pleural Effusions
- Symptoms of Pleural Effusions
- How is pleural effusion diagnosed?
- How is pleural effusion treated?

Students should be able to:

- To collect history and examine the patients with pleural effusion.
- To distinguish tuberculous pleurisy with pleurisy of other etiologies.
- Analysis of Pleural Fluid, Differentiation of Exudates from Transudates
- To know indications for Thoracentesis and to perform this manipulations
- To prescribe treatment of patients with pleural effusion.

3. Interdisciplinary integration

Name of discipline	**Necessary knowledge**
Human Anatomy	Morphology of pleura.
Pathological Physiology	Formal pathogenesis of pleural effusion. Elastic pull the lungs. Pressure between the layers of pleura.
General and Clinical Pharmacology	TB chemotherapy, classification, dosage, methods of administration. Pharmacokinetics of antituberculosis drugs. Adverse reactions to antibacterial drugs, prevention and elimination.
Propedeutics of Internal Medicine	Methods of physical examination of patients. Diagnostic value of epidemiological history, physical methods of examination of patients, puncture of pleural cavity, microscopic examination of fluid for M. tuberculosis.
Hygiene and Ecology	The structure and organization of TB dispensary. Procedure for issuance of disability list for TB patients. Rising incidence of

	tuberculosis among health care workers. The role of the basics of good nutrition, physical education and hardening, quitting bad habits in the prevention of TB.
Radiology	Methods of lung imaging. Interpretation of CT and CXR films.

REMIND

Malignant pleural mesothelioma (MPM)

In the non-invasive diagnosis of MPM the most useful blood-based markers are the serum mesothelinrelated peptides. But the poor sensitivity of mesothelin limits its added value to early diagnosis. In the pathological diagnosis of tissue or fluid the markers CEA, Ber-EP4, and calretinin were most valuable in discriminating mesothelioma from other malignant diseases and EMA and SMRP were most valuable in discriminating mesothelioma from non-malignant diseases.When selecting the preferred biopsy technique the relative sensitivities are 86% for image-guided core-needle biopsy, 94% for thoracoscopy, and 100% for thoracotomy . CT guided biopsy should be considered the primary method of diagnosis in patients with pleural thickening or lesions observed by CT scan, whilst when only pleural fluid is seen on CT scan the primary method of diagnosis should be medical thoracoscopy.
It is important to accurately differentiate between the three main cell types of MPM: epithelioid, sarcomatoid and biphasic since they have significantly different prognoses which may influence treatment selection. The current IMIG TNM staging system for MPM dates back to 1995 and is currently being revised in the IASLC Mesothelioma Staging Project. In the non-invasive staging of MPM, PET-CT had a higher accuracy than CT, PET and MRI for stage II and stage III tumours. PET-CT detects metastases previously undetected. Primary pleural lesions in patients with metastases had higher mean SUVmax and shorter survival.

4. Educational questions

2. Identify the anatomical relationship of the pleural cavities, lungs, kidneys, spleen and liver to the rib cage.
3. Identify the named regions of the parietal pleura and predict where pain from these regions will manifest.
4. Distinguish the following conditions: chylothorax, hemothorax, pneumothorax (open, tension and spontaneous).
5. Distinguish primary and secondary spontaneous pneumothorax and indicate the primary etiologies of each.
6. Compare the management of patients with small and large initial primary spontaneous pneumothorax.
7. Describe the management of patients with a tension pneumothorax.
8. Review the blood supply and innervation of body wall tissues within and adjacent to an intercostal space.
9. Describe the purpose of a tube thoracostomy and indicate where within an intercostal space the chest tube is inserted.
10. List the four most common causes of pleural effusion.
11. Describe the clinical presentation of pneumothorax and pleural effusion.
12. Identify additional physical exam findings that may suggest the etiology of a pleural effusion.

13. List the types of imaging modalities that are used to confirm pleural effusion and compare their strengths and weaknesses.
14. Identify the indication for thoracentesis in cases of pleural effusion.
15. Describe the technique in performing a thoracentesis.
16. Review the location of the intercostal neurovascular bundle within an intercostal space and relate this to the thoracentesis procedure.
17. Review the course of the azygos vein in the thorax and abdomen and predict the significance of this vessel in obstruction of the inferior vena cava.
18. Identify the potential causes of bloody and turbid pleural fluid.
19. Distinguish transudate and exudate effusions physiologically.
20. Define Light's criteria and indicate how they are used to distinguish transudate and exudate effusions.
21. List the primary etiologies of transudate effusions.
22. Identify common causes of exudate effusions.
23. Identify how pleural fluid and serum glucose levels contribute to the diagnosis of patients with exudate effusions.
24. Describe how pleural fluid analysis is used in the diagnosis of cancer.
25. Describe the presenting clinical features of mesothelioma.
26. List risk factors for mesothelioma.
27. Describe how pleural fluid analysis is used in the diagnosis of tuberculosis.
28. Review clinical presentation of lower respiratory tract infections.
29. Describe the assessment of patients with parapneumonic exudate effusions.

5. CASE PRESENTATION

Case1 Chest Pain After Sexual Intercourse

Case Editor - Jeremy Falk

Reviewed By Critical Care Assembly

Submitted by

Nitin Seam, MD
Attending Physician, Pulmonary/Critical Care Section
Veterans Affairs Medical Center
Washington, D.C.
PK Rohatgi, MD
Chief of Pulmonary/Critical Care Section
Veterans Affairs Medical Center
Washington, D.C.

History

A 55-year-old man presented to the Emergency Department 1 hour after developing chest pain.

He described the pain as severe, sharp, left-sided, and abrupt in onset with radiation to his back. He reported that the pain started during sexual intercourse concurrent with an episode of vomiting. He denied any other episodes of nausea or vomiting. He also denied diarrhea, cough, fevers, chills, or recent trauma.

Past Medical History: Significant for HIV without any history of opportunistic infections, as well as gout, hypertension, and insulin-dependent diabetes mellitus.

Social History: Significant for 10-pack-year history of cigarette smoking and intake of two alcoholic beverages per week.

Lab

WBC 11,100/cubic millimeter with 88.1% neutrophils

Hemoglobin 15.6 g/dL

Platelets 82,000/cubic millimeter

Sodium 141 mmol/L

Potassium 3.5 mmol/L

Chloride 107 mmol/L

Bicarbonate 23 mmol/L

Blood Urea Nitrogen 17 mg/dL

Creatinine 1.5 mg/dl

Amylase 122 U/L

Alkaline phosphatase 46 mU/ml

Asparate Aminotransferase 40 U/L

Alanine Aminotransferase 28 U/L

Total bilirubin 1.1 mg/dL

Albumin 4.6 g/dL

Arterial blood gas on 2 liters per minute of supplemental oxygen by nasal cannula: pH=7.43, $PaCO_2$=35 mmHg, PaO_2=58 mmHg

Figures

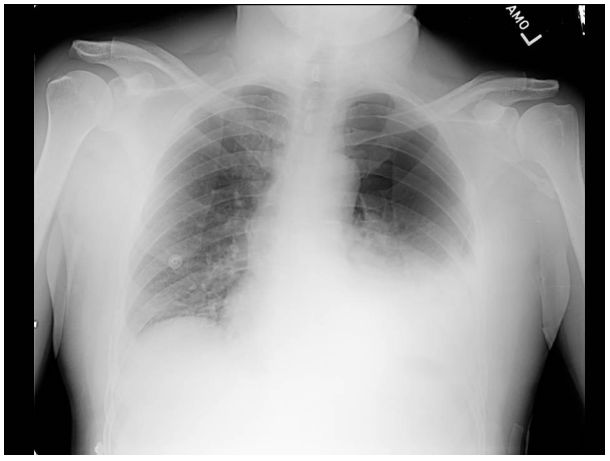


Figure 1. Portable Chest Radiograph

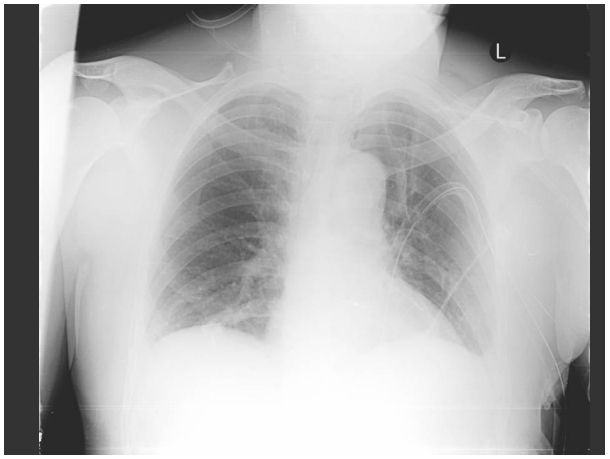


Figure 2. Follow-up Portable Chest Radiograph

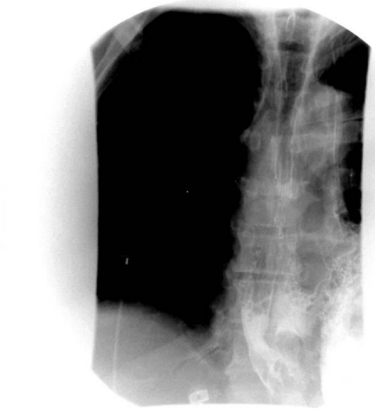


Figure 3. Esophogram

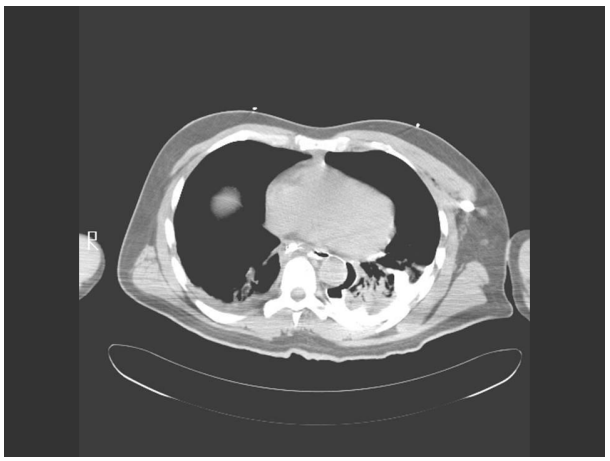


Figure 4. Computed Tomogram (CT) of the Chest

Начало формы

Question 1

What abnormalities are visible on the chest radiograph shown in Figure 1?

- A. Pneumonia due to Pneumocystis jiroveci (formerly known as Pneumocystis carinii)

- B. Left-sided pneumothorax and pleural effusion
- C. Left lower-lobe pneumonia with pleural effusion
- D. Pneumomediastinum with pleural effusion
- E. Pneumoperitoneum and left-sided pleural effusion

Remind

Drug-induced eosinophilic pleural effusion

Although numerous drugs can induce pleuritis and pleural effusion, the list of agents associated with eosinophilic pleuritis is not extensive. Some drugs used in psychiatry and neurology are some of the most important, including valproic acid (and its derivatives) and dantrolene. EPE was also reported as a complication of treatment with tazinidine, trimipramine and fluoxetine.

In order to list the most important drugs associated with EPE, two other groups should also be presented. The first is quite inhomogeneous and includes drugs mainly used in cardiology and internal medicine, these are: warfarin, diltiazem, simvastatin, imidapril, propylthiouracyl and mesalamine. The second group includes the following chemotherapeutics and antibiotics: nitrofurantoin, daptomycin and tosufloxacin.Acomprehensive review on drug-induced pleural effusion was published in 2004.

Pleural Malignancies

- Clinical presentation = usually pleural effusion
- Malignant pleural effusion (MPE) found in 6% of cancers history; reveals the cancer in half cases
- But in necropsy series: pleural effusion is only found in half of pleural tumors
- Dyspnea: most frequent symptom; other NON specific signs: cough, chest pain, asthenia and weight loss…, more rarely fever, pneumothorax

Light RW & Lee YCG. Textbook of Pleural Disease, 2nd ed 2008

Case 2. An adolescent with chest pain

Gwenda
Vleeshouwers,
Roy T. M. Sprooten,
Gernot G. U. Rohde
Dept of Respiratory
Medicine, Maastricht
University Medical Center,
Maastricht, The
Netherlands

An 18-year-old, otherwise healthy, young male reporting a 1-week history of muscular pain, a sore throat and a non-productive cough presented to the emergency room with acute chest pain and pain of the left shoulder. He also experienced some dizziness, without collapse, nausea or vomiting. He reported fever, but this was not objectively confirmed. There was no history of haemoptysis, wheezing, allergic reactions or weight loss. There was no significant family history of similar or other illnesses.

Task 1

What can cause acute chest pain in an otherwise healthy young adult?

On examination he had normal vital signs with a systolic/diastolic blood pressure of 135/65 mmHg, a heart rate of 80 beats·min^{-1}, a regular respiratory rate of 15 breaths·min^{-1}, a temperature of 37°C, normal cardiac examination, normal breath sounds, normal chest percussion and no signs of a deep vein thrombosis (DVT). Ear, nose and throat examination revealed a right-sided submandibular enlarged lymph node, but no enlarged or exudative tonsils. His shoulder examination showed some tenderness in the region of the left deltoid muscle, but no signs of fracture or dislocation.

The laboratory data showed elevated white blood counts with a marked leftward shift, a high C-reactive protein (CRP) and elevated D-dimers (table 2). White blood cell counts were 15.2 × 10^{9}·L^{-1}, with 77% segmented granulocytes, 13% band cells (or stab cells); d-dimers were 1011 ng·mL^{-1}.

An ECG showed a sinus rhythm of 80·min^{-1}, right-sided bundle branch block and up sloping ST-segment in V3-6.

Chest radiograph (fig. 1) showed some increased dorsobasal density in the right lung (arrow), but no lobar infiltrate.

Table 2. Blood results

Blood component	
Haemoglobin	8.6 mmol·L^{-1} (13.76 g·dL^{-1})
White blood cells	15.2 × 10^{9}·L^{-1} (15200·mm^{-3})
Band forms %	13
Neutrophils %	77
Lymfocyten %	8
Monocytes %	1
Eosinophils %	0.62
D-dimers ng·mL^{-1}	1011
CRP mg·L^{-1}	239
Creatinine µmol·L^{-1}	77

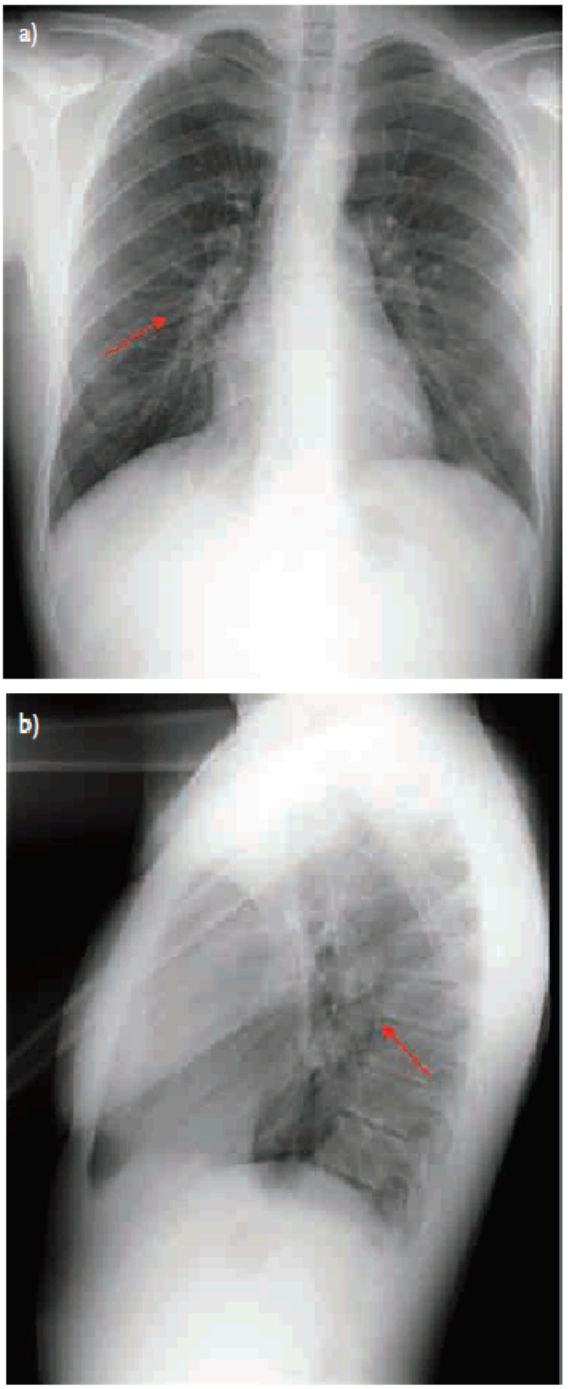


Figure 1
Chest radiograph showing slightly increased density parahilar right (a) and dorsobasal density (b).

Task 2: What is your (differential) diagnosis?

Table 1. Causes of chest pain

Location	Differential diagnosis	Prevalence[#] % [2]
Pulmonary	Pneumonia[¶]/tracheabronchitis	5
	Pleuritis[¶]	
	Pulmonary embolus[¶]	
	Pneumothorax[¶]	
Cardiovascular	Myocarditis/pericarditis[¶]	16
	Cardiac ischaemia	
	Aortic dissection	
	Vasculitis	
Chest wall/ orthopaedic	Myalgia/cramps	36
	Fracture	
	Artritis/arthrosis	
	Costochondritis/bursitis	
	Neuropathic pain	
	Cervical/thoracic disc disease	
Abdominal	Reflux/oesophagitis or oesophageal dysmotility	19
	Peptic ulcer	
	Diafragm spasm	
	Cholecystitis/choledocholithiasis	
	Pancreatitis	
	Nefrolithiasis	
Miscellaneous	Autoimmune disease	Miscellaneous 16; psychiatric 8
	Malignancy	
	Mediastinitis/mediastinal emphysema	
	Somatoform disorders	
	Anxiety disorders	
	Intoxications (e.g. cocaine)	

Data from [1, 2]. [#]: non-emergent chest-pain in primary care. [¶]: Differential diagnoses most likely in this case.

Case 3

Can you identify this uncommon cause of pleural effusion?

Case report

A 51-year-old female was admitted with a history of breathlessness, pain in the left shoulder and difficulty swallowing. A malignant melanoma had been removed from her epigastrium in 1982; in 2002, another pigmented lesion was removed from her cheek. This lesion was benign (Lentigo simplex). On examination, the patient had distended neck veins on the left side and showed clinical signs of left pleural effusion. She also had a highly pigmented lesion over the malar area, present for about 12 months, which was not investigated.

Initial investigations showed haemaglobin 11.4 $g \cdot dL^{-1}$ with mean corpuscular volume 86.2 fL and C reactive protein of 60 $mg \cdot dL^{-1}$ (normal range 0–10 $mg \cdot dL^{-1}$). Renal function, liver function, calcium, phosphorus and serum electrophoresis were normal. Serum lactate dehydrogenase (LDH) was raised to 1,855 IU (normal range 0–400 IU). Chest radiography showed left-sided pleural effusion along with widened mediastinum. The patient went on to undergo a diagnostic pleural aspirate (figure 1).

Figure 1
Pleural fluid aspirate.

Task 1
Comment on the pleural aspirate.

The patient underwent a computed tomography (CT) scan of chest and abdomen (figures 2 and 3).

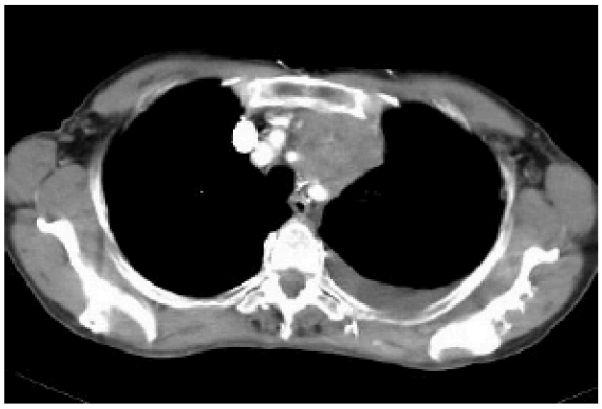


Figure 2
CT scan of the chest.

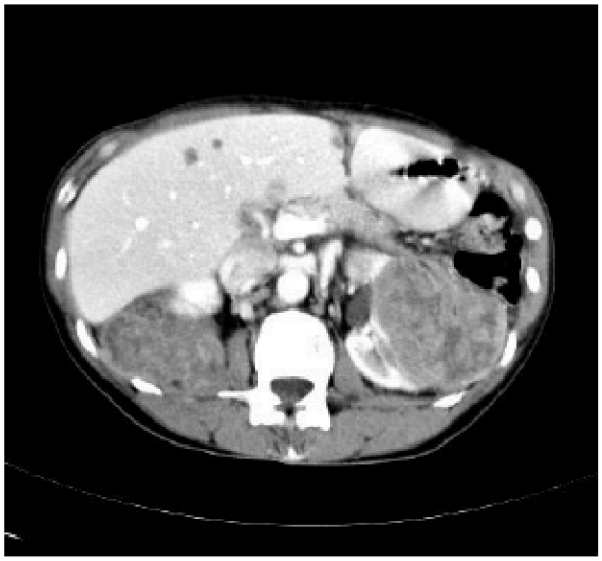
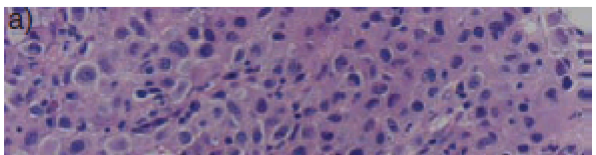


Figure 3
CT scan of the abdomen.

Task 2
Interpret the CT scans.

Pleural fluid analysis confirmed chylothorax and with the radiological findings of anterior-superior mediastinal mass and high serum LDH, lymphoma was first in the list of differential diagnoses. However, malignant melanoma is also likely, given the patient's history of previous melanoma 22 years previously.

The patient underwent ultrasound-guided biopsy of the right-sided pararenal mass (figure 4).



pleural effusion?

Конец формы
Конец формы

Case 4

Images in Pulmonary, Critical Care, Sleep Medicine and the Sciences

An Unusual Cause of Air–Fluid Levels in the Chest

Jihane Faress[1] and Rana Hejal[1]

[1]University Hospitals Case Medical Center and the Cleveland Department of Veterans Affair Medical Center, Case Western Reserve University, Cleveland, Ohio

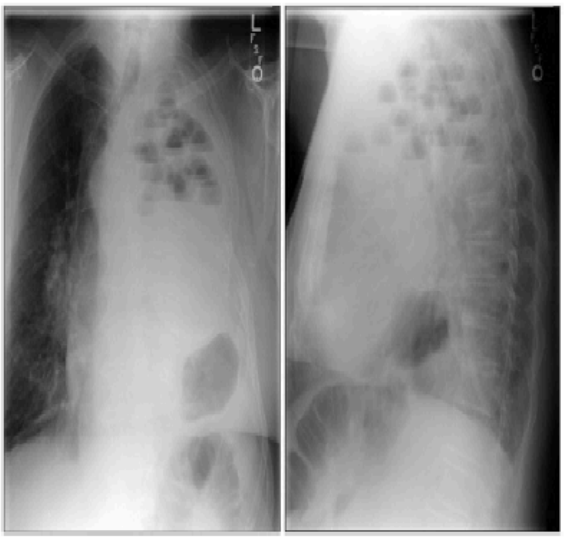


Figure 1

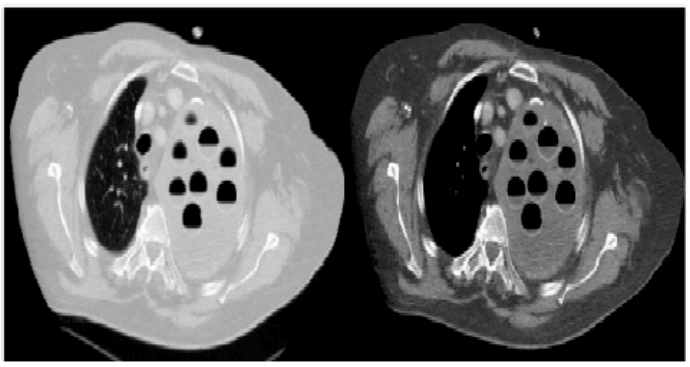


Figure 2

We present the case of a 76-year-old male who underwent pneumonectomy more than 40 years ago for refractory fungal infection. A chest X-ray was performed when the patient presented with dyspnea (Figure 1). To characterize the air–fluid level seen on the chest X-ray, a chest computed tomography was done (Figure 2). Several air–fluid levels were seen in Lucite balls that had been placed in the pneumonectomy space. The placement of space-occupying material in the chest after pneumonectomy is used to re-position the mediastinum for treatment of post-pneumonectomy syndrome, an uncommon late complication of surgery in which the mediastinum shifts into pneumonectomy space, resulting in symptomatic central airway compression (1). Several methods for repositioning the mediastinum have been described. These include suture fixation of the pericardium to the back of the sternum, surgical and chemical phrenectomy, and placement of prostheses to fill the empty hemithorax. Lucite plastic balls, silastic implants, injection of sulfur hexafluoride into the pneumonectomy space, and saline-filled breast prostheses have been used prophylactically and therapeutically (2). Lucite balls are the materials used in this case. It is unusual for the plastic balls to fill with fluid without signs or symptoms of active infection. We speculate that the physiologic fluid that filled the pneumonectomy space leaked into the Lucite balls. No treatment was recommended and the patient has remained clinically stable.

Author disclosures are available with the text of this article at www.atsjournals.org.

References

1. Shen R, Wain JC, Wright CD, Grillo HC, Mathisen DJ. Postpneumonectomy syndrome: surgical management and long-term results. *J Thorac Cardiovasc Surg* 2008;135:1210–1219.
2. Morrow SE, Glynn L, Ashcraft KW. Ping-pong ball plombage for right postpneumonectomy syndrome in children. *J Pediatr Surg* 1998;33:1048–1057.

Am J Respir Crit Care Med Vol 185, Iss. 10, p 1127, May 15, 2012

DOI: 10.1164/rccm.201109-1692IM
Internet address: www.atsjournals.org

Конец формы

6. Practical skills

- Interview (collection) complaints, all histories (present, past), inspectation and physical examination of the patient (revealing of abnormalities in organs and systems).
- To analyze and interpret results of the patient examination, data of chest X-ray, laboratory & instrument investigation.
- Defense of clinical point of view on diagnosis, prescribe adequate chemotherapy, detection of life prognosis and recovery.
- Perform thoracentesis
- Interpretation of laboratory analysis of pleural puncture
- Clinical management of pleural effusion

References

1. Alagha K, Tummino C, Sofalvi T, et al. Iatrogenic eosinophilic pleural effusion. Eur Respir Rev 2011; 20: 118–120.
2 Kalomenidis I, Light RW. Eosinophilic pleural effusions. Curr Opin Pulm Med 2003; 9: 254–260.
3 Light RW, ed. Pleural Diseases. 5th Edn. Philadelphia, Woulters-Kluwer/Lippincott Williams and Wilkins, 2007.
4 Morelock SY, Sahn SA. Drugs and the pleura. Chest 1999; 116:212–221.
5 Bullington W, Sahn SA, Judson MA. Valproic acid-induced eosinophilic pleural effusion: a case report and review of the literature. Am J Med Sci 2007; 333: 290–292.
6 Joshi P, Kasmani R, Hollingsworth J, et al. Divalproex sodiuminduced eosinophilic pleural effusion. Am J Ther 2009; 16: 593–595.
7 Urano T, Nishiumi M, Tajiri S, et al. Eosinophilic pleurisy induced by dantrolene. Tokai J Exp Clin Med 2005; 30: 189–192.
8 Leˆ-Quang B, Calmels P, Valayer-Chale´at E, et al. Dantrolene and pleural effusion: case report and review of literature. Spinal Cord 2004; 42: 317–320.
9 Moufarrege G, Frank E, Carstens DD. Eosinophilic exudative pleural effusion after initiation of tizanidine treatment: a case report. Pain Med 2003; 4: 85–90.
10 Hatzinger M, Stohler R, Holsboer-Trachsler E. Eosinophile pleuritic und Hepatopathie unter Trimipramin-Therapie [Eosinophilic pleuritis and hepatopathy under trimipramine therapy]. Schweiz Med Wochenschr 1991; 121: 910–912.
11 Behnia M, Dowdeswell I, Vakili S. Pleural fluid and serum eosinophilia: association with fluoxetine hydrochloride. South Med J 2000; 93: 611–613.
12 Ferna´ndez-Pe´rez R, Alvarez-Doban˜ o JM, Sua´rez-Antelo J, et al. Eosinophilic pleural effusion associated with the addition of sodium valproate. J Clin Psychopharmacol 2009; 29: 310–311.
13 Kravetz JD, Federman DG. Valproic acid-induced eosinophilic pleural effusion. South Med J 2003; 96: 803–806.
14 Daly JM, Goldberg RJ, Braman SS. Polyserositis associated with clozapine treatment. Am J Psychiatry 1992; 149: 1274–1275.
15 Boot E, de Haan L, Guzelcan Y, et al. Pericardial and bilateral pleural effusion associated with clozapine treatment. Eur Psychiatry 2004; 19: 65.
16 Huggins JT, Sahn SA. Drug-induced pleural disease. Clin Chest Med 2004; 25: 141–153.
17 Adelman M, Albelda SM, Gottlieb J, et al. Diagnostic utility of pleural fluid eosinophilia. Am J Med 1984; 77: 915–920.
18 Krenke R, Nasilowski J, Korczynski P, et al. Incidence and aetiology of eosinophilic pleural effusion. Eur Respir J 2009; 34:1111–1117.
19 Martinez-Garcia MA, Cases-Viedma E, Cordero-Rodriguez PJ, et al. Diagnostic utility of eosinophils in the pleural fluid. Eur Respir J 2000; 15: 166–169.
20 Ozkara SK, Turan G, Bas¸yig˘ it I. Clinicopathologic significance of eosinophilic pleural effusions in a population with a high prevalence of tuberculosis and cancer. Acta Cytol 2007; 51: 773–781.
21 Oba Y, Abu-Salah T. The prevalence and diagnostic significance of eosinophilic pleural effusions: a meta-analysis and systematic review. Respiration 2011; [Epub ahead of print DOI: 10.1159000327200].
22. American Thoracic Society and Centers for Disease Control and Prevention. Diagnostic standards and classification of tuberculosis in adults and children. *Am J Respir Crit Care Med* 2000;161:1376-1395. Available from: http://www.cdc.gov/nchstp/tb/pubs/PDF/1376.pdf

23. Centers for Disease Control and Prevention. Notice to readers: revised definition of extensively drug-resistant tuberculosis. *MMWR* 2006;55(43):1176. Available from: http://www.cdc.gov/MMWR/preview/mmwrhtml/mm5543a4.htm
24. American Thoracic Society and Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. *Am J Respir Crit Care Med* 2000;161:S221-47. Republished *MMWR* 2000;49(No. RR-6):1-51. Available from: http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf
25. Centers for Disease Control and Prevention. Guidelines for using the QuantiFERON–TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54 (RR–15). Available from: http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf
26. Centers for Disease Control and Prevention. Update: Adverse event data and revised American Thoracic Society/Centers for Disease Control recommendations against the use of rifampin and pyrazinamide for treatment of latent tuberculosis infection-United States, 2003. *MMWR* 2003; 52:735-9. Available from: http://www.cdc.gov/mmwr/PDF/wk/mm5231.pdf
27. American Thoracic Society and Centers for Disease Control and Prevention and Infectious Disease Society of America. Treatment of tuberculosis. *Am J Respir Crit Care Med* 2003;167:603-662. Available from: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf
28. Centers for Disease Control and Prevention. Notice to readers: Updated guidelines for the use of rifamycins for the treatment of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors. *MMWR* 2004;53(02):37.

Methodological recommendations were revised and approved at the meeting of the department "30" August 2024. Protocol No. 1.

Prepared methodical recommendations associate Professor of HEI Oksana Litvinyuk MD, PhD