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PLEURAL EFFUSION: A REVIEW

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ABSTRACT: A pleural effusion is an excessive accumulation of fluid in the pleural space. It can pose a diagnostic dilemma to the treating physician because it may be related to disorders of the lung or pleura, or to a systemic disorder. Patients most commonly present with dyspnea, initially on exertion, predominantly dry cough, and pleuritic chest pain. To treat pleural effusion appropriately, it is important to determine its etiology. Laboratory testing helps to distinguish pleural fluid transudate from an exudate. Transudative effusions are usually managed by treating the underlying medical disorder. Malignant effusions are usually drained to palliate symptoms and may require pleurodesis to prevent recurrence. Empyemas need to be treated with appropriate antibiotics and intercostal drainage.

KEYWORDS: pleural effusion, empyema, Light's criteria, thoracentesis.

INTRODUCTION: There is constant movement of fluid from parietal pleural capillaries into the pleural space at a rate of 0.01ml/kg body weight/h. Absorption of pleural fluid occurs through parietal pleural lymphatics. The resultant homeostasis leaves 5-15ml of fluid in the normal pleural space.

A pleural effusion is an abnormal accumulation of fluid in the pleural space. Accumulation of pleural fluid is not a specific disease, but rather a reflection of underlying pathology. With the knowledge of pleural fluid cytology, biochemistry, and clinical presentation, an etiological diagnosis can be established in approximately 75% of patients¹

PATHOPHYSIOLOGY:

1. Increased hydrostatic or decreased oncotic pressure (transudates)
2. Abnormal capillary permeability(exudates)
3. Decreased lymphatic clearance(exudates)
4. Infection in the pleural space(empyema)
5. Bleeding into pleural space(hemothorax)

Parapneumonic pleural effusions are exudates that accompany bacterial pneumonias.

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TRANSUDATES	EXUDATES
Heart failure(>90%cases)	Inflammatory diseases– bacterial
Cirrhosis with ascites	pneumonia, tuberculosis, viral, fungal,
Nephritic syndrome	rickettsial and parasitic infections
Peritoneal dialysis	Pulmonary embolism
Myxedema	Connective tissue disease
Atelectasis(acute)	Neoplasm- mesothelioma, metastasis,
Constrictive pericarditis	Meigs syndrome
Superior venecava obstruction	Pancreatic disease
Pulmonary embolism	Occupational asbestos exposure
	Uremia
	Chylothorax
	Sarcoidosis
	Drug induced- amiodarone, nitrofurantoin,
	dantrolene, bromocriptine, procainamide,
	procarbazine, carmustine,
	cyclophosphamide, docetaxel,
	methotrexate, GM-CSF, methysergide
	Post myocardial injury syndrome
	Chronic atelectasis

Table 1: ETIOLOGY OF PLEURAL EFFUSION:²

Pleural fluid protein: serum protein ratio > 0.5
Pleural fluid LDH: serum LDH ratio > 0.6
Pleural fluid LDH more than two-thirds the upper limit of normal serum LDH
Abbreviation: LDH, lactate dehydrogenase.

Table 2 Light's criteria for exudative pleural effusion³

DIAGNOSIS:

Clinical features: May be asymptomatic. Chest pain is frequently associated in case of pleuritis, trauma or infection. Dry cough may also be present. Dyspnea is common with large effusions.

Physical examination: Reduced tactile vocal fremitus, a stony dull note on percussion and decreased breath sounds over the effusion. Mediastinal shift to the opposite side may be evident in case of a massive pleural effusion.

Chest radiograph: An effusion of more than 75 mL is often visible on chest radiographs⁴. It ranges from blunting of costophrenic angle (small effusion) to dense opacification of the entire hemithorax with mediastinal shift to the opposite side (large effusion). Elevation of hemidiaphragm is seen in sub-pulmonic effusion.

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Ultrasonography: Is useful for detecting small pleural effusions, identifying multiloculated effusions and in localising the site for a diagnostic thoracentesis.

Computed tomography (CT): Chest CT can identify as little as 10ml of fluid. It is useful for delineating loculated pleural effusion or empyema, detecting mediastinal, hilar lymphadenopathy and tumors. The split pleural sign (thickened parietal and visceral pleura separated by pleural fluid) in contrast enhanced CT thorax is a characteristic finding.

Diagnostic thoracentesis: Helps in categorising the pleural fluid as transudate or an exudate.

Percutaneous pleural biopsy: Percutaneous pleural biopsies are of greatest value in the diagnosis of granulomatous and malignant diseases of the pleura. They are performed on patients with undiagnosed exudative effusions and non-diagnostic cytology, and when there is clinical suspicion of tuberculosis or malignancy. Closed percutaneous needle biopsy has traditionally been performed to investigate the etiology of exudative pleural effusions. Abrams and Copes pleural biopsy needles are most commonly used for the procedure.

Positron emission tomography (PET) scans: It helps in differentiating between benign and malignant pleural diseases, with a sensitivity of 97% and a specificity of 88.5%.⁵

Video-assisted thoracoscopy surgery (VATS): It is a minimally invasive method to view and biopsy the pleura and its contents. Apart from its diagnostic use, medical thoracoscopy is also used as a therapeutic tool in chemical pleurodesis for malignant pleural effusion and spontaneous pneumothorax, repair of bronchopleural fistula, performing drainage, and lysis of loculations in pleural infection

Pleural fluid analysis: It includes biochemical, microbiological and cytopathological analysis.

Etiology	Type of fluid	WBC Cells/mcl	Glucose	Other diagnostic features
Malignancy	Turbid to bloody	1000- <100,000 M	Equal to serum levels	Positive pleural biopsy (40%)
Uncomplicated parapneumonic	Clear to turbid	5000- 25,000 P	Equal to serum levels	
Empyema	Turbid to purulent	25,000- 100,000 P	Less than serum levels	

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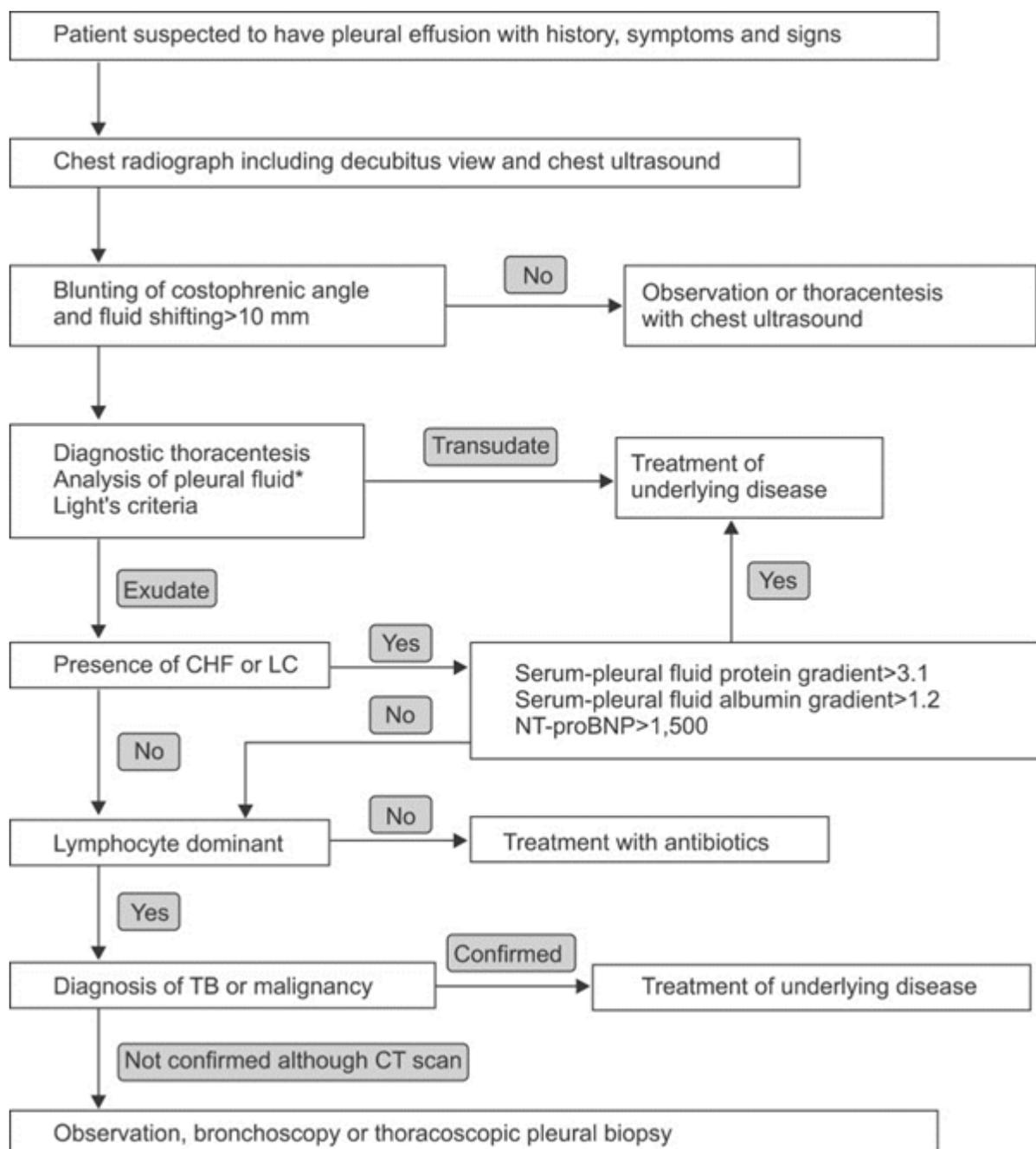
Tuberculosis	Serous to serosanguineous amber	5000-10,000 M	Equal to serum levels	Positive AFB smear/cultures ADA >50U/L Protein >4.0gm/dl Positive tuberculin test Positive pleural biopsy (80%)
Rheumatoid	Turbid, greenish yellow	1000-20,000 M/P	<40mg/dl	Rheumatoid arthritis, rheumatoid factor and anti CCP antibodies High LDH
Pulmonary infarction	Serous to grossly bloody	1000-50,000 M/P	Equal to serum levels	
Esophageal rupture	Turbid to purulent, red-brown	<5000- >50,000 P	Usually low	High salivary amylase level pH <6.0
Pancreatitis	Turbid to serous	1000-50,000 P	Equal to serum levels	High amylase level

Table 3: Characteristic features of exudative pleural effusions:²

LDH- Lactate dehydrogenase, M- mononuclear cell, P- polymorphonuclear leukocytes, ADA- Adenosine deaminase

- Adenosine deaminase – it is predominantly T-lymphocyte enzyme. High in HIV patients with very low CD4 count. Widely accepted cut-off value is 35 U/L (35-47). A meta-analysis of which included 2796 patients with TB pleuritis and 5297 with non-TB effusion demonstrated 92% sensitivity & 90% specificity for ADA as a biomarker.⁶
- Gama-interferon is a cytokine released by activated CD4 (+) T lymphocytes which increases the mycobactericidal activity of macrophages. But it is expensive & hence ADA is preferred.
- BNP and NT-proBNP are biomarkers for congestive heart failure(CHF). Both serum and pleural levels are increased in CHF.⁷ Serum levels >500 pg/ml for BNP & >450-1800 pg/ml for NT-proBNP establish a diagnosis of pleural effusion due to CHF.

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Algorithm for diagnostic approaches for patients suspected of pleural effusions⁸:

*Analysis of pleural fluid includes protein and lactate dehydrogenase of pleural fluids and serum, gross appearance, red blood cell, white blood cell with differential count, pH levels, glucose, amylase, cholesterol, triglyceride, cytology, acid-fast bacilli stain, TB culture, TB-polymerase chain reaction, Gram stain, routine culture, carcinoembryonic antigen and adenosine deaminase of pleural fluids. CHF: congestive heart failure; LC: liver cirrhosis; NT-pro BNP: N-terminal pro-b-type natriuretic peptide; TB: tuberculosis; CT: computed tomography.

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X-ray chest, posteroanterior view, with massive effusion and contralateral mediastinal shift.

Management: Treatment of the specific cause, drainage of fluid, pleurodesis, and surgical management are the therapeutic options for pleural effusion.

Treatment of specific cause: Treatment of the underlying cause helps resolve most transudative effusions. Effusions associated with connective tissue disorders like rheumatoid arthritis and systemic lupus erythematosus are treated with steroids, and resolution may occur within 2 weeks. Congestive cardiac failure-related effusions usually improve quite quickly when diuretic therapy is started.

In India, tuberculosis is the most common cause of pleurisy with effusion in young adults. According to RNTCP they should be treated with DOTS- category 1. A short course of prednisolone (0.5mg/kg/day for 4 weeks) may help to relieve toxæmic symptoms and facilitate rapid absorption of fluid. However poor penetration of drugs through the fibrotic calcified pleura into the empyema cavity leads to sub-therapeutic drug concentrations and promotes development of drug resistance.⁹ Decortication may also be required in few cases. Prognosis is worse than those with non-tuberculous empyema.

In Meigs syndrome, removal of the ovarian mass results in resolution of ascites and pleural effusion within 2–3 weeks. Repeat thoracocentesis should be reserved for patients who reaccumulate pleural effusions slowly after each thoracocentesis, those who are unlikely to survive beyond 1–3 months, and in patients who cannot tolerate other interventions such as pleurodesis. It is the treatment of choice for recurrently filling effusions. Successful pleurodesis requires

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opposition of the visceral and parietal pleurae. Sclerosants (talc or tetracycline) are instilled only when catheter drainage has decreased to less than 150 mL/day. Talc is the most effective sclerosing agent.

Uncomplicated parapneumonic effusions resolve quickly with antibiotic treatment. Empyema is gross infection of pleural space. Its management consists of prompt initiation of appropriate antibiotics, drainage of pus by tube thoracostomy and restoration of lung expansion. Intrapleural streptokinase administration may help if bacterial empyema is loculated. In a recent Cochrane review, it was concluded that intrapleural fibrinolytic therapy confers significant benefit in reducing the requirement for surgical intervention.¹⁰

Pancreatitis-related pleural effusions need conservative management with somatostatins and octreotide for spontaneous closure of fistula.¹¹

Table: Biological Agents for the Treatment of Empyema Thoracis⁹

Fibrinolytics

Streptokinase

Urokinase

Tissue plasminogen activator (alteplase)

Single chain urokinase plasminogen activator

Deoxyribonucleases

Streptodornase

Human recombinant DNase

Antibodies against specific growth factors

Antibodies against transforming growth factor (TGF)

Antibodies against vascular endothelial growth factor (VEGF)

Future prospects: Treatment approaches are being studied that could lead to more effective and less invasive ways of caring for patients with pleural disease. Newer tubes and reservoirs for patients with chronic pleural disease have reduced the need to remain in the hospital. Agents that induce an effective, quick, and painless pleurodesis could greatly improve patient care by speeding and simplifying the process and reducing the complications of lung injury and pleural scarring. Other methods like controlling the inflammatory response or targeting the tumor cells hold promise.

The combination of intrapleural tissue plasminogen activator and deoxyribo nuclease, an enzyme which catalyses extracellular DNA and degrades biofilm formation within the pleural cavity has been found to improve the clinical outcome.

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