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Transudative effusions

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ABSTRACT: Transudative pleural effusions develop because the distribution of hydrostatic and oncotic pressure across the pleura is altered, so that the rate of pleural fluid formation exceeds that of its reabsorption. They are characterized by a low cell and protein content.

Congestive heart failure is the most common cause of transudative effusion. The fluid that accumulates in a hepatic hydrothorax, urinothorax, during peritoneal dialysis, and in many patients with nephrotic syndrome may also have the characteristics of a transudate. The development of a transudative effusion indicates that the pleural membranes *per se* are intact, so that if the underlying problem can be corrected, the effusion will be reabsorbed.
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Transudative pleural effusions develop whenever the hydrostatic and oncotic pressures across the pleural membrane are altered, such that the rate of fluid formation exceeds its rate of absorption. The endothelium of the pleural capillaries is intact and retains its normal sieving characteristics, so that cell and protein content in a transudative effusion is low. If the underlying problem can be corrected, the transudative effusion usually resolves without sequelae.

Congestive heart failure

Congestive heart failure is the most common cause of all pleural effusions in developed countries, and accounts for the overwhelming majority of transudative pleural effusions [1]. The incidence of heart failure is high and over half of these patients will develop pleural effusions during the course of their illness [2]. Indeed, in a large autopsy series, 290 of 402 (72%) patients with congestive failure had pleural effusions. Bilateral effusions were found in 88%; only 8 and 4% had unilateral effusions in the right and left hemithoraces, respectively [3].

A number of derangements in the normal homeostatic mechanisms that serve to keep the pleural fluid volume at a minimum contribute to the development of transudative effusions in patients with congestive heart failure. In health, pleural fluid is formed as an ultrafiltrate from the capillaries in the parietal pleura. Most of the pleural fluid is removed by lymphatics draining the lower costal, mediastinal and diaphragmatic regions of the pleural cavity [4]. The reabsorption of fluid into the capillaries of the visceral pleura and *via* solute-coupled liquid transport across the mesothelium provide additional potential routes for fluid reabsorption. These additional pathways for fluid egress act as a safety mechanism to minimize the accumulation of fluid [5, 6].

The development of pleural effusions in patients with cardiac disease is best correlated with the presence of pulmonary venous hypertension. WEINER-KRONISH *et al.* [7] prospectively examined 37 patients admitted to the Coronary Care Unit (CCU) with congestive heart failure, and observed that 19 (51%) had pleural effusions. The pulmonary capillary wedge pressure in those with effusions was significantly higher than in those without effusions, whereas there was no difference in right atrial pressure between groups (table 1). An increase in pulmonary venous pressure that produces alveolar oedema also increases the interstitial pressure in subpleural regions; oedema fluid leaks from the visceral pleural surface, contributing to the rate of fluid accumulation [8]. To the extent that the elevated left atrial pressure is transmitted to the right heart, systemic venous pressure will also be increased. The elevation of systemic venous pressure should increase the filtration of fluid from the parietal capillaries and simultaneously decrease lymphatic flow from the pleural cavity by increasing the outflow pressure in the thoracic duct [9]. In experimental animals, an acute elevation of systemic venous pressure, even in the absence of pulmonary venous hypertension, will produce pleural effusions [10]. However, pleural effusions are unusual in patients with isolated right heart failure [11]. Thus, the evidence would sug-

Table 1. – Haemodynamic measurements in cardiac patients with or without pleural effusions

	Effusions present (n=19)	Effusions absent (n=18)
Pulmonary arterial pressure mmHg	38.0±1.5	30.7±2.1*
Pulmonary wedge pressure mm HG	24.1±1.3	17.2±1.5*
Right atrial pressure mmHg	12.6±1.5	9.8±1.0

Values are expressed as mean±sgm. *: $p<0.05$, effusion present *vs* effusion absent. (Data from [7]).

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gest that elevated systemic venous pressures are contributory but pulmonary venous hypertension is essential for the development of effusions in humans.

The clinical presentation of patients with pleural effusions due to cardiac failure is usually dominated by the classic symptoms and signs of congestive heart failure. The patient usually complains of increasing dyspnoea on exertion, peripheral oedema, and orthopnoea or paroxysmal nocturnal dyspnoea. Pleuritic chest pain is uncommon. Physical examination frequently reveals signs of biventricular failure: distended neck veins, peripheral oedema and hepatojugular reflux are present, in combination with rales and a left-sided S_3 gallop. Dullness to percussion, decreased fremitus and diminished breath sounds at the bases indicate the presence of pleural effusions.

The chest radiograph shows cardiomegaly and bilateral effusions of relatively equal size. There is usually evidence of pulmonary vascular congestion, and alveolar oedema may be present [2]. Atypical radiographic presentation should arouse clinical suspicion of other causes for the effusion(s). Unilateral effusions do occur but, as noted above, are uncommon [3]. Similarly, bilateral effusions in the absence of cardiomegaly are usually not due to congestive heart failure [12]. A diagnostic thoracentesis should be performed whenever the clinical presentation is atypical. Indications for thoracentesis include: a unilateral effusion or effusions of markedly disparate size; effusions without cardiomegaly; and the presence of fever or pleuritic chest pain. If the effusion is due to heart failure, the fluid will be a transudate with less than 1,000 cells·mm^{-3}. Most of these cells will be lymphocytes and mesothelial cells.

Treatment is directed at the underlying heart failure. Diuretics, digitalis and/or afterload reduction are the mainstays of therapy. Occasionally, large effusions may produce severe dyspnoea. The therapeutic removal of a modest amount of fluid, 500–1,000 mL, can produced marked relief of symptoms. The reduction in dyspnoea occurs before any improvement in arterial oxygen tension (P_{a,O_2}) or lung volumes is observed, and is probably due to a decrease in the distention of the rib cage, which enables the inspiratory muscles to operate on a more advantageous portion of their length-tension curve [13].

Successful treatment of the heart failure results in the reabsorption of the effusions over a period of days to weeks. If water is reabsorbed faster than fluid, the protein concentration will increase over time and the effusion may develop the characteristics of an exudate [14, 15]. However, the lactate dehydrogenase level (LDH) will usually remain below 240 international units (IU)·L^{-1}. Occasionally, one encounters a patient with large pleural effusions and refractory heart failure. If therapeutic thoracentesis relieves the dyspnoea but the effusion cannot be controlled with medical therapy, chemical pleurodesis with doxycycline or talc should be considered. Pleural sclerosis could potentially increase the severity of alveolar oedema by preventing the escape of oedematous fluid into the pleural space. Fortunately, there is no clinical evidence to support this theoretical possibility. Unilateral sclerosis frequently results in an increased accumulation of fluid in the opposite hemithorax [16].

Hepatic hydrothorax

Pleural effusions develop in approximately 6% of patients with hepatic cirrhosis [17, 18]. These effusions are typically unilateral and right-sided, but may occur on the left (16%) or be bilateral (16%). They may vary in size from small to massive. Since hypoalbuminaemia is frequently present in the patient with cirrhosis, it is tempting to attribute these effusions to decreased plasma oncotic pressure, which enhances the formation of pleural fluid. However, these effusions are almost invariably associated with ascites, which is the primary source of the transudative effusion. Even when ascites is not clinically apparent, it can usually be detected with ultrasonography [19].

The ascitic fluid in the abdomen enters the pleural cavity *via* defects in the diaphragm, because the gradient between intraperitoneal and intrapleural pressure favours fluid movement in this direction. When LIEBERMAN *et al*. [17] introduced labelled albumin into the ascitic fluid, the concentration of the labelled protein in the effusion was higher than in plasma or thoracic duct lymph, confirming direct transfer from the peritoneal ascites. When they introduced air into the peritoneum of five patients, it resulted in the development of a pneumothorax within hours. The flow is unidirectional; tracer injected into the pleural effusion does not appear in the ascites [20]. In some patients, the defects are macroscopic and visible at thoracoscopy. Blebs of herniated peritoneum may protrude through defects in the collagen and muscle bundles of the diaphragm [21]. However, in most patients the diaphragmatic defects are microscopic and not visible to the naked eye. If air is introduced into the peritoneal cavity, it may be observed bubbling through otherwise undetectable defects in the diaphragm [17].

The diagnosis of a hepatic hydrothorax should be suspected whenever a patient with the stigmata of cirrhosis and ascites develops a pleural effusion. Large effusions may cause significant dyspnoea. Thoracentesis will reveal transudative fluid, with few cells, predominantly lymphocytes and mesothelial cells. The protein content tends to be slightly higher than that of the ascitic fluid due to the reabsorption of water in excess of protein across the visceral pleura. The transdiaphragmatic movement of ascitic fluid into the pleural space can be verified by imaging over the thorax and abdomen several hours after the intraperitoneal injection of ^{99m}Tc-sulphur colloid into the peritoneal cavity [20]. Patients with cirrhosis and ascites are prone to develop spontaneous bacterial peritonitis. Extension of the peritoneal infection into the pleural cavity may occur [22].

Therapy is directed at reducing the ascites with diuretics and sodium restriction. Therapeutic thoracentesis will only bring temporary relief because the ascitic fluid rapidly reaccumulates in the pleural cavity. Chemical pleurodesis may be attempted, but insertion of a chest tube involves risk. Tube thoracostomy may drain both the pleural fluid and the ascites, resulting in severe hypovolaemia [23]. Whenever a chest tube is inserted, the patient's vital signs and the volume of chest tube drainage should be closely monitored. If hypotension develops, the tube can be clamped and albumin administered to restore the intravascular volume. If pleurodesis is not

successful thoracoscopy or thoracotomy to repair the diaphragmatic defects may be required to control the patients symptoms [24].

Peritoneal dialysis

Pleural effusions can develop in patients undergoing peritoneal dialysis. The dialysate moves from the peritoneal to the pleural cavity across the diaphragm, in a manner analogous to the movement of ascitic fluid in the patient with cirrhosis [25]. This complication is seen in approximately 2% of continuous ambulatory peritoneal dialysis (CAPD) patients [26]. Large, symptomatic effusions can develop within hours of initiating peritoneal dialysis [27, 28]. If this problem is going to occur, it usually develops in the first month after dialysis is initiated [26]. However, it may be a year or more before the effusion is recognized in some patients. Most effusions are right-sided but left-sided or bilateral effusions do occur.

Patients with dialysis-related effusions generally complain of dyspnoea, but approximately 25% of the effusions cause no symptoms and are discovered on routine radiographs [26]. Thoracentesis reveals transudative fluid with an extremely low protein content and a high glucose concentration, similar to that of the dialysate [29]. Stopping the dialysis and draining the peritoneal catheter will usually allow the effusion to resolve. The patient should be switched to haemodialysis. If this is not feasible, chemical pleurodesis should be performed prior to reinstituting CAPD. Small volume peritoneal dialysis in the semierect position may be attempted, while pleurodesis is being performed [30]. The diaphragma tic defect may have to be repaired surgically if pleurodesis is unsuccessful [31].

Urinothorax

A urinothorax is a pleural effusion due to the retroperitoneal leakage of urine that is thought to enter the pleural space *via* the diaphragmatic lymphatics [32]. It generally develops in association with obstructive uropathy, but has been reported in patients with trauma, malignancy, kidney biopsy and renal transplantation [33].

Patients generally present with complaints related to the urinary tract obstruction. The pleural effusion is suspected because of dyspnoea, or may be asymptomatic and recognized on a routine chest radiograph. The pleural effusion is invariably ipsilateral to the urinary obstruction. Thoracentesis yields fluid that looks and smells like urine. The fluid has the characteristics of a transudate, but the pH may be high or low depending on the urine pH [34, 35]. The pleural fluid creatinine is always higher than the serum creatinine in a urinothorax. Relief of the urinary obstruction results in prompt resolution of symptoms.

Nephrotic syndrome

Pleural effusions are frequently present in patients with the nephrotic syndrome. CAVINA and VICHI [36] found radiographic evidence of effusions in 21% of 52 children with nephrosis. Hypoalbuminaemia leads to a decrease in the plasma oncotic pressure, while salt retention produces hypervolaemia and increased hydrostatic pressures, thereby favouring the development of transudative effusions. The effusions are bilateral and are frequently infrapulmonary [37]. They are often associated with the presence of peripheral oedema

Thoracentesis should be performed whenever an effusion is recognized in a patient with nephrotic syndrome, to confirm that the fluid is a transudate. If an exudate is found, thromboembolism is the most likely cause. These patients suffer from a hypercoagulable state and venous thrombosis in the legs and at other sites is common. In a series of 36 patients with nephrotic syndrome, who were studied prospectively with inferior vena cavagrams, 12 with membranous or membranoproliferative glomerulonephritis had renal vein thrombosis [38]. Eight of the 36 patients had pulmonary emboli, including four who did not have renal vein thrombosis. The presence of effusions of disparate size in a patient with nephrotic syndrome should increase the clinical suspicion of thromboembolism.

Treatment is directed at the underlying nephropathy. Therapeutic thoracentesis is indicated if there is severe dyspnoea. Failure to medically control symptomatic effusions is an indication for chemical pleurodesis.

Atelectasis

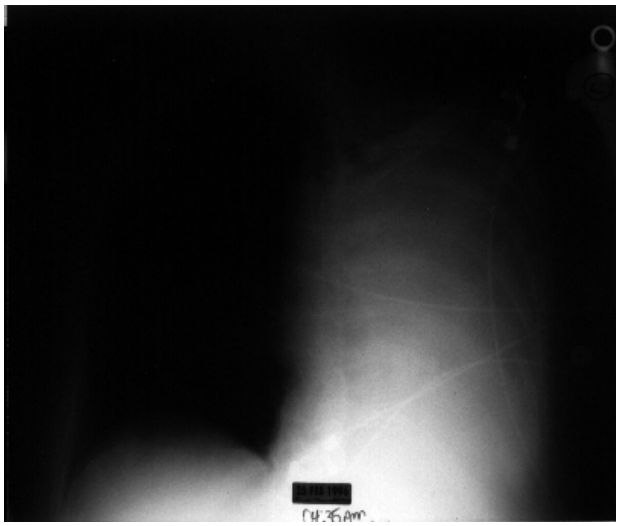
Atelectasis produces a decrease in pleural pressure, which favours the increased filtration of fluid into the pleural space. The small effusions which develop following upper abdomen surgery may be due to basilar atelectasis, which is commonly present in the postoperative period [39]. Effusions may develop following bronchial obstruction by carcinoma or a foreign body (fig. 1). These effusions, termed *ex-vacuo* effusions, have the characteristics of a transudate and will resolve if the underlying problem can be corrected.

Basilar atelectasis due to a gravid uterus probably contributes to the pathogenesis of the small effusions, which commonly occur in the postpartum period [40]. The decrease in oncotic pressure due to volume expansion during pregnancy and the high intrathoracic pressures produced by Valsalva manoeuvres during parturition also promote pleural fluid accumulation [41].

Miscellaneous

Iatrogenic effusions have occurred after introduction of a central line into the pleural space [42]. This complication is recognized by the rapid development of a large effusion, which has a chemical composition similar to the infusate. The use of central venous catheters in infants has been reported to result in superior vena caval obstruction, with leakage of lymph into the pleural space [43]. Whilst effusions are not uncommon in patients with hypothyroidism, most are due to associated disorders, such as congestive heart failure or pneumonia. However, an occasional hypothyroid patient may have a transudative effusion in the absence of obvious cardiac disease [44]. Approximately 20% of the effu-

a)



b)

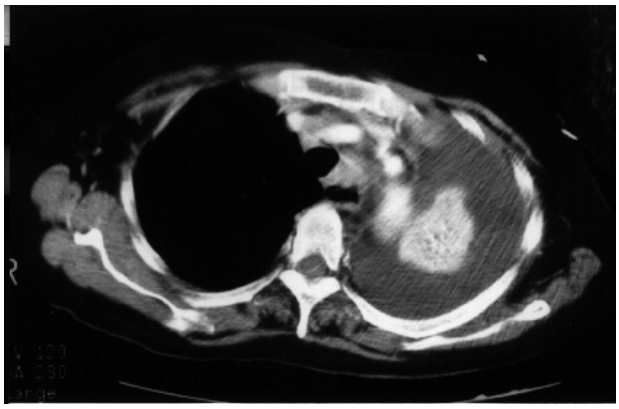


Fig. 1. – a) Chest radiograph reveals opacification of the left hemithorax with mediastinal shift suggesting atelectasis. The left main bronchus was obstructed by a small cell carcinoma. b) Computed tomography (CT) scan just above the level of the carina reveals the atelactalic lung surrounded by a large *ex-vacuo* pleural effusion. Thoracentesis obtained transudative fluid, which did not contain any malignant cells.

sions that develop in patients with pulmonary embolism have the characteristics of a transudate [45]. In some of these patients, the transudative nature of the effusion may reflect the acute effect of venous hypertension on lymphatic outflow, while in others the transudate is due to coexistent congestive heart failure. In the original description of Meigs' syndrome, the fluid was described as a transudate [46]. However, most subsequent reports have found exudative fluid in patients with ovarian ascites and pleural effusion. Pleural amyloidosis is associated with transudative effusions but, since these patients almost always have cardiac amyloid, the effusions are probably due to heart failure [47].

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