THE EFFUSION THAT WOULD NOT GO AWAY

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A 36-year-old man who was undergoing long-term hemodialysis was hospitalized with a two-day history of increasing dyspnea on exertion. He stated that he did not have cough, orthopnea, or night sweats.

On examination, he was found to be in mild respiratory distress, with a blood pressure of 156/68 mm Hg, a respiratory rate of 22, a pulse of 80 per minute, and a temperature of 38.3°C (100.9°F). The site of entry of a right subclavian dialysis catheter appeared unremarkable. There was edema of the left hand and an audible bruit over an arteriovenous shunt in the left forearm. The heart and right lung were normal on examination, but the entire left hemithorax was dull to percussion, with decreased breath sounds. There was no ascites or pedal edema.

A chest film revealed a massive, left-sided pleural effusion (Fig. 1). The blood urea nitrogen level was 73 mg per deciliter (26 mmol per liter), the serum creatinine level was 11.3 mg per deciliter (999 µmol per liter), and the hemoglobin level was 10.6 g per deciliter. Serum levels of potassium, sodium, and bicarbonate were normal. In arterial blood, the pH was 7.33, the partial pressure of carbon dioxide was 41 mm Hg, and the partial pressure of oxygen was 84 mm Hg.

Possible causes of pleural effusion are infection, neoplasm, congestive heart failure, and many other disorders. The clinical findings in this patient help to focus the differential diagnosis. Even low-grade fever in a patient with chronic renal failure suggests the presence of infection; empyema and tuberculosis must be excluded. The presence of a large effusion confined to the left side makes heart failure, fluid overload, and hypoalbuminemic disorders less likely as causes. The presence of both a subclavian catheter and an arteriovenous shunt raises questions about the patient’s history of dialysis. For example, has he also received peritoneal dialysis (which is sometimes complicated by pleural effusion)? Uremic pleuroperticarditis can present in this way, as can diseases that may have been the primary cause of the patient’s renal failure, such as connective-tissue disorders, amyloidosis, and drug-induced syndromes. Additional information and a diagnostic thoracentesis are needed.

The patient had begun hemodialysis three years earlier for end-stage hypertensive nephropathy. Obstructive sleep apnea had been diagnosed a few months before admission. He had missed his hemodialysis appointment the day before admission but no other ones. He had never undergone peritoneal dialysis. He did not smoke cigarettes or drink alcohol. He said he had not been vomiting. Three months before admission, a test for human immunodeficiency virus and a tuberculin skin test with purified protein derivative were negative.

On admission, thoracentesis revealed 3 liters of straw-colored fluid, with a lactate dehydrogenase level of 132 U per liter (serum lactate dehydrogenase level, 228 U per liter), a ratio of pleural-fluid lactate dehydrogenase to serum lactate dehydrogenase of 0.57, a protein level of 3.7 g per deciliter (serum protein level, 7.6 g per deciliter, and serum albumin level, 3.9 g per deciliter), a ratio of pleural-fluid protein to serum protein of 0.48, pH of 7.44, and a normal cell count and glucose level. The results of Gram’s staining and acid-fast smear were negative. The patient’s dyspnea improved after thoracentesis.

In patients who are undergoing dialysis, only a few conditions commonly cause transudative effusions: heart failure, fluid overload, the nephrotic syndrome, and peritoneal dialysis. This patient has no history of peritoneal dialysis, and the normal serum albumin level excludes the possibility of the nephrotic syndrome. Heart failure may be associated with unilateral left-sided pleural effusion (in less than 10 percent of cases), but a massive unilateral effusion would be very unusual. Furthermore, there is no other clinical evidence of heart failure, although the history of sleep apnea is intriguing. Patients with obstructive sleep apnea have negative intrapleural pressures that may contribute to increased formation of pleural fluid.

Uncommon causes of transudative effusions include constrictive pericarditis, myocardia, atelectasis of the lungs, obstruction of the superior vena cava, pulmonary embolism, and urinary leakage into the thorax, a potential complication of retroperitoneal urinary leakage resulting from urinary obstruction, failed nephrostomy, or renal biopsy. Pulmonary em-
bolism causes transudative effusions in 20 percent of cases, but these effusions are rarely massive. Among these possibilities, inadequate dialysis with fluid overload seems most likely.

The morning after admission, an echocardiogram showed no abnormalities; additional details of the history also became available. The patient had been admitted to a local university hospital six times in the preceding six months for the same problem, most recently three days earlier. On each occasion, thoracentesis temporarily improved the patient’s symptoms.

Massive unilateral transudative effusion is unusual in itself, but when it recurs rapidly and repeatedly after thoracentesis, especially in the absence of heart failure or a low plasma oncotic pressure, it is most peculiar. The normal echocardiogram does not completely exclude the possibility of constrictive pericarditis, but it makes cardiogenic causes even less likely. Perhaps we need to consider noncardiac causes of elevated venous pressures in the parietal pleura — the superior vena cava syndrome, for example.

At this point, fluid overload that is somehow related to inadequate dialysis remains the most likely cause of the effusion. I would request records from the other hospital to confirm the patient’s report and to review the results of previous workups.

Records of the patient’s previous hospitalizations were obtained. During each admission, a massive, left-sided pleural effusion was evacuated by thoracentesis, and each time, an analysis of pleural fluid revealed a transudate. Repeated cytologic examinations and cultures for fungal and mycobacterial disease were negative. Despite the transudative nature of the fluid, a pleural biopsy had also been performed and had revealed only benign mesothelial cells. Chest films obtained after thoracentesis had shown no apparent underlying abnormality of the left lung or hilum.

Despite a full evaluation, including thoracotomy, the cause of pleural effusion remains unknown in up to 20 percent of cases. Such effusions are labeled “idiopathic” or “undiagnosed and persistent” but are usually exudates. In many such patients, the pleural biopsy shows nonspecific pleuritis; in some, cancer or tuberculosis is subsequently diagnosed.

In a young nonsmoker, cancer of the lungs is extremely unlikely. However, systemic fluid overload in patients with chronic renal failure may confound the results of pleural-fluid analysis so that exudative effusions appear transudative. With that unlikely possibility in mind, I suspect that the previous pleural biopsy was performed to rule out tuberculosis.

I would observe the patient carefully after the thoracentesis, resume dialysis to rule out confounding fluid overload, and consider computed tomography of the chest. The normal findings on the chest film obtained after thoracentesis are reassuring, but computed tomography of the chest is more reliable in excluding an underlying abnormality of the lung, pleura, hilum, or mediastinum. Impaired lymphatic drainage of the left-sided pleural space as a result of some abnormality of the thoracic duct must also be considered.

On the second hospital day, the patient underwent hemodialysis. The dialysis team was unable to use the arteriovenous shunt in the left forearm because of “poor blood flow”; the shunt appeared normal, with a vigorous thrill and loud bruit. Dialysis was completed uneventfully with the use of the right subclavian catheter.

That evening, the patient’s dyspnea worsened. Computed tomography of the chest (Fig. 2) confirmed that the large pleural effusion had recurred but revealed no other abnormalities. A thoracostomy tube was placed for possible pleurodesis. A pulmonary consultant was called in.

In this clinical situation, pleurodesis is unlikely to help. In fact, suction applied to the chest tube may actually increase the transudation of pleural fluid by increasing the negative intrapleural pressure.

Hemodialysis may cause dyspnea as a result of air embolism, activation of the complement cascade, and the disequilibrium syndrome, but none of these are associated with massive pleural effusion. Vascular perforation by an indwelling subclavian catheter usually
causes ipsilateral pleural effusion, but leakage of intravenous fluids into the mediastinum and contralateral pleural cavity may also occur. However, the dialysis team’s apparent satisfaction with the function of the subclavian catheter makes this possibility unlikely.

I am more concerned now about the possibility of venous obstruction. The obstruction would most likely be proximal to the basilic vein (because the arteriovenous shunt is patent) but distal to the superior vena cava (because there is no clinical evidence of the superior vena cava syndrome). Perhaps the left subclavian or brachiocephalic vein is thrombosed. Did the patient ever have an indwelling left subclavian catheter for dialysis?

In addition to the large left-sided pleural effusion, the consultant noted dilated superficial veins over the proximal part of the patient’s left arm and shoulder, with venous distention of the left, but not the right, jugular vein. There was a small, well-healed scar under the left clavicle; on questioning, the patient reported that he had had a left subclavian dialysis catheter removed about six months earlier, around the time his recurrent problems began.

The consultant asked the patient to stand up. Within seconds, dilated superficial veins appeared over the left side of the patient’s abdominal wall. Forcing the blood from these veins and watching them refill demonstrated caudad flow toward the umbilicus and inguinal ligament. The dilated abdominal veins disappeared when the patient resumed the supine position.

These physical findings indicate well-established collateral venous flow from the left arm, head, and neck to the inferior vena cava and azygos system. The venous obstruction, related to the prior left subclavian catheter, is most likely to be in the brachiocephalic vein where the thoracic duct (which drains the left lung and left-sided pleural cavity) empties into the central venous system. A simultaneous increase in the formation of pleural fluid and impairment in reabsorption by the lymphatic system would explain the massive amount and rapidly recurring nature of the effusion. The functioning arteriovenous shunt in the left forearm probably contributed to the problem by increasing venous pressure and flow.

Venography of the left arm demonstrated nearly complete (90 percent) obstruction of the brachiocephalic vein (Fig. 3). The chest tube was removed; pleurodesis was not attempted. Percutaneous angioplasty successfully opened the vessel without complications.

The patient’s symptoms resolved. He has had no further recurrence of the pleural effusion.

**COMMENTARY**

This patient’s disabling illness defied repeated diagnostic efforts, perhaps because the diagnosis — massive pleural effusion caused by occlusion of the brachiocephalic vein — had been reported only once before in the English-language medical literature. How then did the discussant so confidently solve this unusual problem?

When none of the common or uncommon causes of transudative effusion adequately explained the patient’s problem, the discussant embraced a physiological method of diagnostic reasoning. Physiological (or causal) reasoning is often used as a last resort, when probabilistic thinking proves inadequate. In the diagnosis of pleural effusions, however, physiological reasoning invariably has a role. This approach stimulated the discussant to consider even uncommon causes of increased pleural venous pressure.

Although many diseases can cause pleural effusion, more than 90 percent of all pleural effusions result from one of only five conditions. Among these, congestive heart failure and hypoalbuminemic states (e.g., cirrhosis) typically cause transudative effusions, whereas cancer, infection, and pulmonary embolism typically cause exudative effusions. Because Light’s criteria for the interpretation of pleural fluid have exceptionally high sensitivity for the diagnosis of exudative effusions (0.97 to 0.99), the analysis of pleural fluid combined with the clinical presentation generally leads to the correct diagnosis.
The discussant used heuristic reasoning — trusted “rules of thumb” (if A, think B) — to generate his initial diagnostic hypotheses. If an effusion is very large and confined to the left side, consider neoplasm or infection rather than congestive heart failure, cirrhosis, or pulmonary embolism. If the patient has chronic renal failure, think of causes related to the renal failure itself (uremic pleuropericarditis), its treatment (complications of peritoneal dialysis or hemodialysis), or systemic disorders affecting both the lung and kidneys.

The discussant tested these hypotheses by reasoning probabilistically about the results of pleural-fluid analysis. Although he did not explicitly quantify the test’s receiver-operating characteristics or the relevant pretest and post-test probabilities, he used these probabilities in his clinical reasoning. As a result, he excluded exudative disorders from further consideration, despite their high pretest probability in a patient with a massive, unilateral, recurrent effusion. (The heuristic acronym “SnNOut” — if a highly sensitive test is negative, then it effectively rules out the disease — endorses this approach.)

Thinking physiologically, he immediately understood the relevance of findings of “poor blood flow” in a functioning hemodialysis shunt, dilated veins, and a vascular-access scar.

REFERENCES


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