Chylothorax as Presenting Manifestation of Adenocarcinoma with Probable Gastric Primary

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Chylothorax is an unusual complication of various malignant neoplasms, generally lymphomas. The few reported cases of chylothorax with gastric and other abdominal malignancies have involved large abdominal masses with prominent adenopathy and chylous ascites. We describe a patient in whom chylothorax was the presenting manifestation of an adenocarcinoma with probable gastric primary, developing prior to any clinical or radiologic evidence of tumor.

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Chylothorax, the accumulation of lipid-rich thoracic duct lymph in the pleural space, is an unusual complication of various malignant neoplasms. It may develop either because of obstruction of the thoracic duct by tumor or perforation of the duct wall. Chylothorax has been most commonly associated with lymphoma; where other malignancies have been reported, chylothorax has in almost all cases developed as a late manifestation of advanced disease. This is true of the few cases of chylothorax reported with gastric cancer; all have involved extensive disease with chylous ascites as well as chylothorax. We report a case of chylothorax as a presenting manifestation of adenocarcinoma with presumed gastric primary.

CASE REPORT

A 38-year-old woman was admitted to the hospital for evaluation of a five-day history of increasing right pleuritic chest pain with dyspnea. Five weeks earlier she had undergone cholecystectomy for intermittent upper abdominal pain with nausea of two months' duration; a prior upper gastrointestinal (GI) series had been remarkable, and an abdominal ultrasonogram showed a contracted gallbladder with multiple stones. The cholecystectomy was uncomplicated, and the pathologic findings consisted of only chronic inflammatory changes. Two weeks prior to the current hospital admission, she had repeated abdominal ultrasonogram with amylase and liver function tests for evaluation of recurrent upper abdominal pain, all of which showed unremarkable results. Upper endoscopy showed superficial erosions and inflammatory changes consistent with antral gastritis (no biopsy specimens taken), with some symptomatic response to H₂ blockers. Her medical history was otherwise unremarkable. Her only medications were ranitidine 150 mg twice a day, and conjugated estrogens (Premarin) 0.625 mg every day (D 1-25) for premature menopause.

Vital signs were normal. Physical examination was significant only for dullness and decreased breath sounds at the right base. Hospital admission laboratory studies included the following results: hemoglobin, 14.6 mg/dl; hematocrit, 45 percent; white blood cell count, 9,900/cu mm; platelets, 274,000/cu mm; normal prothrombin time (PT), partial thromboplastin time (PTT), 12-factor automated blood chemistry analysis (SMA-12), amylase, and urinalysis. Room air arterial blood gas showed a pH of 7.45, Pco₂ of 33 and Po₂ of 93. Chest roentgenogram showed a right subpulmonic pleural effusion, with some increased linear markings at the right base most suggestive of atelectasis. A ventilation perfusion (VQ) scan was interpreted as intermediate probability for a pulmonary embolism, but pulmonary arteriogram was negative. Thoracentesis (performed after two days on a nothing by mouth or clear liquid regimen for recurrent nausea) revealed the following: 1,900 white blood cells (45 percent segmented, 10 percent lymphocytes, 45 percent monocytes); 957 red blood cells; pH, 7.48; protein, 3.9 g/dl (peripheral 5.8 g/dl); LDH, 266 U; glucose, 102 mg/dl; amylase, 29 U; and normal rheumatoid factor, cytology, and cultures (including fungal and acid-fast bacilli [AFB]). A Cope needle biopsy subsequently revealed only nonspecific pleural inflammation. Serum rheumatoid factor, antinuclear antibody (ANA), and thyroid function tests were normal, and a purified protein derivative (PPD) was nonreactive (with reactive controls). A computed tomographic (CT) scan of the chest, abdomen, and pelvis revealed only the right pleural effusion, with a much smaller left pleural effusion. Echocardiogram was unremarkable. Recent mammogram, Papanicolaou (PAP) smear, and pelvic sonogram were unremarkable, as were repeated breast and pelvic examinations. The patient's symptoms improved with indomethacin (Indocin) after thoracentesis, and she was discharged from the hospital with close outpatient follow-up.

She was readmitted three weeks later with increasingly symptomatic pleural effusions, as well as bibasilar atelectasis vs early interstitial changes on chest roentgenogram. Complete blood cell count (CBC) and SMA-12 at the time of hospital admission were again unremarkable except for an increased alkaline phosphatase level of 171 U/L (normal, 40 to 125 U/L) and γ-glutamyl transpeptidase (GGT) level of 59 U/L (normal, 5 to 45 U/L). Arterial blood gas on room air was 7.41/39/68. Thoracentesis yielded fluid similar on analysis to the prior thoracentesis, except for the clearly milky, chylous appearance, with triglyceride level of 238 mg/dl (peripheral, 122 mg/dl) and cholesterol level of 96 mg/dl. Repeated chest and upper abdominal CT scans were again without any evidence of masses or lymphadenopathy, although in addition to the pleural effusions, a very small amount of abdominal ascites was seen. On paracentesis, only 50 ml of fluid could be obtained under ultrasound guidance, and this also proved to be chylous, with a protein and lipid content similar to the pleural fluid. On a lymphangiogram, there was generally poor uptake of contrast, with complete absence of contrast in the thoracic lymphatics without clear extravasation or adenopathy.

Pleural fluid continued to reaccumulate bilaterally at a rate of 200 to 300 ml/day after placement of bilateral chest tubes and a regimen of bowel rest and parenteral nutrition. For this reason, and because of progressive interstitial changes on the chest roentgenogram associated with worsening hypoxemia (Po₂, 58 mm Hg) without

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any convincing evidence of edema or infectious cause, the patient underwent open lung biopsy, with ligation of the thoracic duct and pleurodesis. Pathologic study revealed metastatic adenocarcinoma, with small nests and sheets of signet ring cells within the lymphatic spaces of the interstitium and pleura, believed to be highly suggestive of a gastric primary. There was a prominent associated reactive pleural mesothelial proliferation with abundant pleural fibrin deposition. Repeated upper GI series was not obtained because of rapid deterioration in the patient's condition thereafter, and an autopsy was declined.

**DISCUSSION**

The diagnosis of chylothorax is suggested by the finding of milky pleural fluid which on further analysis proves to have triglyceride levels greater than 100 to 150 mg/dl, but cholesterol levels less than 150 mg/dl. Reflecting its origin in the thoracic duct, the fluid is commonly lymphocyte rich and contains chylomicrons and fat globules that stain with Sudan 3 dye. By contrast, "pseudochyloysis" effusions may appear in various chronic inflammatory conditions such as rheumatoid arthritis and tuberculosis, where breakdown of longstanding cell-rich pleural effusions results in fluid high in cholesterol (>250 mg/dl) and relatively low to moderate in triglycerides. Where the lipid content of the pleural fluid is nondiagnostic, lipoprotein analysis showing chylomicron levels can help establish the diagnosis of chylothorax.1,3

Of interest in this case is the fact that, while triglyceride-rich chylos fluid was obtained on a subsequent thoracentesis, the pleural fluid initially obtained was clear. This may be due to the fact that when the initial thoracentesis was performed, the patient had been without anything by mouth or receiving clear liquids for some 48 hours. In fact, dietary restriction aimed at reducing chyle formation by eliminating long-chain triglycerides is, in conjunction with chest tube drainage, recommended as the initial therapy for any kind of chylothorax not requiring emergency thoracotomy. III, hospitalized patients undergoing thoracentesis for evaluation of pleural effusions may often be on restricted diets, which may, as in this case, result in delay in making the diagnosis of chylothorax.

The leading cause of chylothorax is malignancy (50 to 60 percent), followed by trauma, including postsurgical cases (25 to 30 percent). Less common causes include the following: infections, particularly tuberculosis (secondary to disruption of the thoracic duct; a more common cause in the past); parasites such as filariasis and echinococcosis; congenital malformations of the lymphatic system; and idiopathic and miscellaneous rare causes such as lymphangioleiomyomatosis, a rare smooth muscle proliferation involving lymphatic vessels of the lung in young women that was initially considered in the differential diagnosis in this patient.3

Of the malignancy-related causes of chylothorax, about 75 percent are lymphomas.4 Chylothorax may be the presenting symptom of lymphoma.5 Only a few cases of chylothorax in association with gastric or other abdominal malignant neoplasms have been reported. With malignancies other than lymphomas, chylothorax is very unusual and generally a late manifestation of metastatic or locally extensive tumor. For example, the few reported cases of chylothorax with gastric and other abdominal malignancies have involved large abdominal masses and prominent adenopathy; the chylthorax in these patients was secondary in importance to chylous ascites, which has more frequently been reported in association with gastric cancer.4,7

This case is noteworthy in that it involves chylothorax as an early manifestation of an abdominal nonlymphomatous malignant neoplasm, developing prior to any clinical or radiologic evidence of tumor or ascites. The diagnosis of lymphangitic pulmonary involvement by metastatic signet ring cell adenocarcinoma, of presumed gastric origin, was established only by open lung biopsy. The early lymphatic involvement (particularly of the pleural lymphatics, with associated reactive mesothelial proliferation) helps explain the early prominent chylothorax with only minimal chylous ascites. This case underlines the importance of maintaining a high clinical suspicion of occult malignancy in cases of nontraumatic chylothorax.

**REFERENCES**


**Treatment with Acyclovir of Varicella Pneumonia in Pregnancy**

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Varicella pneumonia during pregnancy carries a significant mortality for both mother and fetus. The antiviral drug, acyclovir, appears to have decreased mortality in reported cases. We present a case report and review of the literature summarizing the experience to date with acyclovir in the treatment of varicella pneumonia during pregnancy.

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Since its initial description in 1942 varicella pneumonia has been considered the most frequent and most serious complication of varicella infections in adults.1,4 When varicella pneumonia is associated with pregnancy, a maternal mortality rate of up to 44 percent has been reported.4,5 Recently acyclovir, an antiviral agent, has been used for treatment of varicella pneumonia complicating pregnancy.1,5,13 The effects of this therapy on mortality have not previously been reviewed. We present a case of severe varicella pneumonia during pregnancy which responded rapidly to treatment with acyclovir and review the effects of therapy on maternal and fetal mortality.

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