Chronic massive pancreatic pleural effusion is an uncommon and often unrecognized clinical syndrome which results from an internal pancreatic fistula and usually presents as an exudative effusion of unknown cause. The effusion frequently occurs without clinical evidence of pancreatitis, but occasionally it may be associated with a pseudocyst of the pancreas. Chronic massive pancreatic pleural effusion is usually recurrent and characterized by very high levels of amylase in the pleural fluid. Morbidity and mortality are reduced when a definite diagnosis is established and appropriate therapy rendered. In this report, three cases of chronic massive pancreatic pleural effusions are presented. Two of the three had no demonstrable pancreatic disease, and the condition responded to conservative therapy. The third patient had a pancreatic pseudocyst and an internal pancreatic fistula which was corrected only after multiple surgical procedures.

Chronic massive pancreatic pleural effusion due to an internal pancreatic fistula is a syndrome which is infrequently recognized and diagnosed. The effusion tends to be recurrent and is characterized by very high levels of amylase. Morbidity and mortality can be reduced through appropriate evaluation therapy.

The purpose of this report is to present three cases of chronic massive pancreatic pleural effusion, each having a different clinical course. In the first case, which has been reported elsewhere, there was no evidence of pancreatic disease, and no specific studies were done to attempt to demonstrate an internal pancreatic fistula. The second patient had a large pancreatic pseudocyst with a definite communication between the abdominal cavity and the right pleural space. The last patient had loculated pleural and mediastinal effusions with no detectable pancreatic lesion, and the condition responded to conservative management. The common denominator in all three cases was massive exudative effusion with very high levels of amylase in the pleural fluid.

**Case Reports**

**Case 1**

A 49-year-old man was admitted to the Omaha Veterans Administration Medical Center because of chronic alcohol abuse. On the third day of hospitalization, he complained of orthopnea and pleuritic left-chest pain. Physical examination disclosed an obese

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**Table 1—Findings from Pleural Fluid in Patient 1**

<table>
<thead>
<tr>
<th>Data</th>
<th>Day 3</th>
<th>Day 13</th>
<th>Day 44</th>
<th>Day 55</th>
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<tbody>
<tr>
<td>Protein, g/dl</td>
<td>4</td>
<td>3.8</td>
<td>3.5</td>
<td>3.54</td>
</tr>
<tr>
<td>LDH, IU/ml</td>
<td>264</td>
<td></td>
<td></td>
<td>300</td>
</tr>
<tr>
<td>Amylase, IU/L</td>
<td>6,500</td>
<td>19,400</td>
<td>26,000</td>
<td>47,400</td>
</tr>
<tr>
<td>Serum amylase, IU/L*</td>
<td>423</td>
<td>530</td>
<td></td>
<td>380</td>
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</tbody>
</table>

*Normal range, 20 to 110 IU/L.
lower thorax failed to demonstrate pancreatic edema or a pseudo-
cyst. Multiple thoracocenteses followed by chest tube drainage and
total parenteral nutrition were associated with resolution of the
pleural effusion.

CASE 2

A 37-year-old white man with a known history of pancreatitis was
hospitalized because of increasing shortness of breath and pain in the
left upper quadrant. He had a history of excessive consumption of
alcohol for several years.

On admission the patient was in mild respiratory distress with a
respiratory rate of 24/min, normal temperature, blood pressure of
140/80 mm Hg, and pulse rate of 80 beats per minute. There was
marked dullness to percussion, with complete absence of breath
sounds over the right hemithorax. Chest x-ray film revealed massive
right-sided pleural effusion (Fig 2). Abdominal examination revealed
a large cystic mass, extending from the xiphoid to the umbilicus and
across the entire upper abdomen. Three thousand one hundred
milliliters of yellow-green exudative fluid was drained by thoraco-
centesis. The amylase level of the pleural fluid was 8,100 IU/L, and
the serum level of amylase was 151 IU/L (normal, 25 to 110 IU/L).
Gram stain and cultures of pleural fluid were negative for aerobic and
anaerobic bacteria. An additional 3,000 ml of fluid was removed by
thoracocentesis on the following day, resulting in significant relief
of dyspnea. A computerized tomographic scan of the lower thorax
and upper abdomen showed a moderate pleural effusion and a cystic
mass in the upper abdomen close to the midline and pancreatic
edema.

A consulting surgeon decided to perform an exploratory laparot-
omy. A chest tube was inserted in the operating room just prior to
surgery and drained 2,500 ml of pleural fluid, with reduction in the
abdominal swelling. At laparotomy the pancreas was noted to be
markedly inflamed, and no pseudocysts or fistulous tracts were
identified. Surgical pancreateography was not performed. After sur-
gery the patient received total parenteral nutrition and intravenous
cimetidine for two weeks. He developed an infection in the pleural
space which was treated with antibiotics. Despite these measures,
the patient continued to do poorly, and there was persistent drainage
of 350 to 400 ml from the chest tube. An endoscopic retrograde
cholangiopancreatogram demonstrated good filling of the common
biliary duct and an accessory pancreatic duct, but the main pancre-
atic duct was not visualized. The chest tube was removed despite the
presence of a hydropneumothorax, and the patient was discharged
after 40 days of hospitalization.

The patient was readmitted two months later because of increasing
shortness of breath and recurrence of pleural effusion. At this time,
he was referred to the Mayo Clinic where, after extended observa-
tion, he underwent right thoracotomy and decortication of the lung,
diaphragm, and mediastinum. A 2-mm fistulous tract draining clear
fluid rich in amylase was noted to extend from the right pleural space
into the abdomen. This tract was oversewn by the surgeon. The
patient had a complicated postoperative course, necessitating total
parenteral nutrition to improve nutrition. Multiple computerized
tomographic scans of the abdomen demonstrated slow resolution
of the cystic masses in the pancreas. The patient was discharged four
weeks later. A chest x-ray film at discharge demonstrated pleural and
parenchymal scaring, with no evidence of pleural fluid.

The patient was readmitted six weeks later because of increasing
abdominal swelling. A computerized tomographic scan of the
abdomen demonstrated a large discrete pancreatic pseudocyst (Fig
3), which was internally drained into the stomach through a
gastropseudocystostomy. After surgery the patient did well and was
discharged two weeks later. A chest x-ray film obtained six weeks
after discharge showed no pleural fluid.

Comment: This patient had pancreatitis with an abdominal pseudo-
cyst and pancreatic pleural effusion. Three major surgical proce-
dures were performed in order to resolve the problem. Chest tube

Figure 1. Chest x-ray film obtained at time of third admission, showing
massive left-sided pleural effusion (case 1).

(102°F); however, cultures of blood, urine, sputum, and pleural fluid
were sterile. Two days after the onset of fever, the chest tube
 drainage was minimal, and the tube was removed after six days.
Differential cell counts of the pleural fluid disclosed white blood cell
counts of 1,000/cu mm to 2,000/cu mm, with 75 to 80 percent
mononuclear cells. Levels of amylase in the pleural fluid ranged from
6,500 to 47,400 IU/L, while the highest serum level of amylase was
530 IU/L (Table 1). For three weeks the patient received total
parenteral nutrition and intravenous cimetidine with no oral intake.
He was discharged after four weeks and has remained asymptomatic.
At discharge and after three months, the chest x-ray film revealed
only residual pleural reaction on the left.

Comment: Although there was no attempt to demonstrate an
internal pancreatic fistula, we believe that it was the most likely
cause for the recurring massive pleural effusion with high amylase
content. A computerized tomographic scan of the abdomen and

Figure 2. Chest x-ray film at time of admission, showing massive
right-sided pleural effusion (case 2).
demonstrated (Fig 4). Administration of the pleural fluid was 1,850 ml. Drainage accompanied by infection in the pleural space failed to prevent the reaccumulation of pleural fluid. A fistulous tract connecting the right pleural space to the abdominal cavity was demonstrated during thoracotomy and decortication. The patient ultimately required internal drainage of a pancreatic pseudocyst into the stomach.

Case 3

A 59-year-old white man was admitted to the Omaha Veterans Administration Medical Center with increasing shortness of breath and cough productive of yellow and white sputum. On admission, he was in moderate respiratory distress with a respiratory rate of 44/min, pulse rate of 140 beats per minute, and temperature of 37.4°C (99.4°F). Decreased breath sounds and dullness were noted over the right lower portion of the chest. A chest x-ray film demonstrated a moderate pleural effusion in the right hemithorax (Fig 4). A thoracocentesis performed on the day of admission yielded 1,850 ml of serous exudative fluid (Table 2) with a high level of amylase. Gram stain and cultures of pleural fluid were negative for aerobic and anaerobic bacteria. Acid-fast and fungal stains and cultures were also negative. The sputum grew many organisms of *Hemophilus influenzae*. The patient was treated with intravenous ampicillin (1 g every four hours for ten days). A leukocytosis of 25,000/cu mm with a leftward shift was noted. The serum level of amylase was elevated (Table 2). A skin test with PPD was negative. A repeat thoracocentesis with pleural biopsy was performed. The pH of the pleural fluid was 7.14, and the pleural biopsy showed acute organizing pleuritis with no evidence of malignancy. A chest tube was inserted on the third day of hospitalization, and 400 ml of fluid was drained initially, followed by 150 ml over the next two days. There was no further drainage over the next four days, and a chest x-ray film showed small amounts of loculated pleural fluid posteriorly.

The patient was treated empirically for acute pancreatitis, with intravenous fluids and cimetidine, and his symptoms improved significantly by the fifth day of hospitalization. Computerized tomography of the abdomen and thorax demonstrated small amounts of loculated pleural fluid in the right hemithorax and also a large subcarinal mass which was believed to represent loculated fluid in the mediastinum (Fig 5). There was no evidence of pancreatic inflammation. A barium swallow failed to reveal any esophageal pathologic findings. No endobronchial lesion was noted on fiberoptic bronchoscopy. A regular diet was resumed, with no increase in pleural fluid or worsening of symptoms. Since the patient’s condition continued to improve, it was decided to defer thoracotomy and observe the loculated mediastinal fluid. He was discharged a week after the chest tube had been removed, and a chest x-ray film obtained four weeks later showed some residual pleural thickening. A repeat computerized tomographic scan of the thorax and upper abdomen demonstrated complete resolution of the mediastinal mass.

Table 2—Data from Pleural Fluid and Serum in Patient 3

<table>
<thead>
<tr>
<th>Data</th>
<th>Admission</th>
<th>Day 2</th>
<th>Day 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume, L</td>
<td>1.8</td>
<td>1.5</td>
<td>0.4</td>
</tr>
<tr>
<td>Protein, g/dl</td>
<td>3.8</td>
<td>3.9</td>
<td>2.9</td>
</tr>
<tr>
<td>LDH, IU/L</td>
<td>236</td>
<td>324</td>
<td>64</td>
</tr>
<tr>
<td>Amylase, IU/L</td>
<td>10,285</td>
<td>17,900</td>
<td>7,750</td>
</tr>
<tr>
<td>Serum amylase, IU/L*</td>
<td>1,179</td>
<td>...</td>
<td>145</td>
</tr>
</tbody>
</table>

*Normal range, 20 to 110 IU/L.

*Figures are not relevant to the text.*
Comment: Although an internal pancreatic fistula was not demonstrated, computerized tomographic scans of the thorax and upper abdomen revealed a subcarinal mediastinal mass which was most likely loculated mediastinal fluid or possibly a mediastinal pseudocyst. Nonsurgical treatment was successful in the management of the pleural and mediastinal fluid.

DISCUSSION

Small transient pleural effusions occur in 4 to 17 percent of patients with acute pancreatitis. The effusion is usually left-sided and has a normal or mildly elevated amylase content. Typically, it is an asymptomatic nonhemorrhagic effusion that clears as the acute pancreatitis resolves.

Chronic massive pancreatic pleural effusion may develop weeks, months, or years after an episode of acute pancreatitis, and in the majority of the patients, there is no history of pancreatic disease. Patients commonly present with pulmonary complaints of dyspnea, cough, and chest pain. Most patients do not have abdominal symptoms, but some may have abdominal tenderness or swelling. The serum level of amylase is usually normal or only mildly elevated. When the serum level of amylase is increased, it is thought to be due to back diffusion from the pleural space rather than acute pancreatic inflammation. The concentration of amylase in the pleural fluid is always markedly elevated, usually greater than 1,000 IU/L, with reported values as high as 475,000 Somogyi units/dl. The pleural fluid is an exudate with elevated concentrations of protein and lactic dehydrogenase (LDH). Recurrence of the effusion after repeated thoracocentesis is characteristic, and this was apparent in the three cases presented.

Chronic massive pancreatic pleural effusion is due, in most cases, to posterior disruption of the pancreatic duct into the retroperitoneal space, with tracking of pancreatic secretions along the esophagus or aorta upward into the mediastinum. Penetration into one or both pleural spaces results in unilateral or bilateral pleural effusions. Less commonly, secretions are contained within the mediastinum and present as a mediastinal pseudocyst. In patient 3, there was a large subcarinal mediastinal mass on the computerized tomographic scan, which was due to a loculated mediastinal effusion or a pseudocyst. Formation of a fistula from an abdominal pseudocyst, directly through the dome of the diaphragm and into the right or left pleural cavity, has also been reported, and this was evident in patient 2.

A major pitfall in the diagnosis and management of chronic massive pancreatic pleural effusion is failure to recognize that intra-abdominal disease is responsible for the pleural effusion. The most important clue is the very high level of amylase in the pleural fluid. Lesser elevations in the concentration of amylase in the pleural fluid have been noted in pancreatitis and in thoracic neoplasms, both primary and secondary. Very high levels of salivary amylase may occur with esophageal rupture, but the clinical presentation and natural history usually make this easy to differentiate from chronic massive pancreatic pleural effusion.

Therapy is somewhat controversial, but because of its demonstrated effectiveness in 48 percent of the cases, conservative management should be attempted initially. All three patients were maintained with no oral intake and received total parenteral nutrition and intravenous cimetidine for periods of one to three weeks. Repeat thoracocenteses were required in two patients for relief of dyspnea, and all three patients ultimately had chest tube drainage. Atropine, acetazolamide, and nasogastric suction have been advocated in the medical management of chronic massive pancreatic pleural effusion but are of unproven clinical efficacy. Medical management was successful in two of the three patients, while the third patient required several surgical procedures to resolve the problem.

In summary, chronic massive pancreatic pleural effusion must be considered in the differential diagnosis of massive exudative pleural effusion of unknown cause. The three cases presented provide a spectrum of the clinical presentation of chronic massive pancreatic pleural effusion. Marked elevation of the concentration of amylase in the pleural fluid is virtually diagnostic in the appropriate clinical setting, and a trial of nonsurgical therapy is successful in about one-half of the cases. If this fails, abdominal surgery may be lifesaving. Although infrequently reported, chronic massive pancreatic pleural effusion is probably more common than expected, and as awareness of the syndrome increases, more cases may be identified.

ACKNOWLEDGMENT: We thank Eugene F. Lanspa, M.D., and John D. Boehrns, M.D., for allowing us to include their patient (patient two) in our report.

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5 Tombroff M, Loicq A, DeKoster JP, Engleholm L, Govaerts JP

14th Annual Fleischner Society Symposium
The Fleischner Society will hold its 14th Annual Symposium on Chest Disease, June 17-19, at the Sweeney Convention Center, Santa Fe, New Mexico. For information, please contact Fleischner Society Conference Coordinator, 3770 Tansy, San Diego 92121 (619:453-6222).

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