Pneumocystis carinii Pneumonia after Thoracic Duct Ligation and Leakage

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A case of Pneumocystis carinii pneumonia was induced through immunosuppression following thoracic duct ligation. The patient initially presented with an esophageal adenocarcinoma, which was totally resected. She is human immunodeficiency virus–negative and not undergoing immunosuppressive treatment.

Cell-mediated immunity appears to be the central mechanism by which infection with intracellular pathogens is controlled. This includes all viral pathogens and facultative or obligate intracellular pathogens. A deficit in cell-mediated immunity can occur secondary to lymphocytic depletion, especially involving the CD4 cell subsets. There is no infection in which the importance of cell-mediated immunity is more clearly evident than Pneumocystis carinii pneumonia (PCP), as demonstrated by the susceptibility of AIDS patients to this organism. The majority of infections in adults appear to result from recrudescence of dormant infection, which is held in check by cell-mediated immunity and occurs when the numbers of CD4 lymphocytes fall [1]. Persons most at risk for PCP have low CD4 lymphocyte counts, usually <200 cells/μL [2]. The organism was initially isolated from premature and malnourished children in the 1930s and was a prominent cause of morbidity in the early years of transplant medicine [3]. In the 1980s, PCP was the presenting diagnosis in a high proportion of patients with HIV infection [4].

Thoracic duct damage is a recognized consequence of esophagectomy and leads to extravasation of lymph, with the formation of chylous effusions and depletion of peripheral lymphocytes [5]. Bacterial infections occur secondary to this type of lymphocyte depletion. In the mid-1980s, both gram-negative and gram-positive infections were reported to be associated with lymph loss secondary to thoracic surgery [6, 7]. We present what we believe is the first case report in the literature of PCP secondary to lymphocyte deletion from a thoracic duct leakage.

Case history. A 61-year-old woman first presented in December 1997 with a 2-month history of dysphagia. She was a smoker and had a past history of achalasia for which she had a Heller’s cardiomymotomy in 1975 and esophageal dilatation more recently. She still had persistent symptoms of reflux. Endoscopy of the upper gastrointestinal tract confirmed a Barrett’s esophagus and an esophageal adenocarcinoma. CT confirmed a well-localized tumor at the lower third of the esophagus, and she underwent a subtotal esophagectomy with radical lymph node dissection and splenectomy. Preoperatively, she had normal pulmonary function, with a forced expiratory volume in 1 s of 2.15 L and forced vital capacity of 2.9 L, and a normal complete blood count with a normal differential WBC count. The thoracic duct was ligated at the margins and resected en bloc with the esophageal specimen. There were no visible metastases. Histological examination confirmed a moderately differentiated tumor, and the lymph nodes were clear. The initial postoperative period was unremarkable, and she was discharged. She had no additional antineoplastic chemotherapy. Two weeks later, she developed bilateral pleural effusions and gross ascites and was readmitted when 1 L of serous fluid was drained from the abdominal cavity.

After a subsequent discharge, she was readmitted 2 weeks later with shortness of breath, nausea, and vomiting. A barium swallow and endoscopy were normal. On examination, gross ascites and a large left pleural effusion were noted. The patient was hypoalbuminemic, with a serum albumin level of 25 g/L (normal, 34–50 g/L). The pleural effusion (1.25 L) and the ascites were drained. This fluid from the abdominal cavity was chylous in nature, with lymphocytes and mesothelial cells. There were no microorganisms. The ascitic fluid (13.1 L) was allowed to drain freely for 92 h, and the patient’s breathlessness improved. However, she became edematous and was treated with diuretics. Albumin was replaced, and total parenteral nutrition was begun. Chest radiography at the time revealed extensive consolidation throughout both mid and lower zones, with bilateral pleural effusions.

Over the next few days, she developed a persistent fever, a...
dry cough, and shortness of breath. The bilateral pleural effusion persisted. The pleural fluid was further aspirated, and treatment was begun with 60% oxygen and iv amoxicillin, 1 g q8h, and ciprofloxacin, 500 mg q12h. The pleural aspiration was complicated by a pneumothorax. Thus, a chest drain was placed in situ and she underwent intubation and ventilation. There was a significant air leak through the chest drain, indicating a bronchopleural fistula. Oxygenation was difficult, and a lymphopenia of 9 cells/L was noted. The subsets could not be quantified, because there were <1% lymphocytes; however, the majority of the cells were T cells, ~57% CD3⁺ (T cells), 8% CD19⁺ (B cells), and 40% NK cells. Testing for HIV antibody yielded negative results. Bronchoalveolar lavage showed P. carinii cysts, and treatment was begun with high-dose cotrimoxazole, 120 mg/kg/day (trimethoprim, 20 mg/kg/day), and prednisolone, 40 mg b.i.d. A Swan-Ganz pressure study and an echocardiogram confirmed a low cardiac output state. The patient underwent a transbronchial biopsy. This showed changes consistent with organizing interstitial pneumonia, and the alveolar spaces contained pink foamy exudates containing numerous P. carinii cysts. She failed to respond, and iv pentamidine, 4 mg/kg/day, and methylprednisolone, 500 mg/day, were added to the therapy. Ventilation progressively became more difficult, and she developed a tension pneumothorax. She became hyperkalemic at 6.7 mM (normal, 3.4–5.0 mM), and her urea level rose to 25.4 mM (normal, 2.5–6.4 mM); thus, pentamidine was replaced with iv clindamycin, 900 mg q8h, and oral primaquine, 30 mg/day. She continued to have chylous ascites, and ventilation remained difficult. Continuous venovenous hemofiltration was then commenced but stopped after 1 week’s trial, because no benefit was noted. Co-oximetry showed methemoglobinemia, and the primaquinea treatment was stopped. She remained ventilation-dependent for 32 days. She was also noted to be profoundly hypogammaglobulinemic, and iv immunoglobulins (0.4 g/kg infusion) were added to the treatment. Gradually there was an increase in CD4 T lymphocytes (figure 1). The chest drain was removed, and microbiological culture of repeat bronchoalveolar lavage specimens yielded negative results. She received a total of 21 days of high-dose cotrimoxazole. Her condition improved, and she was weaned off ventilation and onto continuous positive airway pressure by day 50 and was transferred back to the ward with nocturnal pressure support. She was discharged home in September 1998, almost 7 months after her surgery, and after a protracted rehabilitation, she remains well. Prophylactic treatment with cotrimoxazole, 960 mg 3 times weekly, has since been stopped, and her CD4 cells are within the normal range.

Discussion. Infections are not common in patients with chylous ascites and chylothorax [5, 8]. Extensive MEDLINE searches suggest that our case is the first report of PCP after a thoracic duct leakage. P. carinii infections are seen in patients with decreased numbers of helper T lymphocytes (CD4 cells). Experimental exposure to P. carinii of mice selectively depleted of helper T lymphocytes established pulmonary infection [1]. Postoperative chylothorax occurs in 1.1% of patients undergoing transesophagectomy [5]. Conservative management includes intercostal drainage and nutritional support with either enteral formulas enriched with medium-chain triglycerides or total parenteral nutrition [9]. If conservative therapy is not successful after 2–3 weeks, surgical treatment (thoracic duct ligation) is necessary and efficacious [6, 7]. In a series of 18 pediatric patients (ages, 1 month to 9 years) with chylothorax, 5 developed lymphopenia secondary to chylous lymphocyte loss and subsequent infections, 1 of which was a fatal viral pneumonitis. Interestingly there was no correlation between infectious complications and the total lymphocyte count [10]. In a comparison of 2 groups of patients who underwent esophagectomy with or without thoracic duct ligation, the rates of infection were similar [11]. In 13 patients who required pleural drainage for postoperative chylothorax, total protein and albumin levels, body weight, and peripheral lymphocyte counts all decreased substantially during the period of chylous leakage. Four patients developed severe immune impairment and malnutrition but did not develop infections [12].

This case represents a unique manifestation of PCP secondary to lymphocyte depletion following a chylous leak [9]. The incidence of thoracic duct damage with esophagectomy is 2%–9%, and the overall hospital mortality from chylothorax is 10% [13]. Although infection is rare, nutritional support and reinfusion of the drained chyle are recommended as treatment and prevention of sepsis. This case indicates that thoracic duct leaks may occur late after esophageal surgery and should be considered for patients who present with ascites and pleural
effusion, so as to enable early consideration of reinfusion therapy. Prophylactic antibiotics should be given to prevent opportunistic infections.

References