Malignant Pleural Effusions*  
Recent Advances and Ambulatory Sclerotherapy  
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Malignant pleural effusions are a common problem in cancer patients with advanced disease. Patients typically present with progressive dyspnea, cough, and/or chest pain that significantly compromises their quality of life. Treatment is often palliative, usually consisting of sequential thoracenteses or tube thoracostomy with or without sclerotherapy. The traditional method of treatment—tube thoracostomy with large-bore chest tubes connected to continuous wall suction—requires hospitalization, is expensive, limits patient mobility, and can cause significant patient discomfort. More recent trials have explored new techniques, including thoracosopic insufflation of talc and small-bore catheters. Most of these studies have been performed on inpatients, although a recent multi-institutional trial was initiated to evaluate the feasibility and efficacy of ambulatory (outpatient) pleural drainage and sclerotherapy using small-bore catheters. All patients fulfilling eligibility criteria had a small-bore catheter placed in the pleural space that was then connected to a closed gravity drainage bag system. When daily tube drainage was <100 mL, sclerotherapy was performed. Response rates at our institution demonstrated 10 patients (53%) had a complete response, 5 (26%) had a partial response, and 4 (21%) had progressive disease at 30-day follow-up. These preliminary results suggest ambulatory sclerotherapy is a safe, viable alternative to conventional inpatient treatment of malignant pleural effusions in a select group of patients. (CHEST 1998; 113:748-778)

Malig nant pleural effusions are a common problem in cancer patients with advanced disease. Approximately 50% of patients with breast carcinoma, 25% of patients with lung carcinoma, and 35% of patients with lymphoma develop a malignant effusion during the course of their disease. These three malignancies and ovarian carcinoma account for >75% of all malignant effusions.  

Patients usually present with symptoms that compromise their quality of life, including progressive dyspnea, cough, and/or chest pain. Although not all pleural effusions in patients with a known neoplasm are malignant, exudative pleural fluid collections should be considered metastatic in origin until proved otherwise.

Diagnosis  
Thoracentesis is an important step in the initial evaluation of patients with a pleural abnormality. Malignancy is the most common cause of an exudative pleural effusion in adults older than 60 years of age, although a definitive diagnosis is established only by aspiration of malignant cells from the pleural space. Approximately 50% of malignant pleural effusions are diagnosed on initial cytologic study from thoracentesis, with an additional 10% diagnosed on the second cytologic examination. Pleural biopsy specimens are less sensitive in making a definitive diagnosis when used alone, probably because of the focal nature of the metastasis and the blind sampling procedure. Combined cytologic examination and pleural biopsy specimens, however, accurately diagnose metastatic disease in >80% of cases.

Management  
Treatment options for malignant pleural effusion depend on the extent of disease, effectiveness of systemic therapy, and patient performance status. Pleural effusions in patients, particularly those with lymphoma, small cell lung cancer, or germ cell cancer, may be controlled by systemic treatment, although therapeutic thoracentesis is occasionally required to relieve symptoms initially.

Patients with disease that cannot be effectively controlled by systemic treatment usually require local palliative therapy aimed at reducing unnecessary hospitalization, costs, and complications. The most common treatment is tube thoracostomy and drainage, followed by sclerotherapy. Large-bore thoracostomy tubes (>24F) have traditionally been used for drainage and sclerotherapy. This requires hospitalization and can cause patient discomfort. More recently, use of small-bore catheters with radiologic guidance has been studied. Imaging guidance is effective in localizing pleural fluid collections and avoiding unnecessary tube placement in patients with central obstructing mass lesions, a thick pleural peel, or multiple loculated fluid pockets.

Several studies have compared the efficacy of small-bore vs standard large-bore chest tubes, and results indicate that pigtail-catheter drainage and sclerosis are at least as successful as the more traditional drainage with the standard chest tube. In one study, 8 of 13 effusions (61.5%) were adequately treated with pigtail-catheter drainage and sclerotherapy, compared with 4 of 11 effusions (36.4%) treated with standard chest tube drainage and sclerotherapy. Other studies with small-bore tubes have reported similar response rates. Small-bore catheters are typically placed in the midaxillary line at the sixth or seventh interspace so that the tube is not compressed or kinked when the patient is in a supine position. Up to 1 L of fluid is aspirated at the time of tube placement, depending on patient comfort and symptoms. Inpatient chest tubes are connected to a water-seal drainage system with continuous wall suction (approximately 20 cm H₂O). Daily outputs are recorded. When drainage decreases to <100 mL in a 24-h period, a chest radiograph is performed to exclude loculated fluid and assure complete lung reexpansion. All residual fluid is
aspirated, although if >100 mL remains, the tube is flushed with normal saline solution and the patient returned to continuous suction. It is important to completely drain the pleural fluid before instilling the sclerosing agent, since successful pleurodysis requires close contact of the visceral and parietal pleura.

The sclerosing agent is instilled through the drainage tube, after which the tube is clamped. A number of sclerosing agents have been used to treat malignant pleural effusions, including talc, biologies, antibiotics, antineoplastics, and radioisotopes.20,10-20 No single agent has shown a clear advantage over the others.

Once the sclerosing agent is introduced, patient position should be changed every 15 min for 2 h to distribute the agent completely through the pleural space. Following this, the clamp is removed and suction applied for up to an additional 24 h, at which time the tube is removed if <100 mL has drained. Response to sclerotherapy is measured by clinical signs and symptoms, as well as size of effusion on chest radiographs performed at monthly follow-up.

Although unusual, complications include tube malfunction (eg, clotting or kinking) or malposition, infection, loculation, and pneumothorax. Early recognition of these problems ensures they can be managed without difficulty.

Ambulatory Sclerotherapy

One significant advantage of sclerotherapy with small-bore catheters is the potential for outpatient treatment. A study at Duke University Medical Center and the University of Pittsburgh Medical Center has been initiated to assess the feasibility and efficacy of ambulatory sclero¬
thapy.

The study enrolls patients with symptomatic, unilateral malignant pleural effusions meeting eligibility criteria (Table 1). The entrance criteria are somewhat rigid in this pilot study because we want to enroll only patients who can potentially complete outpatient therapy.

All patients have a predrainage baseline chest radio-

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<th>Table 1—Eligibility and Exclusion Criteria</th>
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<td>Characteristics</td>
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<td>Eligibility criteria</td>
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<td>Documented or strongly suspected malignant pleural effusion in patients with a known neoplasm</td>
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<td>Tumor refractory to systemic therapy</td>
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<td>Recurrent pleural effusion after initial thoracentesis</td>
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<td>No prior intrapleural sclerotherapy</td>
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<td>No systemic chemotherapy or ipsilateral radiotherapy within 21 d prior to entry</td>
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<td>Age older than 78 yr</td>
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<td>Karnofsky performance status ≥60%</td>
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<td>Sufficient bone marrow function; WBC count ≥3,000/μL; platelet count ≥100,000/μL; Adequate coagulation profile</td>
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<td>Life expectancy &gt;6 wk</td>
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<td>Exclusion criteria</td>
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<td>Pregnant or lactating women</td>
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<td>Patients with bleeding disorders</td>
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<td>Patients with mesothelioma</td>
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Another chest radiograph is obtained to confirm complete fluid drainage, absence of loculations, and complete lung reexpansion. Any remaining fluid is aspirated prior to installation of the sclerosing agent. Once patients are ready for sclerosis, one dose of 60 U of bleomycin in 50 mL D2W is instilled into the pleural space, and the tube is clamped. Patients are instructed to change positions frequently to distribute the sclerosing agent uniformly. After 2 h, the tube is reopened to gravity drainage, and the patient is sent home. The next day, the patient returns to the clinic for chest tube removal. Postsclerotherapy chest radiographs are obtained immediately after tube removal and at the 50-day follow-up visit. Patients are instructed to call or return to the clinic if they experience any problems. Symptomatic response and complications from sclerotherapy are recorded.

Figure 1. A 600-mL bag used for gravity drainage in outpatient sclerotherapy with small-bore catheters.
To date, 19 patients from Duke University Medical Center have been enrolled. Chest tubes remained in place between 2 and 11 days (mean, 5.1 days). The total pleural drainage ranged from 950 to 3,925 mL (mean, 1,647 mL). At 30 days, 10 patients (53%) had a complete radiographic response and 5 (26%) had a partial response. Four patients (21%) had progressive disease, three of whom had a good initial response but suffered a relapse at 30 days. One patient never had the pleural drainage fall below 100 mL/d. At this patient’s request, sclerosis was performed and the tube removed on day 9. Progressive disease was documented radiographically on day 30. Excluding the latter patient, there was no significant difference in either duration of tube placement or total drainage among the three response groups.

Mild chest pain at the insertion site was reported in six patients (32%). No additional treatment besides oral analgesics was required. There were two tube malfunction secondary to clogging. Both tubes were cleared easily with a guide wire; both patients subsequently had successful scleroses. One patient (5%) developed a subcutaneous wound infection and empyema requiring hospitalization 6 days after tube removal. The patient reported no problems at the time of drainage or sclerotherapy. No patient required hospitalization during therapy. Three patients (16%) reported temporary nausea or vomiting following bleomycin instillation, and four patients (21%) had a transient (<6 h), low-grade fever that resolved without treatment. All patients had significant symptomatic improvement in their respiratory status with drainage.52

In summary, our preliminary findings suggest that small-bore sclerotherapy for management of malignant pleural effusion is feasible on an outpatient basis. Such treatment offers important potential benefits to the patient, including a better quality of life and reduction in overall health-care costs.

CONCLUSIONS

Malignant pleural effusions are a major cause of morbidity in cancer patients. Symptoms usually include chest pain, cough, and dyspnea, and may progress to impair patient quality of life significantly. Treatment is usually palliative, although if possible, initial steps should focus on treatment of the primary malignancy. Some of these patients require a temporizing thoracostesis for symptomatic relief, and others may need repeated thoracostesis for slowly recurring effusions. Most patients, however, will require tube drainage and sclerotherapy. There continues to be controversy regarding the best sclerosing agent, as no single agent has demonstrated a distinct advantage.

Standard sclerotherapy for malignant pleural effusions has been performed routinely using large-bore chest tubes. Pleurodesis using small-bore catheters permits less expensive outpatient ambulatory therapy, which is expected to further reduce patient discomfort and costly hospitalization.

REFERENCES

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