

EPECTM-O

Education In **P**alliative And **E**nd-Of-Life **C**are For **O**ncology

Self-Study Module 3m:

Symptoms; Malignant Pleural Effusions

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Abstract

Many symptoms and syndromes are commonly encountered in patients with cancer. This module first presents general approaches to symptom management, followed by management of the specific symptoms and syndromes, including: anorexia/cachexia, anxiety, constipation, depression, diarrhea, fatigue, insomnia, menopausal symptoms and sexual health, mucositis, nausea and vomiting, and skin problems.

Any symptom can be debilitating and prevent the patient and family from achieving goals that are important to them. As with other aspects of medicine, tailored management is based on the underlying etiology and pathophysiology. When several symptoms occur together, they can be interrelated and management can be complex.

Introduction

Pleural effusions accumulate in the potential space between the visceral (inner) layer covering the lungs and the parietal (outer) layer covering the chest wall. The most commonly associated symptom is dyspnea, although persistent cough and chest pain can also occur.

Prevalence

Malignant pleural effusions occur commonly in patients with cancer. The malignancies responsible for more than 75% of all of pleural effusions in order of frequency are lung, breast, lymphoma, and ovarian cancer.

In a general hospital setting, 25% of all pleural effusions are malignant. In patients with an existing diagnosis of cancer, this increases to 30 to 70% if the fluid is an exudate.

Prognosis

Pleural effusions from a malignancy for which there is no effective treatment portends a poor prognosis. Median survival for patients with an effusion due to metastatic cancer averages 3 months. Drainage alone improves comfort, but does not affect survival. (Ref. 1)

Case

Review the case below, and keep it in mind as you progress through the module. How would you approach the assessment of this patient? What interventions might be appropriate?

F.G., an 84-year-old former truck driver with stage IV lung cancer, reported gradually progressive dyspnea over 2 weeks. He was diagnosed with T4N2M1 adenocarcinoma of the right lung with 3 liver metastases 6 months prior to this visit. He received four cycles of cisplatin and docetaxel with partial response. Treatment was stopped when his performance status deteriorated from 1 to 3. Once chemotherapy was stopped, his performance status improved to 2 until the past 2 weeks when it again deteriorated to 3. Evaluation revealed progressive disease in the liver and a new large left pleural effusion estimated at 3 liters on the chest radiograph. Thoracentesis revealed an exudate and produced partial relief of dyspnea. A radiographically placed catheter was inserted and his wife was taught how to manage the drainage. Sclerosis was considered, but not performed due to high drainage rates (>500 ml/day) and poor performance status. Hospice care was begun. He died comfortably at home 4 weeks later.

Pathophysiology

Normally, there is less than 20 ml of fluid in the pleural space. This provides lubrication during breathing. This volume is normally in equilibrium between secretion by the parietal pleura and absorption by the visceral pleura into the lymphatic system. Up to 10 liters of low-protein fluid flows through the space each day.

Fluid accumulates when this balance is disrupted by decreased oncotic pressure (e.g., decreased serum albumin) or increased lymphatic system pressure (e.g., infiltration by tumor). In addition, metastases to the pleural space can disrupt flow through direct disruption of the pleural surfaces and associated inflammation.

Assessment

A history of worsening dyspnea, cough, and/or pleuritic chest pain may suggest a pleural effusion.

Diminished breath sounds, fremitus, and dullness to percussion on physical examination are suggestive.

Chest radiographs establish the probability of the effusion and provide an estimate of volume. Lateral decubitus views can distinguish free-flowing from loculated effusions. Computed tomography scans are useful when radiographs are inconclusive.

The diagnosis is made with thoracentesis. A clinically significant pleural effusion of unknown cause is an indication for a thoracentesis. (Ref. 2) Collect a small volume of fluid to evaluate its composition, cytology, and complete cell count. Perform culture and sensitivities if infection is suspected.

Measure both pleural fluid and serum total protein, glucose, lactose dehydrogenase, and pH. Effusions are evaluated as transudative or exudative based on Light's criteria. (Ref. 1) Light's criteria state that if the ratio of pleural fluid LDH to serum LDH is >0.6 , and if the ratio of pleural fluid protein to serum protein is >0.5 , and the pleural fluid LDH is $>2/3$ the upper limit of normal (ULN) for the testing lab's serum LDH, then the effusion is likely an exudate. Transudative effusions are rarely malignant. If the clinical appearance of the fluid suggests a transudate but according to Light's criteria it is an exudate, measure the difference between the serum and pleural fluid albumin. Generally, a serum albumin level >1.2 g/dl above the pleural fluid albumin level is consistent with a transudative effusion. (Ref. 3) A meta-analysis of studies that discriminate between exudative and transudative effusions determined alternate thresholds for LDH (pleural LDH >0.45 ULN of serum LDH: this value is used for Light's modified criteria), pleural cholesterol (>45 mg/dl) and pleural protein (>2.9 g/dl). (Ref. 4) This meta-analysis also found that there are two test combinations that include only pleural fluid analysis that are as accurate as using Light's modified criteria (which compares pleural to serum values in ratios): measurement of pleural LDH and pleural cholesterol level (LDH-PF/C-PF) or measuring these two plus pleural protein level (P-PF/LDH-PF/C-PF). That is to say, if pleural LDH is >0.45 of the ULN of serum LDH for the testing lab or if the pleural cholesterol level is >45 mg/dl or if the pleural protein level is >2.9 g/dl, then the effusion is likely an exudate_[a1].

Table 1: Light's Criteria for Transudative vs. Exudative Effusions

	Transudate	Exudate
Malignant cells	Negative	Positive <50%
Cell count	Low	High
Total protein	Pleural : serum ratio <0.5	Pleural : serum ratio >0.5
LDH	Pleural : serum ratio <0.6	Pleura l: serum ratio >0.6 or >2/3 normal serum limit
pH	<7.3	>7.3

In 25% of patients with cancer and recurrent pleural effusion, malignant cells may not be identified by cytology. (Ref. 5) Analyzing three pleural fluid samples increases the yield to 77%. In such cases, thoracoscopy with pleural biopsy is more likely to be diagnostic. (Ref. 2)

Management

Drainage

Establish the goals of treatment before initiating drainage. Consider the patient's symptoms, performance status, primary site of the tumor and its responsiveness to available antineoplastic treatment, and potential for lung expansion following drainage of fluid. Drainage may achieve goals of relieving dyspnea, minimizing hospitalization, improving function, and providing the patient and family with a sense of control.

A new diagnosis of non small-cell lung cancer, breast cancer, lymphoma, or germ cell cancer may best be managed with chemotherapy if the patient has an adequate performance status.

A variety of options, as listed below along with the advantages and disadvantages of each, are available for drainage.

Table 2: Thorax Drainage Options

	Advantages	Disadvantages
Serial thoracentesis	Technically simple. Can be performed at home or in outpatient setting. Volumes large enough to cause symptoms make pneumothorax unlikely. Avoid removal of >1,500cc.	Impractical with quickly reaccumulating fluid. Recurrence rate at 1 month approaches 100%. (Ref. 6)
Chest tube insertion with intra pleural sclerosant	Success rate >60%; low incidence of complications. Small bore (10-14F) equally as effective as large bore tubes. (Ref. 7)	Side effects of sclerosants and pain. Requires hospitalization.
Permanent or semi permanent catheter	Placed by interventional radiology or surgery. Can be continuous or intermittent drainage. Family can manage catheter.	Highly proteinaceous fluid may clog. Local cellulitis most common complication.
Thoracoscopy with talc	High success rate >90%. Perioperative mortality<0.5%.	Surgery required/invasive procedure. Most common major complications: empyema, respiratory failure.
Pleuroperitoneal (Denver) shunt	No external catheters. May be effective for patient with failed pleurodesis.	Patient or caregiver must press pump to be effective. Occlusion, infection risk, tumor seeding.

Thoracoscopy

Thoracoscopy is now the most widely used technique for the management of pleural effusions. It should be considered for the diagnosis of suspected but unproven malignant pleural effusion, and for control of recurrent malignant effusions. (Ref. 6)

Video-assisted thoracoscopy offers multiple advantages over other surgical methods. It offers detailed visualization of the hemithorax, allowing for directed pleural biopsies, therapeutic pleurectomies, mechanical pleurodesis, chemical pleurodesis with improved distribution of the sclerosing agent, and catheter placement for thoracic drainage. (Ref. 6) (Ref. 8)

Patients undergoing video-assisted thoracoscopy have reduced operative time, drainage time, and postoperative morbidity compared with the open surgical technique. (Ref. 8) They also experience less pain and less pulmonary dysfunction during the post-treatment period than those undergoing mini-thoracotomy. (Ref. 8)

Patients with “trapped lung” from a “rind” of tumor or fibrosis, or an obstructed bronchus will not experience relief of dyspnea, chest pain, or cough after thoracentesis. Vigorous manipulation of a chest tube is more likely to cause discomfort, intrapleural infection, and emphysema as it is to re-expand the collapsed lung. In carefully selected patients, video-assisted thoracoscopy may offer a therapeutic benefit. (Ref. 6) (Ref. 8)

Pleurodesis

Selected patients who have undergone thoracentesis may be candidates for pleurodesis. Typically, patients are candidates if thoracentesis resulted in lung re-expansion with apposition of the visceral and parietal pleura and relief of symptoms and they have <200 ml/day of drainage.

Pleurodesis is performed to scar the visceral and parietal pleura together and obliterate the potential pleural space. Pleurodesis requires a diffuse inflammatory response and local activation of the coagulation system with fibrin deposition. Talc is generally considered the preferred agent. (Ref. 9) Pleurodesis can be achieved via chest tube or with a long-term indwelling pleural catheter. To date, the only randomized trial compares use of each of the above treatments in patients with symptomatic, recurrent malignant pleural effusions. Doxycycline pleurodesis was compared with use of an indwelling long-term intercostal catheter. The degree of improvement of dyspnea was equal and the hospitalization time was shorter for patients with the long-term catheter. (Ref. 10)

Sclerosing agents can produce severe pain. Therefore, adequate medication with opioids before and after the procedure is required. In addition, sclerosing agents can produce fever, tachycardia, and nausea. Talc, doxycycline, and bleomycin have all been reported to be effective in ≥50% of cases.

Pleuroperitoneal shunts may be useful for patients with a trapped lung or failed pleurodesis.

Summary

Presence of a malignant pleural effusion is associated with an average prognosis of 3 months. In addition to managing dyspnea and pain with opioids, physical drainage of the fluid may relieve symptoms quickly. For fluid that reaccumulates, pleurodesis may prevent the effusion from recurring. A semi permanent catheter may be placed for frequent drainage in cases where pleurodesis is not possible.

Key Take-Home Points

1. History, physical examination, and plain radiograph of the chest usually provide the diagnosis.
2. Drainage with video-assisted thoracoscopy can provide a diagnosis and definitive management.
3. Serial thoracentesis or semi permanent catheters may be used for effusions for which pleurodesis is not possible, or has failed.

Pearls

1. Drainage of a large pleural effusion may safely be tapped at home; ultrasound guidance is not required.
2. Make a partnership with your patient and the family caregiver; draw them into the interdisciplinary team and foster their active participation in the care plan.

Pitfalls

1. Failing to use medical management alone when a patient has a short time to live.
2. Failing to realize that an asymptomatic pleural effusion cannot have its symptoms improved.

References

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The authors provide a review and meta-analysis of randomized controlled studies of talc as the sclerosant of choice, and thoracoscopic pleurodesis as the preferred technique for pleurodesis based on efficacy.

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One hundred forty-four patients (61 men and 83 women) were randomized in a 2:1 distribution to either an indwelling pleural catheter or doxycycline pleurodesis. The median hospitalization time was 1.0 day for the catheter group and 6.5 days for the doxycycline group. The degree of symptomatic improvement in dyspnea and quality of life was comparable in each group.