Malignant Pleural Effusion

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Injury/Disease Demographics

- Malignant pleural effusion (MPE) is defined as tumor cells in pleural fluid and result from cancer cells invading pleural membranes.
- The majority of patients who develop MPE have incurable malignant disease with disseminated, advanced stage malignancy. Median survival for patients who develop MPEs is reported to be 4-6 months.
- Lung cancer is the most common malignancy associated with MPEs. Other common malignancies include breast cancer, gastrointestinal tract carcinomas, and lymphoma.
- Patients with an unknown primary cancer can also present with MPEs as the initial manifestation of malignancy.
- Paramalignant effusions are effusions associated *indirectly* with malignancies
    - Examples are effusions due to chemotherapy or radiation treatment; post-obstructive pneumonia from the tumor; effusion from pulmonary embolism which occur because of the hypercoagulable state of malignancy.
    - Distinguishing paramalignant effusions and MPEs is crucial in patient prognosis and in treatment considerations.

Clinical Presentation

- Most patients will present with dyspnea. Occasionally patients will also complain of persistent cough and pleuritic chest pain.
- Uncommonly, patients who are asymptomatic will have a MPE found incidentally on radiographic imaging, prompting further workup for the underlying primary malignancy.

Evaluation/Diagnostics/Imaging

- All patients suspected to have a MPE should have a thorough history and physical examination performed. Attention on history and examination should be guided by evaluating for a primary underlying etiology for the MPE.
- Sampling of the pleural fluid to confirm the diagnosis of an MPE can be done by thoracentesis, preferably by ultrasound guidance when the pleural fluid collection is small.
    - At least 60 ml of pleural fluid should be sent for cytological evaluation; flow-cytometry studies should be considered in patients with or suspected to have hematological malignancies.
- Computed tomographic (CT) imaging is useful to guide subsequent interventional strategies for managing symptomatic MPEs.
    - Evidence of dense tumor burden in the pleura space, multiple loculations, lung collapse, or endobronchial obstruction are more likely to fail attempts at pleurodesis (procedure to induce symphysis between the parietal and visceral lung pleura)
- Large symptomatic MPEs should be drained (large-volume thoracentesis/chest tube drainage) as completely as possible.

- Relief of symptoms with drainage suggests benefit with subsequent interventions to try to prevent recurrence.
- Absence of symptomatic relief with drainage of the effusions may indicate alternative explanations for a patient's dyspnea.
- The presence of an *ex vacuo* pneumothorax due to unexpanded lung (trapped lung) after drainage of the MPE suggests that pleurodesis would likely be unsuccessful.

Role of Nonoperative Management and Associated Considerations

- Management of MPE is entirely palliative and is to relieve the symptoms attributed to the effusion such as dyspnea. Therefore, informed patient preference is central to any management options to control MPEs.
  - Multi-disciplinary team management with expertise in the different treatment modalities of the underlying type of malignancy is fundamental to individualizing the optimal approach to managing a patient with a MPE.
- Options for non-surgical management of MPEs include: no intervention; repeated large-volume thoracentesis; chest catheter-directed pleurodesis; and insertion of an indwelling pleural drainage catheter.
- Sterile talc is the most common chemical sclerosant used in the U.S. to instigate pleurodesis.
  - Intrapleural administration of talc can be uncomfortable to the awake patient, when administered at the bedside.
    - Administering 1% lidocaine (3mg/kg) intrapleurally just before the talc slurry can reduce the discomfort.
    - Talc slurry can be prepared sterilely in a syringe by mixing 5grams sterile medical grade talc powder in 30-50 ml sodium chloride 0.9%. The talc slurry is mixed thoroughly in the syringe by gentle shaking and then flushed in the intercostal chest tube. Often this is followed by an additional 30-50ml sodium chloride 0.9% flush.
    - The chest tube should be clamped for 2-4 hrs after talc slurry administration and the patient is rotated to ensure good spread throughout the pleural space. The chest tube can be unclamped after the clamped period and allowed to drain.
    - Once there is good pleural fluid drainage and the lung is expanded radiographically, the chest tube can be removed within 24-48 hrs after talc slurry administration.
  - Other sclerosing agents that have been used include bleomycin and doxycycline.
- The patient with poor functional performance status (e.g. Karnofsky ≤ 30; ECOG > 3) portends poor prognosis overall and is usually not well-suited for surgical pleurodesis.

Indications for Operative Intervention

- Surgical pleurodesis by a video-assisted thoracic surgery approach (VATS) should be considered for patients who present with recurrent symptomatic MPEs.
    - The optimal timing for surgical intervention has not been well-studied, but commonly, patients whose expected life expectancy is < 3 months should be recommended less invasive approaches for palliation of the symptoms caused by the MPE (e.g. indwelling pleural drainage catheter placement; repeat large-volume thoracenteses).
- Surgical intervention for diagnostic purposes may be undertaken whenever there is strong suspicion for MPE despite repeated cytology-negative pleural fluid evaluation by thoracenteses.

Pre-operative Preparation

- Patients should be assessed to determine if they will tolerate single lung ventilation. This often is based upon careful review of the individual patient's co-morbidities and clinical judgment, and it is important to discuss such concerns with the anesthesiology team. When deciding on whether a patient will tolerate undergoing surgical pleurodesis, it should be remembered that patients with large unilateral pleural effusions often already are dependent primarily on single lung function, and may subsequently improve with evacuation of the pleura fluid during VATS.
- Flexible bronchoscopy to evaluate airway patency should be performed first if there is concern for an endobronchial lesion causing lung collapse.

Operative Techniques

- VATS is the preferred operative approach for treating MPE when surgery is indicated. This approach is less invasive than open thoracotomy, which should be uniformly avoided given the greater morbidity associated with thoracotomy and the palliative intent of surgery.
- VATS pleurodesis provides wide access to the pleural space and the visualization to assess the extent to which the lung will re-expand against the chest wall.
    - Talc pleurodesis administered during VATS is less painful to patients. The sterile talc is available in aerosolized canisters and 4-5 grams can be more evenly dispersed under thoracoscopic visualization directly onto the pleural surface when the patient is under general anesthesia
    - A single thoracoscopic incision can often be used for the thoracoscope as well as to provide sufficient access to spray the aerosolized talc.
        - Attempts to lyse intrapleural adhesions and evacuate of pleural loculations in order to allow optimal pleural drainage and facilitate complete lung expansion, should be performed first. This may require additional thoracoscopic port sites.

- 1-2 chest tubes are then placed to drain the pleural space and are placed on water suction to evacuate the pneumothorax created during thoracoscopy and allow lung expansion.
- During the operative procedure, if lung expansion with adequate pleural apposition is not feasible, alternatively, a long-term indwelling pleural catheter (e.g. PleurX®, BD can be placed during the same operative session.

Postoperative Management

- Chest tubes placed during VATS pleurodesis are typically removed when drainage is < 200 ml/day.
- Typically chest tubes are able to be removed within 48 hrs after VATS pleurodesis if there is no air leak and the lung appears well-expanded radiographically.

Complications

- Reports of acute respiratory failure from talc instillation have been reported after VATS talc pleurodesis
  - This complication is thought to be associated with talc particle size rather than the quantity of talc instilled

Considerations for Special Populations

- Patients on chronic steroid therapy are at higher risk for failure of pleurodesis to achieve a durable prevention of MPE recurrence given the systemic anti-inflammatory state

Suggested Readings

- Thomas JM and Musani AI. Malignant pleural effusions: a review. Clin Chest Med. 2013;34(3):459-71.
- Zahid I, Routledge T, Billè A et al. What is the best treatment for malignant pleural effusions? Interact Cardiovasc Thorac Surg. 2011;12(5):818-23.
- Davies HE, Mishra EK, Kahan BC et al. Effect of an indwelling pleural catheter vs chest tube and talc pleurodesis for relieving dyspnea in patients with malignant pleural effusion: the TIME2 randomized controlled trial. JAMA. 2012;307(22):2383-9.