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Management of Malignant Lung Entrapment, the Oncothorax

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INTRODUCTION

Metastatic pleural disease is a tragic but relatively common occurrence in patients with most types of cancer. It is estimated that up to 30% of patients with advanced malignancy will have pleural metastasis, with lung cancer followed by breast and ovarian cancer the most common.¹ The presence of malignant pleural metastasis is almost always classified as distant metastasis or stage IV, even from ipsilateral lung cancer with the sole exception of mesothelioma, a primary malignancy of the pleura. A malignant pleural effusion (MPE) inevitably confers poor prognosis. In a meta-analysis of 417 patients with MPE, the median survival was 4 months, shortest for patients with lung cancer.¹ However, due to the often-incapacitating symptoms, including dyspnea, pain, and cough, the goal of therapy for this devastating disease should always focus on palliation of symptoms.

Usually, when MPE first occurs, it is a free-flowing collection that is not loculated. This can often be easily managed with simple thoracentesis or pleurodesis. However, much like its benign counterpart, with time, the lung may form adhesions to the lung, causing entrapment and loculation of the fluid. The additional effect of lung entrapment causes the equivalent of a fibrothorax, indeed it is an “oncothorax.” This causes a restrictive lung disorder in addition to that caused by the malignant hydrothorax. Unfortunately, these adhesions that entrap the lung are often malignant and not typically amenable to surgical decortication. The standard approach for managing these patients is to place an indwelling catheter with the hope of preventing further compression of the lung by the fluid. However, this will not allow full reexpansion of the lung in most situations.

This article focuses on the unique situation of malignant lung entrapment from pleural metastasis. We use the term “oncothorax” to describe this phenomenon. To our knowledge, this name has not been previously used but does inherently describe the process and

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differentiates it from the more common MPE without entrapment of the lung. We present the therapeutic modalities available to manage this difficult syndrome.

PATHOPHYSIOLOGY

The pleural cavity contains a small amount of lubricating fluid (0.3 mL/kg body mass) between the visceral and parietal pleura under normal conditions.² This fluid is in continuous movement between the pleural membranes, and it is thought that the lymphatic system plays an important role in its homeostasis and balance.³ The clearance of fluid within the pleural space is not fully understood, even though it is felt that fluid accumulation originates from the visceral pleura and is drained by the parietal pleura.⁴ Transmission electron microscopy of human parietal pleura has also revealed the presence of lymphatic pleural stomata on the diaphragmatic surface of parietal pleura that serves to drain the pleural space of fluid and particles.^{5,6} Malignancies can cause dysfunction of the pleural fluid flow dynamics and drainage by different means. First, obstruction of lymphatics or obstruction by enlarged mediastinal lymph nodes can increase the hydrostatic pressure of the interstitial tissue, leading to an increased fluid volume. Second, fluid absorption can be impaired by tumor involvement of the visceral and parietal pleura, inducing an inflammatory response and resulting in increased capillary permeability.⁷ Third, cancers can also produce proliferative stimulants, such as cytokines, neurotransmitters, and growth factors that can promote pleural effusions.⁸ Lung entrapment, or fibrothorax, occurs in long-standing benign pleural effusion from buildup of a fibrous layer of connective tissue over the collapsed lung, preventing its full reexpansion. This frequently results from inadequately treated parapneumonic effusions or empyema. This scenario is more challenging in mesothelioma or metastatic pleural disease, as the malignant pleural deposits tend to form effusions at a high volume. In addition, the adhesions that form are usually due to direct malignant invasion of the chest wall and lung. This combination of massive malignant effusion and malignant pleural rind will distort the respiratory mechanics by preventing normal chest wall excursion and enhancing the ventilation perfusion mismatch. A persistent pleural space due to lung atelectasis will invariably lead to further production of pleural fluid, thus perpetuating this vicious cycle.

DIAGNOSIS

Initial diagnosis of pleural effusion is usually based on chest radiography. A unilateral process should raise a high suspicion of malignancy or an infectious etiology. Computed tomography of the chest offers better resolution and anatomic definition of the process, showing a thick rind and fluid loculation, both of which are characteristic for entrapped lung (Fig. 1). Drainage of the fluid will confirm the latter, with lack of lung expansion and persistence of a pleural space. A thoracentesis is the least-invasive initial step to accomplish initial drainage, and the fluid is sent for analysis (cultures, cell count, cytology, and biochemical tests). A MPE or an infectious process will typically reveal an exudative pattern according to the criteria of Light and colleagues.⁹ The sensitivity of thoracentesis and cytology to establish a diagnosis of malignancy ranges between 40% and 87%.^{10,11} Repeat drainage and analysis may be required then, or alternatively, thoroscopic exploration and pleural biopsies.

MANAGEMENT OF RECURRENT MALIGNANT PLEURAL EFFUSION

Most cases of MPE will recur within a month of drainage,¹² but a repeat thoracentesis can be considered in cases of slow reaccumulation and/or short life expectancy. Even though chemotherapy can help control a MPE in certain cancers (breast, small cell carcinoma of the lung, germ cell tumors, and lymphoma^{13,14}), definitive management is usually required. This should take into account the functional status of the patients and their preferences, as well as the life expectancy, nutritional status, and tumor burden. As such, goals of therapy mostly focus on palliation of symptoms and providing comfort with minimization of hospitalization.

Pleurodesis

The goal of pleurodesis is to obliterate the pleural space by creating a seal between the visceral and parietal pleura, preventing reaccumulation of the effusion. Mechanical pleurodesis and induction of pleural abrasions are not typically recommended in malignant processes, mainly because of bleeding risk and high morbidity in terminally ill patients. Chemical pleurodesis can be performed using a variety of drugs, such as Adriamycin, tetracycline, doxycycline, bleomycin, talc, and even iodine.¹⁵ Talc pleurodesis is a procedure that enjoys wide clinical applications. Initially introduced in the 1930s by Canadian thoracic surgeon Norman Bethune,¹⁶ it induces a severe inflammatory and fibrotic response to multiple foreign bodies/talc particles.

Technique

Talc for pleurodesis can be used in the form of talc slurry via chest tube or as aerosolized insufflations (poudrage) during video-assisted thoracic surgery (VATS) (Fig. 2). The latter can be performed via a uniportal approach. On entrance of the pleural cavity, aerosolized talc spray can be used to disperse talc particles over the pleural lining. When talc is supplied in glass containers, it can be insufflated by connecting it to suction tubing and oxygen flow at 6 L per minute. That provides very even dispersion of the talc over pleural surfaces. The chest ports should be covered with wet towels to prevent contamination of the air.

Talc slurry is achieved by instilling suspension of 4 g of talc in 50 mL of normal saline through an already existing chest tube. A local anesthetic can be added in the mixture to help reduce the ensuing pain from pleurodesis. The procedure is performed at the bedside and the patient is encouraged to roll in bed for approximately 2 hours to assist in equal distribution of the talc over pleural surfaces. Not infrequently, the patient requires conscious sedation and/or close observation in a telemetry unit during and after the procedure.

Results

In a randomized trial of 482 patients, Dresler and colleagues¹⁷ demonstrated similar efficacy of talc slurry (71%) and thorascopic talc insufflation (TTI) (77%). However, subgroup analysis showed better results in patients with primary lung or breast cancer who underwent TTI (82% vs 67%), as defined by absence of effusion recurrence on imaging 30 days after the procedure. Additionally, quality of life appeared to be better in the TTI group. Similarly, the success rate has been reported as high as 93% in a series of 614 consecutive patients

with pleural effusions who underwent thoracoscopic talc poudrage, although 11% of the patient population was excluded due to trapped lung or early death.¹⁸ The most common adverse events following talc pleurodesis include fever and pain. More serious morbidity includes respiratory failure, reexpansion pulmonary edema, hypoxia, empyema, atrial fibrillation, and even death.^{17,19} Furthermore, concerns were raised of the safety of talc regarding development of systemic inflammatory response syndrome (SIRS), acute respiratory distress syndrome (ARDS), and potential malignancy related to contamination with asbestos and particle size.²⁰ In fact, experimental animal models suggest systemic distribution of the talc after intrapleural administration.²¹ In an analysis of clinical application of graded talc (with particles <10 nm removed) and mixed talc, Maskell and colleagues²² demonstrated more SIRS and oxygen gradient in patients who received mixed. Additionally, Janssen and coauthors²³ conducted a large multicenter international study with inclusion of 558 patients with MPE. The investigators used 4 g of large-particle calibrated talc and reported no incidence of ARDS and a low rate of postoperative complications.²³

The other chemical agents that have been used in pleurodesis include hypertonic saline, silver nitrate, nitrogen mustard, and sodium hydroxide.^{24–26} However, in a meta-analysis of available literature, talc poudrage was found to be more effective in managing MPE than most other frequently used methods, including tetracycline and bleomycin.²⁷

It is necessary that apposition of visceral and parietal plurae will occur for pleurodesis to be successful. This is rarely the case with oncothorax or malignant lung entrapment. It is therefore attempted only in the rare cases in which the surgeon was able to reexpand the lung after minor dissection.

INDWELLING PLEURAL CATHETER

Indwelling tunneled pleural catheters are a therapeutic alternative to recurrent MPE, and allow intermittent drainage on an outpatient basis. In cases of lung entrapment, they provide symptom palliation by preventing reaccumulation of the effusion, and they can help achieve pleural symphysis in cases of lung reexpansion. Two systems currently exist in the United States: the PleurX catheter (CareFusion, San Diego, CA), which uses a vacuum bottle, and the Aspira pleural catheter drainage system (Bard Access Systems, Salt Lake City, UT), which uses a low-vacuum siphon pump (Fig. 3).

Technique

Tunneled pleural catheters are placed percutaneously using a Seldinger technique and under ultrasound guidance, to best identify the pleural fluid pocket/area. Even though they can be performed at the bedside, we recommend an operative and strict sterile setting with monitored anesthesia care (MAC), with the patient in a mild decubitus position. In cases in which a sufficiently large fluid pocket cannot be identified, or early resistance is met when threading the wire or the peel-away sheath, concerns regarding the intrapleural location of the catheter are raised. In these cases, we advocate placing the catheter using VATS under either MAC or general anesthesia. After placement, drainage of the fluid should be stopped when the patient has a significant cough or air is encountered in the catheter itself. An

airtight and sterile dressing is applied at the end. In cases of clogging, a solution of 10 to 20 mg tissue plasminogen activator can be instilled into the catheter to recanalize the lumen.

Results

In a randomized trial comparing indwelling pleural catheter to doxycycline pleurodesis, Putnam and colleagues²⁸ revealed excellent palliation of symptoms, a shorter median length of hospital stay (1.0 vs 6.5 days) and a lower rate of recurrence in the pleural catheter group. Another randomized trial of daily versus every other day drainage of indwelling pleural catheters in 149 patients demonstrated a higher rate of spontaneous pleurodesis (47% vs 24%) at an earlier date (54 vs 90 days), with no difference in the rate of adverse events.²⁹ Very high success rate as defined by improved dyspnea and/or quality of life has been reported by many retrospective series.^{30–32} Similarly, a randomized prospective trial by Demmy and colleagues³³ compared bedside talc slurry with indwelling pleural catheter placement. The primary endpoint was combined success defined as consistent drainage/pleurodesis, lung expansion, and 30-day survival. The investigators found that combined success was higher with indwelling catheter than with bedside talc slurry (62% vs 46%, $P = .064$), and that patients who underwent catheter placement had a better survival with effusion control at 30 days compared with the pleurodesis group ($P = .024$). However, the trial had to be terminated early because of insufficient accrual (total $n = 58$ patients).³³

A recent meta-analysis of 68 randomized trials showed that although pleurodesis is best at cessation of fluid production, indwelling pleural catheters may be better for patient-centered outcomes, particularly control of dyspnea.²⁷

Adverse events include the risk of catheter track seeding with potential for local infection, empyema and metastases, or catheter dysfunction or blockage requiring thrombolysis and even possible fracture and retained material during bedside removal.^{34,35}

Cost analysis comparing pleural catheters with pleurodesis is relatively difficult, as expenses should take into account not only the lower cost of initial catheter placement, but also later expenses related to visiting nurses and chronic drainage.³⁶ A recent analysis from the United Kingdom appears to favor indwelling pleural catheter over talc pleurodesis in patients with limited survival (<14 weeks).³⁷

Indwelling Catheter and Pleurodesis

Thoracoscopy and tunneled pleural catheters are not mutually exclusive procedures, as both can be performed to achieve pleurodesis and potentially shorten the duration of hospitalization. Pleurodesis can be performed through the catheter with talc slurry, as reported by Ahmed and colleagues.³⁸ After instillation of 4 g of talc in 50 mL of normal saline, patients underwent daily drainage of the effusion. Based on ultrasound imaging, pleurodesis was achieved in 92% of patients 3 days after the procedure. At that point, drainage was held and catheter removed after 2 weeks. Similar success was reported in another series, in which a pleural catheter was placed during medical pleuroscopy and talc poultice in 30 patients.³⁹

PLEUROPERITONEAL SHUNT

Pleuroperitoneal shunts are rarely performed in the management of MPE, because indwelling tunneled catheters became available. They can still be used in cases of lung entrapment with inadequate lung expansion. In a large series, Genc and colleagues⁴⁰ placed pleuroperitoneal shunts thor-acoscopically in 160 patients and reported a 95% successful palliation rate with 1.87% mortality and 14.8% complication rate. That included shunt occlusion requiring revision or replacement, skin erosion, and structural failure. Interestingly, tumor implants were reported at the site of insertion but not in the peritoneum.⁴⁰ Similar results were reported by other series, including tract seeding in cases of mesothelioma.^{41,42}

MANAGEMENT OF MALIGNANT LUNG ENTRAPMENT (ONCOTHORAX)

Compared with benign empyema, management of malignant lung entrapment is particularly challenging. Patients are usually more debilitated, and both the parietal and visceral pleura can be involved with tumor infiltration, not only preventing lung expansion but also impairing chest wall excursion. Besides indwelling pleural catheters and pleuroperitoneal shunts, a few other therapeutic options are available in this scenario.

PLEURECTOMY AND DECORTICATION

Whereas entrapped lung in benign diseases develops as a result of fibrotic rind over the visceral pleura, it is usually due to infiltration and thickening of the visceral pleura in malignant processes.⁴³ Thus, the plane of dissection is deeper and involves removal of the visceral pleura. This procedure is more widely accepted in the treatment of malignant mesothelioma as an alternative to extrapleural pneumonectomy.⁴⁴ It is usually of less value in the setting of metastatic pleural disease due to limited expected survival and poor patient condition from advanced malignancy and systemic effects of antitumor therapy.

Technique

A pleurectomy decortication is performed with the patient in lateral decubitus position, under general anesthesia and lung isolation. Using the VATS approach, the initial port can be placed anterior and inferior to the scapular tip, or in the fourth to fifth intercostal space in the midaxillary line, potentially away from the disease process. Digital exploration can help free adhesions and avoid parenchymal tears on first entry, and the other 2 ports are placed under direct camera vision. Alternatively, a single-port approach can be used with the 30° camera and curved instruments fitting through a 2.5-cm anterior incision in the sixth or seventh intercostal space. A wound protector is used to retract the subcutaneous and muscle tissue. Pleural fluid is initially drained and the decortication is carried in a similar fashion to an empyema. The visceral pleura is incised with endoscopic shears and carefully peeled off from the underlying trapped lung. This can be achieved using blunt dissection with a peanut dissector or the Yankauer suction tip. A thick cortex can be held with a Kocher device, and gynecologic curettes can sometimes be helpful to follow and extend the plane of dissection. Intermittent continuous positive airway pressure can be applied to the operative lung to facilitate the dissection. The goal is to allow adequate lung expansion and apposition of the

parenchyma against the chest wall. A partial or even a subtotal pleurectomy/decortication can be achieved with the VATS approach, but an extended pleurectomy decortication with removal of the diaphragm and pericardium usually necessitates a posterolateral thoracotomy, extending anteriorly and inferiorly. This is particularly true in cases of malignant mesothelioma, in which the goal of surgery is to achieve a complete macroscopic resection and improve survival in fit patients with reasonable life expectancy. The sixth rib is removed and the parietal pleura dissected in an extrapleural plane using finger blunt dissection (Fig. 4). After placement of the Finochietto chest retractor, dissection is carried to the apex with special care not to injure major vessels, and the mediastinal pleura mobilized with a peanut sponge. The diaphragm is then mobilized by freeing its insertion from the chest wall, and cautery used in the dissection plane from lateral to medial. Reconstruction of the diaphragm is performed with 2-mm-thick polytetrafluoroethylene mesh. Decortication of the visceral pleura is carried with a needle tip cautery, with care to clear the tumor burden down to the fissures. If the pleura is attached to the pericardium, the latter is excised and the ensuing defect closed with absorbable mesh. Adequate chest tube drainage is essential to ensure full expansion of the lung and avoid space problems.

Results

Benefits of visceral pleurectomy include lung reexpansion and improvement of hypoxia and ventilation perfusion mismatch. In fact, persistent lung expansion has been demonstrated by Sensakovic and colleagues,⁴⁵ where 83% of patients with mesothelioma achieved 44% increase in their lung volumes until at least 4 months after the intervention. Approximately a similar percentage of patients with mesothelioma achieved significant improvement in pulmonary function tests, especially when the diaphragm was preserved.⁴⁶ However, the impact of pleurectomy on survival was not demonstrated in the mesoVATS study, in which 175 patients with mesothelioma and pleural effusion were randomly assigned to VATS partial pleurectomy (VATS-PP) or talc pleurodesis. The overall survival at 1 year was in fact similar between the 2 groups (52% vs 57%, respectively), but surgical complications and pulmonary complications (including prolonged air leak) were significantly more prevalent in the VATS-PP group.⁴⁷

DECORTICATION WITH INTRAOPERATIVE HYPERTHERMIC CHEMOPERFUSION

Most treatment modalities of MPE and metastatic disease are palliative in nature, and do not confer a survival benefit. Intraoperative chemoperfusion represent a paradigm shift in managing these patients, and the procedure can be done in conjunction with decortication and pleurectomy if indicated. The interest for intraoperative chemotherapy was sparked by Dedrick and colleagues⁴⁸ in 1978. The rationale for local administration of chemotherapy agents is potential dose escalation with limited systemic absorption and toxicity. In fact, intrapleural cisplatin administration has been shown to be associated with lower plasma concentrations compared with the pleural cavity, even more so if a pleurectomy is performed. This is presumed to be due to the absorptive properties of the pleura.^{49,50} Furthermore, hyperthermia as high as 44°C can potentiate the cytotoxic effect of drugs,

overcome chemoresistance, and promote apoptosis of cancer cells, without causing much harm.⁵¹

Technique

At the completion of pleurectomy via VATS or thoracotomy, preparation is made for chemoperfusion. The chest is inspected to determine the degree of residual disease. Incomplete resection with presence of tumor fragments larger than 2 cm is usually considered a contraindication for intrapleural chemoperfusion. Retractors are removed and an occlusive adhesive drape is placed over the incisions. Inflow and outflow catheters are introduced through the drape and infusion of the chest with the agent (usually cisplatin diluted in saline) at a temperature of 42.0 to 45°C for 60 to 90 minutes (Fig. 5). Sodium thiosulfate can be administered intravenously to limit the systemic absorption and provide renal protection whenever cisplatin is used. In addition, urine output is maintained at 100 mL/h during chemotherapy infusion using intravenous fluids, furosemide, and/or mannitol. Patient body temperature is monitored with an esophageal temperature probe; cooling blankets and/or ice packs are used if necessary to maintain body temperature lower than 40°C. An additional temperature probe is placed into the thorax to confirm a continuous temperature of the perfusion solution. At the completion of perfusion, all fluid is suctioned out of the thorax, which is irrigated with normal saline.

Results

The effect of intraoperative hyperthermic chemoperfusion on survival has been thoroughly reported. Sugarbaker and colleagues⁵² showed a longer interval to recurrence and improved survival in 103 low-risk patients with malignant pleural mesothelioma who underwent extrapleural pneumonectomy. This modality also can be applied in lung cancer with pleural dissemination, as reported by Yi and colleagues.⁵³ The investigators used a 90-minute perfusion of 150 mg/m² of cisplatin with mannitol and thiosulphate protection at 43 to 45°C. There was statistically significant improvement of overall survival at 6 months, 1 year, and 3 years (95.7%, 91.3%, and 38.6% vs 80.0%, 80.0%, and 37.5%) and trend toward improved progression-free survival (87.0%, 47.8%, and 24.3%, vs 44.4%, 33.3%, and 0.0%). No mortality was noted in that series. Other applications of hyperthermic pleural lavage include stage IV thymoma with pleural dissemination.⁵⁴ Future technologies involve immobilizing chemotherapy agents on carrier molecules to increase the intrapleural concentration and duration of exposure, therefore reducing systemic reabsorption.^{55,56}

INTRAPLEURAL PHOTODYNAMIC THERAPY

Having a long-standing history in the treatment of endoluminal esophageal and lung cancer, photodynamic therapy (PDT) has recently been proposed for the management of pleural disease in patients with malignant mesothelioma. A light-based treatment, PDT consists of 3 components: a nontoxic porphyrin-based photosensitizing agent, oxygen, and visible light. It is believed that PDT can directly kill cancer cells, destroy the tumor neovasculature, and induce a tumor-directed immune response.⁵⁷ Because the visible light penetrates several millimeters into tissue, PDT will treat for a short depth below the surface. Encouraging results were reported by Friedberg and colleagues⁵⁸ in 38 patients with stage III/IV

mesothelioma who underwent lung-sparing pleurectomy and intraoperative PDT. The overall median survival was 31.7 months (41.2 months for epithelial type), which is superior to results reported in many surgical series, especially in patients with such advanced disease. Similarly, Chen and colleagues⁵⁹ used PDT and radical surgical resection in 18 patients with malignant pleural disease (lungs n 5 10 and thymoma n 5 8). There was no procedure-related mortality, and the 3-year and 5-year survival were as high as 68.9% and 57.4%. In a study by Chen and colleagues⁵⁹ of 51 patients who underwent intrapleural PDT for metastatic pleural disease from metastatic lung and thymic cancer, the median survival of patients with lung cancer who underwent PDT was better than those who had chemotherapy or targeted therapy (39.0 vs 17.6 months).

Although the experience with PDT in pleural disease is limited, it appears that the technology may help control residual microscopic disease after radical resection. Further work is needed to better clarify its role in clinical practice.

THE INFECTED ONCOTHORAX

Although rare, a loculated malignant effusion may become superinfected, especially if drainage interventions have been attempted. This may cause a pleural abscess and lead to severe sepsis. This situation in benign disease is normally managed by drainage and decortication; however, in malignant entrapment, the lung is unlikely to reexpand after drainage or decortication, leaving a chronic space that will be a nidus for recurrence.

Our approach to this difficult situation is to attempt closed catheter drainage and instillation of antibiotics. If this fails to resolve the ongoing infection (and the patient can tolerate surgery), it may be warranted to perform a pleurectomy for decortication with muscle flap coverage of any residual space (modified Clagett procedure).⁶⁰ In cases of MPE, any attempt at creating a permanent drainage window (Eloesser flap) may be complicated by massive drainage and skin seeding.

SUMMARY AND RECOMMENDATIONS

Development of metastatic pleural disease with trapped lung (oncothorax) is usually extremely debilitating in patients with a limited prognosis. Traditional options for free-flowing MPE, such as thoracentesis or pleurodesis, are not reasonable options because pleural apposition is necessary for development of pleural symphysis. Placement of an indwelling catheter lately has been the primary modality used in these situations. Although it does not address fluid production, it may partially palliate dyspnea and allow transition of the patient to independent home care.

There are currently new approaches available, such as pleurectomy and intraoperative hyperthermic chemoperfusion, which have been occasionally offered with curative intent. However, these procedures are complex, require significant expertise, and can be applied only to a very select group of patients with excellent performance status, controlled primary disease, established disease-free interval, and localized unilateral metastases. They should be performed preferably within the confines of clinical trials and in centers with significant expertise.

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KEY POINTS

- It is estimated that up to 30% of patients with advanced malignancy will have pleural metastasis, with lung cancer followed by breast and ovarian cancer the most common.
- The additional effect of lung entrapment causes the equivalent of a fibrothorax, indeed it is an “oncothorax.”
- The standard approach for managing these patients is to place an indwelling catheter with the hope of preventing further compression of the lung by the fluid. However, this will not allow full reexpansion of the lung in most situations.

Fig. 1.
(A) Chest radiograph and (B) computed tomography showing a chronic MPE and lung entrapment in a patient with history of metastatic ovarian cancer. Pleural thickening can be seen along with rounded atelectasis affecting all lobes and resulting in a contracted right hemithorax.

Fig. 2.
Sterile talc in aerosolized spray and powder form. (© Novatech S.A, France.)

Fig. 3.
Pleurx system, by carefusion. (*Courtesy* and © Becton, Dickinson and Company.)

Fig. 4.

The parietal pleura being mobilized away from the chest wall and the endothoracic fascia, in a patient with malignant pleural mesothelioma. (*From Rusch VW. Pleurectomy and decortication: how I teach it. Ann Thorac Surg 2017;103(5):1376; with permission.*)

Fig. 5.

The patient is connected to the extracorporeal circulation circuit to apply hyperthermic pleural chemoperfusion, with an inflow and outflow chest drain. (*From Asteriou C, Kleontas A, Barbetakis N. Recent advances in surgical techniques for multimodality treatment of malignant pleural mesothelioma. In: Firstenberg MS, editor. Principles and practice of cardiothoracic surgery. Rijekak (Croatia): Intech; 2013. p. 167–93; with permission.*)