Medical Thoracoscopic Talc Pleurodesis for Chylothorax Due to Lymphoma*

A Case Series

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Study Objectives: Recurrent chylothorax as a complication of lymphoma has had unsatisfactory outcomes. Serial thoracentesis, tube thoracostomy, and pleurodesis via chest tube have been ineffective and compromise the nutritional and immune status of the patient. Medical thoracoscopic talc pleurodesis has been safe and effective in the treatment of some other varieties of recurrent pleural effusions. Our objective was to investigate the safety and efficacy of medical thoracoscopic talc pleurodesis in the palliation of chylothorax related to lymphoma.

Design: This is a report of 24 hemithoraces treated in 19 consecutive patients with lymphoma-related chylothorax, failing chemotherapy or radiation therapy. The average patient age was 55 years.

Interventions: Medical thoracoscopy was performed under local anesthesia and conscious sedation in a bronchoscopy suite. Sedation included midazolam (mean dose, 6 mg; range, 2-14 mg) with either meperidine (mean dose, 94 mg; range 25-140 mg), or morphine (mean dose, 18 mg; range 4-40 mg). Pleurodesis was performed with insufflation of sterile asbestos-free talc, (4-8 g). After pleurodesis, chest tubes were placed, with the mean duration of chest tube placement being 4 days, range 3 to 10 days.

Results: One patient died a few days after the procedure due to causes related to the primary disease process. Follow-up was for at least 90 days following the procedure. Patients were assessed at 30, 60, and 90 days following the procedure. At each of these endpoints, all patients remaining alive were without recurrence of pleural effusions, which was confirmed by chest radiography. Eight patients in the series died of the effects of their malignancy during the 90-day evaluation interval. Complications included medication reactions in two patients (8.3%) and ARDS in one patient (4.1%).

Conclusion: Many patients with lymphoma-related chylothorax are refractory to chemotherapy and/or radiation therapy. In this group, medical thoracoscopic talc pleurodesis has an acceptable complication rate and a 100% success rate in the prevention of recurrence of pleural effusions at 30, 60, and 90 days following the procedure.

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Abbreviations: CLL=chronic lymphocytic leukemia; MCT=medium chain triglyceride

Patients with lymphoma and other malignancies metastatic to the mediastinum are occasionally troubled by dyspnea caused by recurrent accumulations of chylous pleural fluid due to extrinsic compression or invasion of the thoracic duct. These patients require frequent thoracenteses for symptomatic control of dyspnea. While treatment of the underlying disease process with either radiation therapy or chemotherapy may be of benefit, there are treatment failures, recurrences of the malignancy, and eventual resistance to these therapies.1 In these situations, more aggressive efforts are made to provide palliative symptomatic relief.

Several therapies are currently available for the treatment of recurrent chylothorax refractory to chemotherapy and radiation therapies. These include multiple thoracenteses, tube thoracostomy, gastrointestinal rest, thoracic duct ligation, pleuropertitoneal shunt, and pleurodesis via thoracostomy tube or thoracoscopy. Recurrent thoracentesis and tube tho-
ractomy with gastrointestinal rest lead to severe protein malnutrition and lymphopenia, and are ineffective as therapy for malignant chylothorax.\textsuperscript{1-3} Thoracic duct ligation is frequently difficult due to massive mediastinal lymphadenopathy and may be too aggressive in this extremely debilitated patient population.\textsuperscript{4} While pleuroperitoneal shunt placement may effectively treat dyspnea, it is contraindicated in the presence of chylous ascites, a common finding in patients with malignant chylothorax.\textsuperscript{4,5} Pleurodesis via tube thoracostomy has been attempted using multiple agents, and has been of limited effectiveness.\textsuperscript{6-9} A few small series have reported successful thoracoscopic talc pleurodesis in several etiologies of chylothorax, but they either have not reported the etiologies or have very small numbers of patients with malignant chylothorax.\textsuperscript{10-12}

Medical thoracoscopic talc pleurodesis is well tolerated and is highly effective in treatment of other etiologies of recurrent pleural effusion.\textsuperscript{13} The procedure can be done in a bronchoscopy suite with conscious sedation and local anesthesia.\textsuperscript{14} This study describes the clinical utility, efficacy, and safety of medical thoracoscopic talc pleurodesis in the management and palliation of recurrent chylothorax due to lymphoma.

**Materials and Methods**

**Procedures**

All thoracoscopic procedures were carried out with a rigid thoracoscope (Karl Storz Endoscopy America, Inc; Culver City, Calif). Pleurodesis was done via insufflation of 4 to 8 g of sterile asbestos-free talc applied through a talc atomizer.\textsuperscript{13,14} The procedures were all done in a bronchoscopy suite with routine cardiopulmonary monitoring devices and conscious sedation. Conscious sedation was induced with midazolam (mean dose, 6 mg; range, 2-14 mg) with either meperidine (mean dose, 94 mg; range, 25-140 mg) or morphine (mean dose, 18 mg; range, 4-40 mg). Supplemental oxygen was given, and arterial oxygenation was monitored by pulse oximetry. Prior to the procedure, all patients were evaluated by obtaining routine clinical data, coagulation studies, and chest radiography.

After obtaining informed consent, medical thoracoscopy was performed as reported previously.\textsuperscript{14} Local anesthesia and conscious sedation were administered, sterile preparation was completed, and access to the pleural space was obtained by blunt dissection.\textsuperscript{15} Under direct visualization, the pleural space was entered and pleural fluid within the hemithorax was removed with a suction cannula. The pleural space was examined and, if necessary, adhesions were lysed. Asbestos-free sterile talc was insufflated into the pleural space through the working channel. Talc insufflation was done under direct visualization and with directed motions of the bronchoscope to uniformly spread talc over the entirety of the pleura, requiring a total of 4-8 g of talc.\textsuperscript{13,14} Two chest tubes were used to completely drain the pleural space and maintain drainage during the scarification of the pleura. The first tube was directed posteriorly and advanced as close as possible to the apex under thoracoscopic visualization.

The thoroscope was then removed and a second tube was placed through the trocar site. The tubes were then sutured into place, connected to suction and drainage collection chambers, and dressed. The tubes were kept at ~20 cm water suction. Chest radiography, evaluation of the tube for position and air leakage, and drainage quantification occurred on a daily basis. The markers for tube removal were drainage less than 150 mL per 24 h and absence of air leak. The average duration of chest tube drainage was 4 days (range, 3-10 days). After hospital release, the patients were evaluated with chest radiography at 30, 60, and 90 days following the procedure.

**Patients**

Patients in this study had medical thoracoscopic talc pleurodesis for lymphoma-related chylothorax failing radiation and/or chemotherapy from November 1989 through January 1997. Nineteen patients were included, five of which had bilateral disease; thus, the total number of hemithoraces treated was 24. A single patient had chronic lymphocytic leukemia (CLL) and adenocarcinoma of the colon. The CLL presentation in this case was a lymphoma variant and was characterized by bulky mediastinal lymphadenopathy and chylothorax. For this reason, this patient was included in our series. The average patient age was 55 years (range, 15-75 years). Male to female ratio was 1:1. Eighteen patients had lymphoma and the remaining patient had CLL and adenocarcinoma of the colon. All patients studied had chylothorax by accepted standards,\textsuperscript{16} and all had recurrence of pleural effusion and were symptomatic with dyspnea.

**Results**

Results were judged by length of time with tube thoracostomy in place, symptom recurrence, and chest radiography at 30, 60, and 90 days following the procedure. The chest tube duration was, on average, 4 days (range, 3-10 days) and no patients had continued drainage requiring further therapies. At 30 days, 18 of 19 patients were alive, and 23 of 23 hemithoraces free of recurrence of pleural effusion as proved by chest radiography. Similarly, by the 60-day visit, two more patients had succumbed to their malignancies, and 16 patients were left in the study group. Of these, all 21 hemithoraces were without recurrence. Again, by 90 days there were 12 patients remaining alive with all 17 hemithoraces free of recurrence of pleural effusion as proved by chest radiography (Table 1). The high rate of attrition of the patients in our study group was related to their underlying malignancies. All of the patients in our study group had end stage lymphoma, refractory to multiple therapies both specifically for their chy-

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lyothoraces and in general for their malignant processes. The attrition in this group appeared to be consistent with that expected in their stage of disease.

Complications

There were three complications, two minor and one major. Two patients had minor difficulties that we believe were related to the medications used for conscious sedation; one of these two patients had medication-induced confusion that resolved quickly. The second patient with a minor medication-related complication involved a short ICU stay for hypoxemia and hypoventilation. This patient quickly responded to supportive measures, did not require intubation, and had no evidence of pulmonary edema or ARDS. The patient with a major complication developed ARDS that we believe was related to talc pleurodesis. Intubation and mechanical ventilation were instituted and the patient responded to supportive measures, was extubated on the fifth post-procedure day, and recovered without further difficulties. Finally, one patient died several days following the procedure due to causes related to the primary malignancy. No late complications of the procedure appeared in the study group during the follow-up interval. The minor complication rate was 8.3% and the major complication rate was 4.1%.

Discussion

Chylothorax is caused by malignancy in greater than 50% of cases, with lymphoma causing greater than 70% of this group.16 Other malignant causes include tumors that cause mediastinal mass effect, either primary or metastatic, disrupting or compressing the thoracic duct.5 Certain varieties of lymphoma are very responsive to chemotherapy or radiation therapy, and these options should be considered early in the disease process, after removing pleural fluid to treat symptoms.4 As reported by Roy et al,1 mediastinal radiation therapy was effective in controlling chylothorax in 68% of patients with lymphoma-related chylothorax, and in 50% of patients with other malignant processes. Two other smaller studies5,17 have found similar results, specifically in the lymphoma group, with a 50% to 100% response to chemotherapy or radiation therapy. Interestingly, two patients described had persistent problems with chylothorax reaccumulation even after effective chemotherapy had induced tumor remissions.

Repeated thoracentesis and tube thoracostomy effectively treat the dyspnea related to pleural effusion, but the continued drainage of chyle from the body quickly depletes protein stores and also significantly impacts the immune system by causing lymphopenia.2,3 It is the profound nutritional and immune compromise that occur with prolonged chyle drainage that have resulted in the reported 50% mortality associated with this process.16 In attempts to decrease the chyle flow and promote healing of the leak, gastrointestinal rest has been used with nasogastric suction to remove gastric secretions. Dietary supplementation has been undertaken either with medium chain triglycerides (MCTs) orally18 or parenteral hyperalimentation.19 Since MCTs are absorbed directly into the portal vein, they minimally increase chyle flow while effectively supplementing the diet with lipids. The MCTs are, however, not as effective as parenteral hyperalimentation, which is quickly becoming the desired method of dietary supplementation in the therapy of chylothorax.19 While either of these drainage therapies may effectively treat a traumatic chylothorax where spontaneous healing is expected in several days, neither of these procedures are good options in the patient with a malignant chylothorax.1 In one series of 35 patients with chylothorax due to malignancies, none were adequately treated by drainage via thoracostomy or repeated thoracenteses.1

Considering the relative value of chyle to the body, attempts have been made to steriley collect the vital substance and reinfuse it promptly. Some of the earliest attempts were unfortunately complicated by anaphylaxis and death,20 whereas in other cases, prolonged infusion of chyle back into the venous system has seemed to prevent the progressive nutritional and immunologic decline.21 There have been no large series evaluating this therapeutic option. Surgical or thoracoscopic ligation of the thoracic duct has been reserved in the past for cases of chylothorax unresponsive to less aggressive therapies.5,22,23 These procedures would, however, need to be planned prior to the development of nutritional or immune compromise to minimize operative risk and promote healing.2,3,24 These procedures have also been used effectively in other etiologies of chylothorax, but based on the poor operative candidacy and short life span of patients with malignant chylothorax, corrective operative management is usually not undertaken.23

Pleuroperitoneal shunting has become an option for palliation of dyspnea by decreasing pleural fluid levels while placing the fluid into the peritoneal cavity where it may be quickly absorbed, maintaining its nutritional and possibly its immunologic value.25-26 This procedure is contraindicated if chylovus ascites is concurrently present, a common finding in chylothorax due to lymphoma (up to 70% of patients in some series).4,5 Shunt occlusion also is a problem,
 occurring in approximately 10% of patients, and necessitating a second surgical procedure in this already compromised population.27

Pleurodesis has been a successful therapeutic option in many other diseases of the pleural space when performed either via tube thoracostomy or via thoracoscopy. Pleurodesis via chest tube, however, has not shown the high pleural symphysis rates in chylothorax as it has in other forms of chronic and recurrent pleural effusions. A few case reports using fibrin glue or talc slurry via chest tube report success, but other situations with tetracycline derivatives or other agents have met only with failure.6-9 Based on these problems, it is generally not suggested that pleurodesis via tube thoracostomy be attempted in chylothorax. In contrast, some significant successes have been found with thoracoscopic talc pleurodesis. Weissberg and Ben-Zeev10 reported 360 thoracoscopic talc pleurodeses, including nine patients with chylothorax, with success in seven (77%). Vargas et al11 reported a series of 22 patients, including 5 with chylothorax, of which 3 were due to lymphoma. This group had a 100% success rate with thoracoscopic talc pleurodesis. Graham et al12 reported eight patients treated exclusively with talc pleurodesis for chylothorax with 100% success rate, although four patients had requirement for thoracostomy tube for up to 12 d following the procedure for high pleural fluid outputs. Of these patients, none had lymphoma and only one was due to malignancy.12

The complications of medical thoracoscopic talc pleurodesis include medication reactions, persistent drainage, empyema, and ARDS.28 Of the previously mentioned studies, the only complications were minor, consisting of high tube output requiring 10-12 d of drainage and a single patient with empyema. No patients developed ARDS. While talc pleurodesis via tube thoracostomy has infrequently been complicated by ARDS in multiple case reports and series, it is not an insignificant complication because the mortality can be high. This complication has been much less frequent in thoracoscopic talc pleurodesis, possibly due to the lesser amount of talc used in the thoracoscopic procedure. In a recent report, Campos et al29 described ARDS in 4 of 255 patients (1.6%) treated with thoracoscopic talc pleurodesis for malignant pleural effusion, with 75% mortality. All of those patients were treated with 2 g of talc. While our incidence of this morbidity complication was 4.1%, we hope this is overestimated due to our small population.

In conclusion, medical thoracoscopic talc pleurodesis is a very effective and safe method of palliating the symptoms of recurrent pleural effusion in lymphoma-related chylothorax without causing the progressive immune and nutritional compromise caused by many of the other available therapies. As for other applications of talc pleurodesis, ARDS has been an uncommon but morbid complication. Medical thoracoscopic talc pleurodesis can be safely performed by pulmonologists in a procedure suite with local anesthesia and conscious sedation.

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