Thoracentesis in Patients With Hematologic Malignancy*

Yield and Safety

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Background: Pleural effusions occur in patients with hematologic malignancies, particularly during periods of hospitalization. Thoracentesis is often performed to diagnose infection and to exclude the presence of complicated parapneumonic effusions. The efficacy and safety of thoracentesis in this setting has not been well-studied.

Design: Retrospective chart review of hospitalized patients with hematologic malignancies undergoing thoracentesis. The aim of this study was to assess the role of thoracentesis in establishing a diagnosis of infection in this population and to determine the risk of complications.

Results: A total of 100 thoracentesis findings were analyzed in patients with lymphoma (52 patients) and leukemia (27 patients), and in patients who had undergone bone marrow or stem cell transplantation (21 patients). The indication for performing thoracentesis was to exclude infection in 69% of cases. Fever was present in 59% of the patients, and a concomitant lung parenchymal abnormality was present in 69% of cases. Effusions were moderate to large in size (87% of cases), and were both bilateral (62%) and unilateral (38%). Exudates were documented in 83% of the cases. A specific diagnosis was found in 21 patients and was more frequently established in those with lymphoma (31%) compared to the other groups of patients. Diagnoses found included malignancy in 14 cases, chyloous effusions in 6 cases, and infection in 1 case. The one patient in whom empyema was found required drainage. The criteria for a parapneumonic effusion were not found in any other patients. The complication rate of 9% (pneumothorax, seven patients; hemothorax, two patients) was comparable to that in other populations of patients.

Conclusions: Despite a high propensity for developing pulmonary infections, hospitalized patients with hematologic malignancies rarely developed complex parapneumonic effusions. The etiology of many of the effusions that occurred in this setting was unclear.

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Key words: cancer; empyema; pleural effusions; thoracentesis

Abbreviation: LDH = lactate dehydrogenase

Pleural effusions, either as isolated entities or associated with parenchymal lung abnormalities, occur regularly in patients with hematologic malignancies.1 The etiology of these effusions include pleural involvement by malignancy, chyloous effusion secondary to lymphatic obstruction, infection, radiation or chemotherapy effects, heart failure, and fluid overload. Hospitalized patients often require frequent transfusions and therapy with IV antibiotics, making states of fluid overload common. The presence of a pleural effusion in a patient with a hematologic malignancy always presents a diagnostic challenge, and, unless the effusion is very small, thoracentesis is typically considered. If fever is present, thoracentesis is usually performed to exclude infection and a complicated parapneumonic effusion or empyema. Performing a thoracentesis may carry an increased risk for some patients with hematologic malignancies because of coagulation abnormalities and multiple medical comorbidities. The data that have been published on the ability of thoracentesis to identify infections or on its safety in this population are sparse. In a report2 on children with cancer and neutropenia, an evaluation of pleural fluid during febrile episodes in 22 patients found infection in 2 patients (9%), both of which were fungal infections. Therapy was changed in both cases, and the procedures were performed with no

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complications. There are also a few reports of the identification of unusual infections in the pleural space in this population. We reviewed the outcomes of thoracenteses that were performed in hospitalized patients with hematologic malignancies to clarify the role of this procedure in the diagnosis of infection and to determine its complication rate.

**Materials and Methods**

We retrospectively reviewed all findings from thoracenteses performed on patients with hematologic malignancies who were hospitalized at Memorial Sloan Kettering Cancer Center from September 1, 1998, to December 31, 2001, as identified from a search of the electronic record. This study was approved by the Institutional Review Board of Memorial Sloan Kettering Cancer Center.

The patients included in the study were those with lymphoma, leukemia, multiple myeloma, and amyloidosis, and those who had undergone bone marrow or stem cell transplantation. For purposes of analysis, patients were placed into the following three groups: (1) lymphoma patients; (2) leukemia patients, including those with multiple myeloma and amyloidosis; and (3) patients who had undergone bone marrow or stem cell transplantation. All patients had received a diagnosis of a hematologic malignancy at the time of the thoracentesis, and this procedure was not the basis of the diagnosis. The decisions about whether to perform a thoracentesis and about the side on which to perform thoracentesis in those with bilateral effusions were made by the clinician caring for the patients.

Each chart was retrospectively abstracted for age, sex, hematologic diagnosis, radiographic characteristic of effusion, other radiographic abnormalities, clinical symptoms, indication for thoracentesis, laboratory data at the time of the procedure, blood products administered prior to thoracentesis, pleural fluid analysis, complications, results of the procedure, and outcome of the effusions at the time of hospital discharge. The size of the effusion was characterized, as described on the radiographic study prethoracentesis record, as being small, moderate, or large. The presence of an exudate or transudate was determined by the pleural fluid analysis showing a polymorphonuclear-predominant exudate and an infectious agent isolated from respiratory tract specimens. The data were expressed as the mean ± SD.

**Results**

**Patients**

A total of 110 patients were identified who had undergone thoracentesis during the study period. Ten patients were excluded from the study because no analysis of pleural fluid had been performed. The remaining 100 patients were the subjects of this study, and all had had at least a bacterial culture of pleural fluid performed. There were 55 men and 45 women, and the mean age was 55 ± 21 years. Lymphoma was present in 52% of patients, including 46 with non-Hodgkin lymphoma and 6 with Hodgkin disease. The leukemia/other group contained 27% of the cases, including those with acute myeloid leukemia (9 patients), multiple myeloma (7 patients), chronic lymphocytic leukemia (6 patients), acute lymphocytic leukemia (2 patients), chronic myelogenous leukemia (1 patient), and amyloidosis (2 patients). Bone marrow or stem cell transplants had been performed in 21% of patients, including 14 autologous transplants and 7 autologous transplants.

A total of 81 of the patients had received chemotherapy prior to the occurrence of the pleural effusion, including 38 patients with lymphoma and 22 with leukemia, and all 21 patients who had received transplants. The thoracentesis occurred from 2 weeks to 3.3 years after they had undergone transplantation.

At the time of the thoracentesis, neutropenia (ie, absolute neutrophil count, < 1,000 cells/µL) was present in 11 patients, a platelet count of < 50,000 cells/µL in 13 patients, and coagulopathy with prothrombin time of > 15 s and/or a partially activated thromboplastin time of > 40 s in 14 patients.

**Thoracentesis**

The main indication for performing thoracentesis was to rule out infection in 69% of cases, relieve dyspnea in 23% of cases, and restage/document cancer in 8% of cases. Most patients were symptomatic. Fever was present in 59% of cases, dyspnea in 74% of cases, and chest pain in 21% of cases. A coexisting pulmonary infiltrate or nodule/mass was present in 69% of the patients. Ultrasound localization was used in 32% of all cases.

Characteristics of the effusions are given in Table 1. They were most frequently moderate to large in size (87%), bilateral (62%), and exudative (83%). There were no significant differences in these characteristics among the three groups of patients. In the two effusions with a pleural fluid pH of < 7.2 and/or a glucose level of < 60 mg/dL, one was related to infection and the other to malignancy. A sample of pleural fluid was sent for bacterial culture in all 100 cases, fungal culture in 94 cases, and mycobacterial culture in 92 cases. Specimens from 99 cases were sent for cytologic analysis for cancer.
Diagnostic Yield

A specific diagnosis was made in 21% of cases (Table 2). A diagnosis was established more frequently in patients with lymphoma compared to the other groups of patients (31%). Infection was identified in only one patient who had empyema. No other effusion met all of the criteria for a parapneumonic effusion. A total of 13 patients had fever with a new infiltrate and an ipsilateral effusion, but a neutrophil-predominant effusion was documented in only three of these patients, and none had a pleural fluid or a respiratory tract culture that was positive for an organism. Another 2 of the 13 patients did not have a pleural fluid cell count performed, and, additionally, all cultures were negative for an organism. The remaining eight patients had lymphocyte-predominant or monocyte-predominant effusions.

The one patient with an empyema was a 70-year-old woman with multiple myeloma that had been treated with corticosteroids. She presented with fever, dyspnea, and chest pain. The chest radiograph showed a left lower infiltrate and small unilateral effusion. She was started on therapy with antibiotics and antifungal agents. Infiltrates progressed, and the fever persisted. She underwent catheter drainage of a persistent loculated effusion, which revealed purulent fluid. The pleural fluid pH was 7.19, the glucose level was 4 g/dL, and the serum LDH level was 8,364 U. Gram-positive cocci were present on the Gram stain, and the culture was positive for penicillin-resistant Streptococcus pneumoniae. Vancomycin was added to therapy after the thoracentesis, and the patient’s condition improved with the resolution of the infiltrates and effusion.

Complications

Prior to the pleural fluid tap, platelet transfusions were performed in 18% of cases, and fresh-frozen plasma was administered in 7% of cases. Complications are shown in Table 3. Despite a concern for
bleeding due to thrombocytopenia and coagulation defects, complications related to bleeding occurred in only two cases in which a hemothorax occurred. In both of these cases, platelet counts and coagulation study findings were normal, but one patient had an elevated creatinine level of 2.0 mg/dL. All complications were successfully treated.

Outcome

At the time of hospital discharge, 22 patients who had undergone thoracentesis had died. None of the deaths were directly related to the presence of the pleural effusion or thoracentesis, and deaths were due to the progression of cancer, organ system failures, or sepsis. Of the remaining 78 patients who had been discharged from the hospital, outcomes could not be determined in 10 patients because of inadequate follow-up. In 62 patients, the effusion resolved or markedly improved spontaneously or with treatment, including antibiotics, diuretics, and chemotherapy. Six patients required pleurodesis for management of the effusion.

Discussion

Pleural effusions occur regularly during the hospitalization of patients with hematologic malignancies, and thoracentesis is frequently performed. Most of the effusions in which a thoracentesis was undertaken were moderate to large in size (87%) and were associated with parenchymal pulmonary abnormalities (69%). Both bilateral effusions (62%) and unilateral effusions (38%) were subject to thoracentesis. Although fluid overload, cardiac dysfunction, and hypoalbuminemia were a concern in this population, only 10% of the effusions that had been analyzed using thoracentesis were documented to be transudates. Exudates were documented in 83% of patients, and 7% were unclassified because of a lack of data. A specific etiology for the effusions was identified in only 21 patients, with 20 effusions due to malignancy or chylos effusions, while 1 effusion was due to infection. The yield for a malignant or chylos effusion was highest in patients with lymphoma (yield, 31%) compared to the other patient groups. This higher yield is not unexpected since, among the hematologic malignancies, lymphomas have been most commonly associated with the development of malignant effusions.1 In patients with Hodgkin lymphoma and non-Hodgkin lymphoma, pleural involvement due to the underlying disease is seen in up to 20 to 30% of patients, while malignant involvement is much less common in patients with the acute and chronic leukemias.1

The most common reason to perform thoracentesis was to identify an infection and exclude a complicated parapneumonic effusion (69%). Documented infection was unusual, with only one case (1%) of empyema reported. A total of 13 other patients had fever and a new infiltrate with an ipsilateral pleural effusion, but in only 3 of these patients was a neutrophil-predominant effusion found. Given the high risk of pulmonary infection in this population, and the significant immunosuppression from the underlying disease or treatments given, it is somewhat surprising how infrequently parapneumonic effusions were documented. Studies of thoracentesis in ICU patients have shown a higher incidence of parapneumonic effusions and empyema. One study7 of 82 patients in a medical ICU in whom a thoracentesis was performed found empyema in 17% of patients and parapneumonic effusions in 26% of patients. Another study8 of 100 consecutive medical ICU patients found an uncomplicated parapneumonic effusion in 23% of patients, but empyema in only 1 patient.

The reason for the infrequency of infection is not known, but we think that it is likely that the very early institution of therapy with antibiotics in patients with hematologic malignancies sterilizes the pleural fluid early and also decreases the likelihood of obtaining positive sputum or other respiratory specimens. Additionally, in these immunosuppressed patients, inflammatory cells such as neutrophils may be less likely to be recruited to the pleural space,

Table 3—Complications of Thoracentesis

<table>
<thead>
<tr>
<th>Complications</th>
<th>All Patients</th>
<th>Lymphoma Group</th>
<th>Leukemia Group</th>
<th>Post Transplant Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effusions</td>
<td>100 (100)</td>
<td>52 (100)</td>
<td>27 (100)</td>
<td>21 (100)</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>7 (7)</td>
<td>5 (10)</td>
<td>1 (4)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Hemothorax</td>
<td>2 (2)</td>
<td>1 (2)</td>
<td>1 (4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Required chest tube</td>
<td>4 (4)</td>
<td>2 (4)</td>
<td>1 (4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Total complications</td>
<td>9 (9)</td>
<td>6 (12)</td>
<td>2 (8)</td>
<td>1 (5)</td>
</tr>
</tbody>
</table>
resulting in fewer neutrophil-predominant effusions, and possibly in less fibrin deposition and pleural loculation with the resultant complicated parapneumonic effusions. It would be helpful to have the results of additional studies of the yield of thoracentesis for infection in this patient population from other centers to further assess the applicability of our findings.

At the time of discharge from the hospital, only 6% of patients required pleurodesis for the management of their effusions, while effusions in 62% of patients resolved or significantly improved, even though a diagnosis was not established. Most effusions due to the hematologic malignancy itself will respond to therapeutic agents for the underlying disease.1,9

Our hospitalized patients needing thoracentesis appeared to represent a group with a poor prognosis, as 22% of this group died during the hospitalization in which the procedure was performed. The deaths were not directly related to the effects of the effusion or the thoracentesis but were probably a marker for the seriousness of the underlying disease.

The etiology of many of the effusions remains unknown. They may represent parapneumonic effusion that could not be diagnosed using the standard criteria. Studies in animals10–12 have shown that following acute lung injury lung edema with increased permeability and high-protein pleural effusions can occur. It is possible that noninfectious lung injury in the immunocompromised host can contribute to the development of bilateral exudative effusions.

The complications of thoracentesis in our patients were consistent with the rates reported in other nonimmunocompromised patients. We found that 7% of patients had a pneumothorax and 2% had a hemothorax, with tube thoracostomy required in 4% of patients. Pneumothorax is reported to occur in 8 to 12% of patients undergoing the procedure.13,14

Bleeding was of concern in only two patients without a specific diagnosis was made in only 21% of cases. Almost all of the diagnoses were related to malignancy. Infection was rarely documented, and the results of the thoracenteses led to a change in treatment for infection in only one case. Although this population of patients has a high incidence of pulmonary infection, our results suggest that complicated pleural effusions are uncommon. Studies are needed to assess the reasons for the development of effusions in this population and to determine better criteria for the need for diagnostic thoracentesis.

**Conclusions**

In 100 consecutive thoracenteses performed in hospitalized patients with hematologic malignancies, a specific diagnosis was made in only 21% of cases.