Percutaneous Image-Guided Cutting Needle Biopsy of the Pleura in the Diagnosis of Malignant Mesothelioma*

Rosie F. Adams, BM BCh; Winifred Gray, MB BS; Robert J. O. Davies, DM; and Fergus V. Gleeson, MB BS

Study objectives: Pleural fluid cytology and non–image-guided Abrams or Cope biopsies have sensitivities of approximately 30% for detecting malignant mesothelioma, and thoracoscopic biopsy has a sensitivity of approximately 90%. The difference between these two probably relates to obtaining adequate tissue. The use of immunohistochemical stains allows a firm diagnosis to be made from relatively small samples. This study explores whether percutaneous image-guided cutting needle biopsy (CNB) combined with immunohistochemistry is accurate in diagnosing pleural thickening due to mesothelioma.

Design: Retrospective review of image-guided CNB of pleural thickening performed on consecutive patients over 7 years by a single radiologist.

Setting: Teaching hospital chest radiology department.

Patients: Twenty-one adult patients with a final diagnosis of malignant mesothelioma were identified from 53 consecutive patients who underwent percutaneous image-guided CNB. All 21 patients had pleural thickening identified on contrast-enhanced CT, and all had a final histologic diagnosis of mesothelioma confirmed by postmortem examination or thoracoscopy.

Interventions: Fourteen-gauge and 18-gauge cutting needles were used. Biopsy guidance was by ultrasound in 6 patients and by CT in 15 patients.

Measurements and results: A correct histologic diagnosis of malignant mesothelioma was made by CNB in 18 patients (86% sensitivity and 100% specificity). Complications included one chest wall hematoma and a small hemoptysis. Four patients with a pleural thickness of ≤ 5 mm underwent biopsy, and all specimens were diagnostic for mesothelioma.

Conclusions: Image-guided percutaneous CNB of pleural thickening is a safe procedure, with 86% sensitivity for detecting malignant mesothelioma. Pleural thickening of ≤ 5 mm may be successfully sampled.

(CHEST 2001; 120:1798–1802)

Key words: biopsy; CT; image guidance; mesothelioma; ultrasound

Abbreviations: CNB = cutting needle biopsy; EMA = epithelial membrane antigen; FNA = fine-needle aspiration

Most cases of mesothelioma are caused by occupational asbestos exposure. The peak industrial use of asbestos was in the 1960s and 1970s in Western Europe but several decades earlier in the United States. Hence, while the incidence of mesothelioma has just reached its peak in the United States, the incidence of malignant mesothelioma in Western Europe is forecast to almost double over the next 2 decades. It has been predicted that malignant mesothelioma will kill almost 1 in 150 western European men born between 1945 and 1950.2

Clinicoradiologic suspicion of malignant mesothelioma can be difficult to confirm cytohistologically. The radiologic manifestations tend to be those of pleural effusion and/or pleural thickening. Pleural effusions are initially investigated by thoracentesis. A positive diagnosis by pleural fluid cytology has been reported as low (26%).3,4 Although in centers where the incidence of mesothelioma is high, this may rise to 76%.5 Pleural biopsy in the presence of a pleural effusion has traditionally been performed using a reverse bevel needle, such as Abrams or Cope needles, without image guidance, with a sensitivity of 21 to 43% for the detection of malignant mesothelioma.3,4 In many patients in whom malignant pleural...
thickening is suspected, with nondiagnostic pleural fluid cytology and Abrams or Cope biopsies, the investigator often proceeds straight to thoracoscopic biopsy. Thoracoscopic biopsy has a sensitivity of 91 to 98% in detecting malignant pleural disease, including mesothelioma, but is an expensive and invasive procedure. The purpose of this study was to examine the accuracy of image-guided, pleural cutting needle biopsy (CNB) in the diagnosis of malignant mesothelioma.

Materials and Methods

We identified 53 consecutive patients with pleural thickening demonstrated on contrast-enhanced CT, who had been referred for image-guided pleural CNB. The patients were identified from radiology department biopsy records. The biopsies were performed over a 7-year period at a single teaching hospital with a referral population of 550,000. The case notes and radiology and histology reports of this group of patients were reviewed to ascertain the final diagnosis of each patient. Twenty patients received a final diagnosis of nonmesothelial malignant pleural disease; 12 patients received a final diagnosis of benign pleural disease; and 21 patients received a final diagnosis of malignant mesothelioma.

All patients included in the study had another form of histologic confirmation of the diagnosis of malignant mesothelioma in addition to the CNB result. Mesothelioma was confirmed by immunohistochemistry, and the patient previously showing only inflammatory changes and no evidence of malignancy. In one of these cases, thoracoscopic biopsy performed 3 months prior to CNB had also shown only inflammatory changes and no evidence of malignancy; in the other case, biopsy could not be performed due to technical factors.

The CNB specimens were processed routinely in the laboratory, and comprised one or two cylinders of tissue up to 1.8 cm in length. The amount of tissue generally sufficed to provide routine hematoxylin-eosin stains on a set of three levels, with Alcian blue/periodic acid-Schiff staining. Spare sections for immunostaining were cut at the same time. A panel of antibodies (cytokeratin cocktail, epithelial membrane antigen [EMA], carcinoembryonic antigen, and Ber EP4, with the additional use of cytokeratin 5/6 and thrombomodulin) was applied for distinguishing metastatic carcinoma from mesothelioma and reactive mesothelial proliferation. The FNAs and CNBs were reported independently of each other. The CNBs were reported by a single pulmonary histopathologist.

Results

The results are summarized in Table 1. There were 19 men and 2 women (age range, 47 to 84 years; median, 65 years). The mode of biopsy guidance was by CT in 15 patients and by ultrasound in 6 patients. The size of automated cutting needle used was 18 gauge in 16 patients, 14 gauge in 3 patients, and both 18 gauge and 14 gauge in 2 patients. There were a total of 31 cutting needle passes and 20 FNA passes, giving an average of 2.4 passes per patient (1.5 cutting needle passes per patient).

Complications comprised a small hemoptysis after biopsy under CT guidance, and one chest wall hematoma after biopsy performed under ultrasound guidance. These complications did not require active management.

Mesothelioma was correctly diagnosed by CNB histology in 18 of the 21 cases (sensitivity of 86% and specificity of 100%). CNB was nondiagnostic in two cases; adequate specimens were obtained that showed fibrosis and chronic inflammation but no malignancy. In one of these cases, thoracoscopic biopsy performed 3 months prior to CNB had also shown only inflammatory changes and no evidence of malignancy; in the other case, biopsy could not be performed at thoracoscopy due to technical factors. A third case of postmortem examination-proven mesothelioma was considered more likely to be carcinoma on the basis of the CNB histology and immunohistochemistry, and the patient previously underwent two thoracoscopic biopsies showing no malignancy. Four patients with CNB diagnostic of mesothelioma had thoracoscopic biopsies, of which only two biopsies were diagnostic. In total, seven patients underwent thoracoscopy and attempted biopsy either before (three patients) or after (four patients) CNB. No patients underwent closed pleural biopsy.
The range of pleural thickness at the biopsy site was 0.3 to 10.0 cm (median, 1.5 cm). The thickness of pleura at the biopsy site of the two nondiagnostic biopsies was 1.5 cm and 3.0 cm, respectively. Four patients had a pleural thickness of 0.5 cm at the site of biopsy, and all of these CNBs were diagnostic. The largest core lengths obtained in each of these four patients were 0.8 cm, 1.0 cm, 1.0 cm, and 1.5 cm, respectively. Fourteen of the 21 patients had a pleural effusion at the time of biopsy. Of the 17 patients with mesothelioma who underwent FNA, the FNA cytology was diagnostic in 2 patients, suggestive of mesothelioma in 7 patients, diagnostic of carcinoma in 1 patient, showed atypical mesothelial cells in 2 patients, and nondiagnostic in 5 patients. The addition of FNA to the CNB episode in the three undiagnosed cases of mesothelioma on CNB had no effect on the diagnostic outcome. In all patients with a pleural effusion, pleural fluid cytology was nondiagnostic.

**DISCUSSION**

Around the world, the incidence of malignant mesothelioma has either risen to a peak or will continue to rise for the next few decades, depending on the pattern of asbestos use in that region. Although there is no current curative treatment for malignant mesothelioma, it is an important diagnosis to make for prognostic reasons and palliative treatment.

Both pleural fluid cytology and nonguided hook needle biopsy have low sensitivities for diagnosing malignant mesothelioma, and require the presence of a pleural effusion. Abrams or Cope needle pleural biopsies may be complicated by pneumothorax, vasovagal syncope, hemothorax, biopsy site hematoma, and ipsilateral shoulder pain.9–11 FNA of the pleura is also poor at detecting mesothelioma; 53% of FNAs in our study were diagnostic or suggestive of mesothelioma, similar to the 58% sensitivity of Sterrett et al,12 but only conclusively diagnostic of mesothelioma in 12%. Thoracoscopy is frequently used to establish a diagnosis of malignant mesothelioma because it produces large, visually guided biopsy samples. Its sensitivity for malignant disease is about 90%.7,8 However, the financial cost of this examination is high because it requires an operator, an assistant, operating theater space, an anesthetist (for thoracoscopy performed under general anesthetic), and because the patient is usually in the hospital for at least 24 h. Complication rates from thoracoscopy are usually low,7,13,14 although rates as high as 15% have been reported.15 The demonstration that CNB of the pleura is capable of yielding a secure diagnosis in the majority of subjects from a day-case procedure performed by one operator and with few complica-

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Maximum Pleural Thickness, mm</th>
<th>Pleural Fluid Present</th>
<th>Pleural Fluid Cytology</th>
<th>Pleural FNA Cytology</th>
<th>Pleural CNB Histology</th>
<th>Thoracoscopic Biopsy Histology</th>
<th>How Final Diagnosis Confirmed</th>
<th>PM Histology</th>
<th>Diagnostic for Mesothelioma</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>No</td>
<td>NA</td>
<td>Yes</td>
<td>Yes</td>
<td>NP</td>
<td>PM</td>
<td>PM elsewhere</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>100</td>
<td>No</td>
<td>NA</td>
<td>Yes</td>
<td>Yes</td>
<td>NP</td>
<td>PM</td>
<td>PM elsewhere</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>25</td>
<td>No</td>
<td>NA</td>
<td>NP</td>
<td>Yes</td>
<td>NP</td>
<td>PM</td>
<td>PM elsewhere</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>12</td>
<td>No</td>
<td>NA</td>
<td>NP</td>
<td>Yes</td>
<td>NP</td>
<td>PM</td>
<td>PM elsewhere</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>15</td>
<td>No</td>
<td>NA</td>
<td>Atypia</td>
<td>No</td>
<td>Biopsy failed</td>
<td>PM</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>20</td>
<td>No</td>
<td>NA</td>
<td>Carcinoma</td>
<td>Carcinoma</td>
<td>No, 20/12 before</td>
<td>PM</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>70</td>
<td>No</td>
<td>NA</td>
<td>?</td>
<td>Yes</td>
<td>NP</td>
<td>PM</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>25</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>NP</td>
<td>PM</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>14</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>NP</td>
<td>PM</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>40</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes, Pleurodesis</td>
<td>NA</td>
<td>PM</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>10</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes, 4/12 before</td>
<td>PM</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>3</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes, 3/12 before</td>
<td>PM</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>40</td>
<td>Yes</td>
<td>No</td>
<td>?</td>
<td>Yes</td>
<td>NP</td>
<td>PM</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>15</td>
<td>Yes</td>
<td>No</td>
<td>?</td>
<td>Yes</td>
<td>NP</td>
<td>PM</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>20</td>
<td>Yes</td>
<td>No</td>
<td>?</td>
<td>Yes</td>
<td>NP</td>
<td>PM</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>5</td>
<td>Yes</td>
<td>No</td>
<td>?</td>
<td>Yes</td>
<td>NP</td>
<td>PM</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>5</td>
<td>Yes</td>
<td>No</td>
<td>?</td>
<td>Yes</td>
<td>No</td>
<td>PM</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>20</td>
<td>Yes</td>
<td>No</td>
<td>?</td>
<td>Yes</td>
<td>NA, Thoracoscopic biopsy</td>
<td>PM</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>7</td>
<td>Yes</td>
<td>No</td>
<td>Atypia</td>
<td>Yes</td>
<td>NP</td>
<td>PM</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>10</td>
<td>Yes</td>
<td>No</td>
<td>NP</td>
<td>Yes</td>
<td>NP</td>
<td>PM</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>5</td>
<td>Yes</td>
<td>No</td>
<td>NP</td>
<td>Yes</td>
<td>No, 2/52 before</td>
<td>PM</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

*? = suspicious for mesothelioma; NA = not applicable; NP = not performed; PM = postmortem.
tions suggests it may have substantial advantages over thoracoscopy in this setting.

The use of immunostaining allows a secure diagnosis of mesothelioma to be made from a relatively small tissue sample, as provided by a CNB. Immunostaining for confirmation of mesothelioma involves the use of a panel of antibodies that exclude metastatic carcinoma and, to a lesser extent, confirm mesothelioma. Carcinoma markers used in these cases include carcinoembryonic antigen, Ber EP4, and EMA with cytoplasmic staining. Ber EP4 has activity similar to Leu M1 and B72.3, and also to AUA 1. Confirmatory stains for mesothelioma include calretinin, cytokeratin 5/6, and thrombomodulin. Vimentin findings are usually positive but nonspecific, so it is not included in our regular panel. EMA frequently gives a delicate membranous staining of mesothelioma cells that differs from the diffuse cytoplasmic staining seen in metastatic carcinoma. No one single immunostain is entirely conclusive either for mesothelioma or metastatic carcinoma, hence the need for applying a panel of markers in all cases.

Pleural thickening, whether benign or malignant, is frequently not uniform, and image-guided biopsy facilitates selection of the most appropriate biopsy site (Fig 1). Image guidance also enables biopsies to be performed safely in the absence of a pleural effusion. There have been several reports over the years indicating the diagnostic efficacy of percutaneous image-guided CNB of the pleura, with diagnostic sensitivities for detecting all types of malignant pleural disease of 70 to 83% and were performed under CT guidance or ultrasound guidance. There has only been one report on the value of image-guided CNB in the diagnosis of mesothelioma: Heilo et al did not address the degree of pleural thickness required for biopsy nor its value in the presence or absence of a pleural effusion, and ultrasound was the only image guidance used. The authors reported a minor complication rate of 3% in 70 patients, and 52 patients had a final diagnosis of malignant mesothelioma, with 77% sensitivity at the first biopsy attempt, and no false-positive results. Metintas et al described CT-guided closed pleural biopsy (using Cope, Ramel, or Abrams needles) in 30 patients with a final diagnosis of mesothelioma with a sensitivity of 83% and a specificity of 100% in diagnosing mesothelioma.

In our study, we achieved 86% sensitivity and 100% specificity for detecting mesothelioma by image-guided CNB in 21 patients. Our report suggests that image-guided pleural CNB of pleural thickening is an accurate and safe procedure that can be performed in the presence or absence of a pleural effusion. In addition, by performing the biopsy along the line of the pleura rather than tangentially, a pleural thickness ≤5 mm may be safely and accurately sampled (Fig 2), and may continue to provide cores for histologic diagnosis, with a similar sensitivity to thoracoscopy.

Tumor seeding down needle, chest drain, or surgical tracks for malignant mesothelioma occur in approximately 20% of patients. Consequently, all patients in our center with a diagnosis of malignant mesothelioma are offered local radiotherapy to reduce the chance of tumor seeding down biopsy or thoracoscopy tracks. Nevertheless, a test likely to produce a diagnosis with the minimum number of pleural passes is desirable. The poor sensitivity of blind Cope or Abrams biopsies for detecting mesothelioma makes these procedures difficult to justify in such patients when image-guided pleural CNB could be performed. We propose that in

**Figure 1.** Contrast-enhanced chest CT showing a large solitary pleural nodule (arrow) that was hidden on chest radiographs by a large pleural effusion (E). Mesothelioma was diagnosed from the CT-guided CNB.

**Figure 2.** Contrast-enhanced chest CT showing CNB performed along the line of the pleura in a patient with pleural thickening up to 0.5 cm. Two cores of 1.5 cm were obtained that provided a diagnosis of mesothelioma.
patients with suspected malignant mesothelioma, and pleural thickening identified on contrast-enhanced CT, image-guided pleural CNB may be the optimal investigation.

References