The Role of Closed Pleural Needle Biopsy in the Diagnosis of Malignant Mesothelioma of the Pleura*


Malignant mesothelioma of the pleura is a disease that requires a biopsy procedure for a definitive diagnosis. In the past, closed pleural needle biopsy (CPNB) has given poor yields due to the small amount of tissue obtained, and the patient has subsequently been subjected to a diagnostic thoracotomy. In recent years, the availability of more accurate histopathologic tests have enabled the pathologist to make a diagnosis more easily on samples obtained at CPNB. In this retrospective study of 20 consecutive cases of malignant mesothelioma of the pleura diagnosed between 1980 and 1990, we found that a blind CPNB was diagnostic in five of seven procedures and CT-guided CPNB was diagnostic in five of six procedures. An open pleural biopsy (OPB) was diagnostic in ten of ten procedures performed. There were no complications associated with any of the CPNB procedures. We conclude that CPNB is a safe and effective manner of diagnosing malignant mesothelioma of the pleura, and should be attempted prior to OPB.

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CEA = carcinoembryonic antigen; CPNB = closed pleural needle biopsy; OPB = open pleural biopsy

Closed Pleural Needle Biopsy in Malignant Mesothelioma (Beauchamp et al)

The incidence of malignant mesothelioma is increasing1 and consequently the need to diagnose more cases accurately can be appreciated. Establishing a diagnosis of malignant mesothelioma of the pleura frequently requires large amounts of pleural tissue. In many cases, a thoracotomy is necessary, but this procedure may spread the tumor into the chest wall2 and cause chronic intractable pain.3 In addition, open pleural biopsy (OPB) requires general anesthesia with its associated complications and use of an operating room.

A diagnosis made with use of closed pleural needle biopsy (CPNB) may eliminate the need for a diagnostic thoracotomy. In the past, CPNB has not been considered a good diagnostic technique. Recently available histopathologic tests, however, may have improved its diagnostic yield. To address this possibility, we retrospectively studied the effectiveness of CPNB in the diagnosis of malignant mesothelioma of the pleura.

METHODS

We reviewed the records of 20 consecutive patients with a histopathologic diagnosis of malignant mesothelioma of the pleura made at St. Elizabeth’s Hospital and Quigley Memorial Hospital, Boston, from 1980 to 1990 for documentation of age and sex, diagnostic procedure performed, and staining methods used in making the pathologic diagnosis.

Twelve patients initially underwent either a blind CPNB with use of an Abram’s needle (seven patients), or a CT-guided CPNB using a 19-gauge Greene needle (five patients). One of the patients undergoing a blind CPNB subsequently had a CT-guided CPNB. Eight patients had an OPB initially. One patient had a blind CPNB and one had a CT-guided CPNB before an OPB.

The biopsy material was subjected to extensive histologic evaluation and histochemical examinations using various stains, including colloidal iron, alcian blue, and periodic acid-Schiff (PAS) with and without diastase.

Immunohistochemical studies were performed using a polyclonal antibody to carcinoembryogenic antigen (CEA), a mixed high and low molecular weight pan keratin antibody, and a monoclonal antibody to vimentin. All antibodies were obtained from one company (Signet Laboratories, Inc, Dedham, Mass).

Differences between groups were compared with the use of a Student’s t test.

RESULTS

Nineteen men and one woman were included in the study. The age at diagnosis ranged from 54 to 82 years (mean, 67.5 years). Of the 20 cases of malignant mesotheliomas of the pleura, ten were epithelial, four were sarcomatous, and six were mixed. Of the seven patients who underwent blindly directed CPNB, a histologic diagnosis of malignant mesothelioma of the pleura was made in five (71 percent). Of the six patients who had a CT-guided CPNB (one of whom had previously had a negative blind CPNB), a histologic diagnosis of malignant mesothelioma of the pleura was made in five (83 percent). Therefore, 13 CPNBs were performed in 12 patients and ten (77 percent) of the 13 were diagnostic. Two patients (17 percent) whose conditions were not diagnosed with use of CPNB had OPB. There were no pneumothoraces, hemotheraces, or infectious complications due to CPNB. An OPB was performed in ten patients, one of whom had previously had a nondiagnostic blind CPNB and one who had had a nondiagnostic CT-guided CPNB. OPB yielded a diagnosis of malignant mesothelioma of the pleura in all ten patients.

Eight (40 percent) of the 20 biopsy specimens were subjected to alcian blue staining with positive results in all cases (Table 1). One specimen stained positive

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to PAS, but after pretreatment with diastase and reexposure to PAS, it stained negative. Three (14 percent) of the 20 biopsy specimens were subjected to colloidal iron assessment, two of which stained positive. One specimen was subjected to vimentin and did not stain. Sixteen (80 percent) of the 20 biopsy specimens (nine from CPNB and seven from OPB) were subjected to keratin antibodies and all reacted positively. Seventeen (85 percent) of the 20 biopsy specimens (nine from CPNB and eight from OPB) were subjected to CEA antibodies and all reacted negatively.

**DISCUSSION**

There is no single pathognomonic diagnostic test for malignant mesothelioma. Diagnosis of malignant mesothelioma of the pleura is based on an accumulation of supportive data, including clinical findings (especially a history of exposure to asbestos), roentgenographic characteristics, and an extensive histopathologic evaluation of biopsy samples obtained by CPNB, thoracoscopy, or OPB.

Histologically, malignant mesothelioma is most commonly classified as epithelial, sarcomatous, or mixed.\(^4\) Epithelial malignant mesothelioma is the most common type, accounting for approximately 50 percent of cases. When small biopsy specimens are taken, such as with CPNB, there can be considerable difficulty in distinguishing epithelial malignant mesothelioma from pulmonary adenocarcinoma.

In attempting to distinguish epithelial malignant mesothelioma from pulmonary adenocarcinoma, the pathologist employs certain ancillary tests. These ancillary tests include histochemical staining, immunohistochemical studies using antibodies to various antigens in the mesothelioma or adenocarcinoma, and electron microscopy where available.

Hyaluronic acid is produced by the epithelial component of mesotheliomas found in the epithelial and mixed types of mesothelioma, but it is not produced by adenocarcinomas.\(^5\) The histochemical stains alcin blue and colloidal iron demonstrate the presence of acid mucopolysaccharides such as hyaluronic acid; thus, a positive stain implies that the tissue is a mesothelioma. That the substance stained is indeed hyaluronic acid and not, for example, chondroitin sulfate can be verified by pretreatment of the tissue with hyaluronidase.\(^6\) However, not all mesotheliomas produce hyaluronic acid, and therefore a negative reaction to alcin blue or colloidal iron does not rule out malignant mesothelioma.\(^6\) More recently, PAS staining with diastase has been used. PAS stains glycogen found in mesotheliomas and mucin found in adenocarcinomas.\(^7\) The glycogen found in epithelial malignant mesotheliomas is usually thinly dispersed throughout the cytoplasm as granules and is easily digested by diastase. The mucin of adenocarcinomas is resistant to diastase digestion. In this manner, the PAS with diastase test can add further support to a diagnosis of malignant mesothelioma or adenocarcinoma. However, not all adenocarcinomas produce mucin and therefore a negative stain to PAS with diastase does not rule out an adenocarcinoma.\(^5\)

For immunohistochemical studies, the most widely employed antibody is that to CEA.\(^8\) Since CEA is found in most adenocarcinomas but few epithelial mesotheliomas,\(^g\) a positive result is highly suggestive of adenocarcinoma. Even if an epithelial mesothelioma does react positively with CEA, the reaction is usually extremely weak and easily distinguished from the strong reaction seen with adenocarcinoma.\(^10\) However, occasionally intense staining to CEA can be seen with epithelial mesotheliomas. A high molecular weight antibody to cytoplasmic keratin has a high positive yield in epithelial mesotheliomas, but it is also often positive in adenocarcinomas.\(^11\) However, using a noncommercial cytoplasmic keratin antibody, Conron and Pinkus\(^12\) found that all 14 epithelial mesotheliomas exhibited moderate or strong staining with a predominantly diffuse and homogenous pattern, while nine of 20 adenocarcinomas failed to stain and seven of 20 exhibited weak staining that was predominantly peripheral in location. A monoclonal antibody to vimentin can also be used but it is less sensitive and less specific. There are many antibodies that can be used to aid in the diagnosis of epithelial mesotheliomas, although no single antibody to date is diagnostic.\(^11\) The US-Canadian Mesothelioma Panel uses a battery of antibody tests. Recently, promising results have been reported with an antimesothelial antibody.\(^13\)

Ultrastructural evaluation with electron microscopy can also be used to aid in the diagnosis of epithelial malignant mesothelioma. Churg\(^4\) claims the ultrastructural features are generally nonspecific in the difficult-to-diagnose cases. Others have found electron microscopy to be quite useful in establishing the

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**Table 1—Results of Ancillary Tests Used in This Study to Help Diagnose Malignant Mesothelioma of the Pleura**

<table>
<thead>
<tr>
<th>Test for adenocarcinoma</th>
<th>No. of Specimens</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vimentin</td>
<td>1 (O)</td>
<td>None</td>
<td>1 (O)</td>
</tr>
<tr>
<td>Antibody to CEA</td>
<td>9 (O)</td>
<td>None</td>
<td>9 (O)</td>
</tr>
<tr>
<td>PAS with diastase</td>
<td>8 (C)</td>
<td>8 (C)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 (O)</td>
<td>None</td>
<td>1 (O)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test for mesothelioma</th>
<th>No. of Specimens</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcian blue</td>
<td>7 (O)</td>
<td>7 (O)</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>1 (C)</td>
<td>1 (C)</td>
<td></td>
</tr>
<tr>
<td>Colloidal iron</td>
<td>2 (O)</td>
<td>1 (O)</td>
<td>1 (O)</td>
</tr>
<tr>
<td></td>
<td>1 (C)</td>
<td>1 (C)</td>
<td></td>
</tr>
<tr>
<td>Antibody to keratin</td>
<td>8 (O)</td>
<td>8 (O)</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>8 (C)</td>
<td>8 (C)</td>
<td></td>
</tr>
</tbody>
</table>

\(^*\) PAS = periodic acid-Schiff; CEA = carcinoembryonic antigen; O = open pleural biopsy; C = closed pleural biopsy.
diagnosis of mesothelioma.14

OPB with direct visualization and palpation of the pleura has been the usual method of diagnosing malignant mesothelioma. This method supplies enough tissue for an accurate pathologic assessment. However, OPB can result in seeding of the mesothelioma into the thoracotomy wound and subsequently the chest wall, as well as chronic intractable postoperative pain along the incision site. In addition, general anesthesia is necessary. Seeding has also been reported in CPNB and care must be taken to excise the needle tract if aggressive surgery is subsequently undertaken.

Thoracoscopy under local or general anesthesia has been used recently to obtain samples for diagnosing malignant mesothelioma of the pleura; diagnostic yields of 60 to 75 percent have been reported. However, the use of this procedure is still uncommon in the United States.16

In the past, CPNB has been thought to deliver insufficient tissue to allow a definite pathologic diagnosis of epithelial malignant mesothelioma. The diagnostic yield for CPNB has generally been reported as 20 to 30 percent.17 We found, however, that a blindly directed CPNB using an Abram's needle produced a yield of 71 percent. A CT-guided approach using a Greene needle had a yield of 83 percent. Combining the two approaches gave a yield of 77 percent. The higher yield obtained in this study probably reflects the use of the newer, more accurate diagnostic ancillary tests that have become available in the past 10 to 15 years. Of the two patients in this study in whom the blind approach resulted in nondiagnostic findings, one patient was subsequently given a diagnosis based on analysis of tissue obtained at a subsequent CT-guided CPNB. Although CPNB can have a number of possible complications, none occurred in our patients.

These observations suggest that CPNB may be attempted before OPB in patients in whom a definitive diagnosis of malignant mesothelioma of the pleura is required. If a nondiagnostic result is obtained when a blind approach is used, a CT-guided approach may be done before proceeding to OPB.

REFERENCES

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8 The Pleura. In: Fraser RG, Pare JAP, Pare PD, Fraser RS, Generous GP, eds. Diagnosis of diseases of the chest. Philadelphia: WB Saunders, 1991; 4:2763-93