Diagnosis of Malignant Pleural Mesothelioma by Axillary Lymph Node Biopsy*

S. Brian Kim, M.D.; Basil Varkey, M.D., F.C.C.P.; and Hongyung Choi, M.D.

Diffuse malignant mesothelioma was diagnosed by axillary lymph node biopsy in a patient with brief asbestos exposure and extensive pleural masses. The clinical, radiographic, and pathologic findings of this case are reported and lymph node involvement in DMM is briefly discussed.

Extrathoracic lymph node metastasis is a very rare occurrence in diffuse malignant mesothelioma. Herein we describe a patient with axillary lymph node enlargement, the biopsy of which showed metastatic malignant mesothelioma. To our knowledge, this is the first case of diffuse malignant mesothelioma (DMM) in which the diagnosis was made by an extrathoracic lymph node biopsy.

CASE REPORT

A 52-year-old white man presented with progressive dyspnea on exertion, fatigue and weight loss of 10 pounds over a three-month period. He was an ex-smoker with a 45-pack-year history of smoking. He was exposed to asbestos in his childhood when his grandfather was installing pipe insulation. Examination of the patient revealed a 2 cm lymph node in the right axilla which was hard, movable and not tender. There was no chest wall tenderness or mass. On percussion, the right lower lung field was dull and breath sounds were markedly decreased in the same area. The routine laboratory findings were normal except for a hemoglobin of 13.3 g/dl, hematocrit of 40.5 percent, and a sedimentation rate of 59 mm/hr (Westergren). The chest radiograph, posteroanterior view (Fig 1A), showed the right lung surrounded by pleural-based densities, and a paraaortic density suggestive of mediastinal lymph node enlargement. Computed tomography of the chest (Fig 1B) showed that the right lung was encased with about a 2 cm-thick pleural mass. Multiple enlarged lymph nodes were seen in the mediastinum. Another tomographic cut also revealed moderate pleural effusion on the right side. The enlarged right axillary lymph node was biopsied and extensive metastatic neoplasm was noted. The tumor cells had abundant eosinophilic and focally vacuolated cytoplasm, and large vesicular often hyperchromatic nuclei, which contained single or multiple prominent nucleoli. These cells were arranged in diffuse, solid sheets and was focally papillary in pattern (Fig 2A). Occasional mitotic figures and multinucleated giant cells were present. On the basis of these findings, asbestos exposure history and consistent clinical and radiographic findings, a diagnosis of DMM was made. Further confirmatory evidence was obtained from histochemical, immunocytochemical and electron microscopy studies. Histochemical stains of the biopsied lymph node showed negative mucicarmine and positive intracellular and extracellular alcin blue and immunocytochemical studies showed negative carcinoembryonic antigen and positive keratin.1,3 Electron microscopy (Fig 2B) showed numerous long and slender complex microvilli and prominent tonofilaments.5 The patient expired on the 11th hospital day due to progressive cardiorespiratory failure, and his family denied permis-sion for an autopsy. However, with the family's consent, a small piece of pleural tumor was removed, and the excised tumor exhibited the same characteristics as the axillary node.

DISCUSSION

The lymphatic vessels of the parietal pleura drain anteriorly to the parasternal lymph nodes, posteriorly to the paravertebral lymph nodes, and centrally to the hilar nodes. The lymphatic drainage of the chest walls is to the axillary lymph nodes; anterior and lateral thoracic wall lymphatics drain to the anterior or pectoral group of nodes and the posterior thoracic wall lymphatics to the other axillary nodes. Chest wall involvement is a recognized complication of malignant mesothelioma, but the incidence of this complication varies in the published literature. In one study,4 six of 44

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**Figure 1. A (upper). Chest radiograph (PA view) shows right-sided densities and markedly reduced aeration of right lung. A paraaortic density is seen on the left side. B (lower). Computed tomography of the chest shows encasement of right lung with a 2 cm-thick pleural mass. Multiple enlarged lymph nodes (arrows) are seen in the mediastinum.
cases (14 percent) of DMM had chest wall involvement while Whitwell and associates\(^4\) noted chest wall involvement in all 32 autopsied cases. In those with chest wall involvement, a higher frequency of axillary lymph node metastases is expected because of the pattern of lymphatic drainage. However, our review of the reported studies on DMM does not bear this out.

We reviewed a number of articles on DMM,\(^4\),\(^8\) which described a total of 401 cases (Table 1). At least 183 of these cases had autopsies, 81 (44 percent) of whom had neoplastic

Table 1—Lymph Node Involvement in DMM

<table>
<thead>
<tr>
<th>Authors</th>
<th>Total Cases Reported</th>
<th>Autopsy Cases</th>
<th>Hilar and Mediastinal Node</th>
<th>Axillary Node</th>
<th>Cervical Node</th>
<th>Abdominal Node</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>McCormack et al(^7)</td>
<td>149</td>
<td>48</td>
<td>18</td>
<td>12</td>
<td>15</td>
<td></td>
<td>All cases had surgery for diagnosis and treatment. Axillary node involvement by physical exam or surgical resection was not noted in any case (Dr. McCormack—personal communication). At least 48 cases had autopsy.</td>
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<tr>
<td>Wanebo et al(^4)</td>
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<td>Total autopsy cases were 36 but the information regarding lymph node involvement was available in only 32 cases.</td>
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<tr>
<td>Ratzer et al(^8)</td>
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<td>Autopsy rates not given in 29 surgical cases. All 17 nonsurgical cases had autopsies.</td>
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<tr>
<td>Whitwell et al(^5)</td>
<td>52</td>
<td>32</td>
<td>14</td>
<td>1</td>
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<tr>
<td>Roberts(^9)</td>
<td>32</td>
<td>32</td>
<td>17</td>
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<tr>
<td>Butchart et al(^10)</td>
<td>46</td>
<td>17</td>
<td>7</td>
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<tr>
<td>Adams et al(^7)</td>
<td>16</td>
<td>16</td>
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<td>Urschel et al(^8)</td>
<td>21</td>
<td>11</td>
<td>9</td>
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<td>Semb(^11)</td>
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<td>10</td>
<td>4</td>
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<td>Manguikian et al(^12)</td>
<td>5</td>
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<tr>
<td>Manfredi et al(^13)</td>
<td>4</td>
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<td>Shearin et al(^14)</td>
<td>19</td>
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<td>Geschichter(^15)</td>
<td>25</td>
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<tr>
<td>Heller et al(^16)</td>
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<td>Taryle et al(^16)</td>
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<tr>
<td>Kahn et al(^17)</td>
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<tr>
<td>Total</td>
<td>401</td>
<td>183</td>
<td>81</td>
<td>2</td>
<td>13</td>
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Malignant Pleural Mesothelioma (Kim, Verhey, Cho)
involvement of the hilar or mediastinal nodes. In marked contrast, only two cases with axillary lymph node involvement were noted. In an additional case, axillary lymphadenopathy was detected clinically, but there was no histopathologic diagnosis. The discrepancy between the expected frequency of axillary lymph node involvement and observed frequency in the autopsied cases is not well explained. One probable reason is that the autopsies may not have included axillary lymph node dissections, particularly in those without obvious axillary lymph node enlargement on physical examination. A prospective multicenter clinical and autopsy study of lymph node involvement in DMM would establish the true frequency of peripheral lymph node involvement. Our case points to the importance of axillary lymphadenopathy in DMM and suggests biopsy of an enlarged node as a method of diagnosis of DMM.

REFERENCES


8 Ratzer ER, Pool JL, Melamed MR. Pleural mesotheliomas; clinical experiences with thirty-seven patients. AJR 1967; 99:863-80


Pulmonary Ceroidosis


We describe a patient with pulmonary ceroid histiocytosis. Skin pigmentation, chest x-ray film and laboratory findings were normal. Only pulmonary function tests were abnormal (TLC = 63 percent, DLco = 52 percent). Based on these functional data, the patient was submitted to a lung biopsy by thoracotomy. Brown pigmented histiocytes were shown occupying alveolar spaces. Similar brown pigmented hepatocytes were seen in the liver biopsy.

There are 30 kinds of disease in which systemic or localized deposition of ceroid occurs in the reticuloendothelial system. These diseases include sea-blue histiocytosis, since the materials stored in sea-blue histiocytes are a kind of ceroid. Among the diseases, systemic or localized deposition are described as acquired or heredofamilial forms. The lung is involved in 11 percent of cases of the sea-blue histiocyte syndrome.

In the Hermansky-Pudlak syndrome the pulmonary manifestations are very frequent. Clinically, this appears as dyspnea on exertion and evolves similarly to idiopathic fibrosis. Patients also have albinism and hemorrhagic diathesis. The ceroid pigment present in alveolar macrophages and interstitial fibrosis is also demonstrated.

In 1967, Maeda described the occurrence of a ceroid-like pigment in the alveolar macrophages in the pulmonary tissues of eight autopsies of patients with gastric carcinoma. In 1978, Takahashi described a new entity in a Japanese patient who died from vascular collapse after injection of a contrast medium. The entity is characterized by marked proliferation of brown pigment-laden macrophages in pulmonary tissues (mainly in alveolar spaces), viz., idiopathic pulmonary ceroidosis.

We describe a patient with pulmonary ceroid histiocytosis without evidence of any basic disorder.

CASE REPORT

A 27-year-old woman from the Canary Islands is presented. She was well until five years ago, when episodes of cough with sputum production appeared. These episodes became more frequent and two years later she complained of dyspnea on exertion. She had smoked 20 cigarettes a day for eight years. She denied having used hair sprays or having had any contact with other noxious vapors. Her father suffers from chronic bronchitis and is a heavy smoker. Her mother is well. Ten brothers are asymptomatic.

Physical examination: Skin pigmentation was normal. No lymphadenopathy was found. The lungs were clear and no abnormal cardiac sound was heard. No hepatosplenomegaly was felt. Results of neurologic and funduscopic examinations were negative.

Laboratory examination: A Coulter "S", SMAC 20 (Technicon), and urinalysis were normal. The platelet count, bleeding time and prothrombin time were normal. Other determinations included serum electrophoretic pattern, immunoelectrophoresis, Singer and from the *Allergy, †Pathology, Pneumology Departments, Fundación Jiménez Díaz, Universidad Autónoma, Madrid, Spain. ‡Pneumology Section, Ntra Sra del Pino, Las Palmas, Canary Islands.

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