Liposarcoma of Pleural Cavity with Recurrence as Malignant Fibrous Histiocytoma*

DOUGLAS H. MCGREGOR, M.D.,†‡ ANITA Y. DIXON, M.D.,†‡ LUIS MORAL, M.D.,†‡ and SUMIO KANABE, M.D.†‡

†Laboratory Service, Veterans Administration Medical Center, Kansas City, MO 64128 and ‡Department of Pathology and Oncology, University of Kansas Medical Center, Kansas City, KS 66102

ABSTRACT

The case of a 54-year-old male, with a massive right pleural liposarcoma weighing over 3200 g, is presented. The tumor was found by light and electron microscopy to be of well-differentiated and pleomorphic subtypes, and it apparently represents the sixth reported case of liposarcoma primary to the pleura. Two years after excision of the primary tumor, it recurred as a neoplasm with histologic and ultrastructural features characteristic of malignant fibrous histiocytoma. The histogenetic and pathologic implications of the above findings are discussed, and the literature regarding intrathoracic liposarcoma and malignant fibrous histiocytoma is reviewed.

Introduction

Liposarcoma is one of the most common soft tissue sarcomas among adults. Liposarcoma of the internal thorax is relatively uncommon, however, and primary liposarcoma of the pleura is rare, with apparently only five cases having been previously reported. Recently, three cases of liposarcoma (two of retroperitoneum, one of arm) were reported to recur with focal features of malignant fibrous histiocytoma. The following report presents a case of a massive liposarcoma of the right pleura, which was resected and then recurred as a neoplasm with morphologic features characteristic of malignant fibrous histiocytoma.
Case Report

A 54-year-old black man complained of shortness of breath for two months, dyspnea on exertion after walking two or three blocks, sputum production of one-half cup per day, and mild right chest pain accentuated with breathing. Past history included a 50-year history of smoking and chronic alcoholism.

A chest x-ray revealed a homogeneous density which obscured the lower two-thirds of the right lung and extended into the apical area. The left lung appeared to be expanded and clear. There was a slight shift of the heart and mediastinal structures to the left. Bronchoscopy revealed compression of the right, lower, and middle lobe bronchi. A bronchial biopsy demonstrated only squamous metaplasia and basal cell hyperplasia. Repeated thoracenteses failed to reveal malignant cells or to alleviate significantly the apparent pleural effusion. A right pleural biopsy demonstrated only inflammatory and reactive changes. A right thoracotomy revealed two large lobulated masses (one of which initially appeared to be a lung) and fatty appendages protruding into the pleural cavity, resulting in displacement of the lung inferiorly and superiorly. These masses and appendages were excised. Frozen and permanent section diagnoses were liposarcoma, well-differentiated and pleomorphic types. No radiation or chemotherapy was instituted.

During the subsequent two years, the patient developed evidence of recurrence of the right thoracic tumor. A chest x-ray showed a large soft tissue mass involving the anterior region of the right upper lung. A right thoracotomy revealed an eight cm dark yellow mass underlying the anterior fourth and fifth ribs, which was freed and resected from the lung and chest wall. Histologic sections were interpreted as malignant mesodermal neoplasm with features characteristic of malignant fibrous histiocytoma but probably representing recurrent liposarcoma. Three years later, recurrence of tumor in the right, lower, and middle lobe lung fields was identified radiologically, when the patient was admitted for a hypertensive-associated cerebrovascular accident. Further diagnostic studies or therapy were not instituted, and the patient died of unknown causes four years later, nine years after the original surgery, at the age of 63 years.

Materials and Methods

Surgery to obtain the tissue was performed at 22-month intervals. Tissue for light microscopy was fixed in 10 percent neutral buffered formalin, dehydrated and embedded in paraffin, except for frozen tissue sections processed for oil red 0 staining for lipid. Paraffin sections (multiple sections each from 40 blocks of original tumor and 18 blocks of recurrent tumor) were stained with hematoxylin-eosin, Masson’s trichrome, and Wilder’s reticulum stain.

Tissue for electron microscopy was immediately fixed in four percent glutaraldehyde in 0.1M phosphate buffer at pH 7.4. After one hour, the tissue was washed in 0.1M phosphate buffer with sucrose and postfixed in one percent osmium tetroxide in 0.1M phosphate buffer. It was then dehydrated through a series of graded alcohols and propylene oxide and embedded in epoxy resin. Sections one cm thick were stained with toluidine blue for light microscopy. Ultrathin sections were stained with a saturated solution of uranyl acetate and lead citrate and examined with an electron microscope.

Results

GROSS FINDINGS (ORIGINAL TUMOR)

Four portions of tumor tissue were resected from the right thorax, one (figure 1a) measuring 22 X 12 X 10 cm and weighing 1040 g, one measuring 25 X 25 X 18 cm and weighing 2160 g, one measuring 2.5 X 1.5 X 0.6 cm, and one measuring 2 X 1.5 X 1 cm. Each of these tissue specimens had a homogeneous yellow-tan to pink-tan external surface which was smooth but focally lobulated and soft but focally indurated. The cut surfaces (figure 1b) were similar in color and consistency and had focal hemorrhage and mucoid areas. There was no lung tissue identified.

LIGHT MICROSCOPIC FINDINGS

(ORIGINAL TUMOR)

Multiple histologic sections of the first-received 1040 gm specimen (figure 2) demonstrated mature adipose tissue with interspersed lipoblasts having nuclei with marked enlargement, moderate to marked hyperchromasia, finely
to coarsely granular chromatin, and small to moderate sized nucleoli. Also present were scattered, multinucleated, giant cells with similar appearing nuclei and with a large amount of pale eosinophilic cytoplasm having diffuse, fine granularity, or multiple clear vacuoles. These vacuoles were positive for lipid in frozen sections stained with oil red 0. The tumor periphery was limited in some areas by loose fibrovascular tissue, which was focally infiltrated by neoplasm and which occasionally had an outer layer of flattened mesothelial-like cells.

These findings were interpreted as liposarcoma, predominantly the well-differentiated type. Multiple histologic sections of the subsequently received 2160 g and two smaller specimens (figure 3) demonstrated similar findings except that the mature adipose tissue component was much less evident and that the

**Figure 1. Gross appearance of original tumor; A showing smooth focally lobulated external surfaces, and B showing homogeneous yellow-tan focally hemorrhagic cut surface.**
pleomorphic multinucleated cellular component was much more prominent. These were scattered throughout a variably proteinaceous and myxoid matrix, with an interspersed fibrovascular stroma and moderate numbers of chronic inflammatory cells, predominantly lymphocytes and plasma cells. These find-
ings were interpreted as liposarcoma, predominantly pleomorphic type. Lung tissue was not identified in any of the specimens.

Electron Microscopic Findings (Original Tumor)

An electron microscopic study of the first-received 1040 g specimen demonstrated mature adipose cells and scattered lipoblasts, the latter having large, irregular nuclei and prominent nucleoli. Also present were scattered more poorly differentiated mesenchymal cells, with large, irregular nuclei, peripherally located heterochromatin, prominent nucleolus, several to many lipid droplets, several lysosomes, moderate numbers of irregularly-shaped mitochondria, moderate amount of rough endoplasmic reticulum (sometimes dilated and containing proteinaceous material), interspersed microfilaments and polyribosomes, and an irregular tortuous cytoplasmic shape with focal, finger-like projections. These mesenchymal cells were dispersed in a proteinaceous and myxoid matrix with focal collagen fiber deposition (figure 4).

An electron microscopic study of the subsequently received 2160 g specimen demonstrated findings similar to the first specimen, except that the more poorly differentiated mesenchymal cell component with lipid droplets was much more prominent.

Gross Findings (Recurrent Tumor)

Two portions of tumor tissue were removed from the right thorax, one measuring $5.5 \times 3.5 \times 1\ cm$ and one measuring $8 \times 5.5 \times 2\ cm$. The first had an irregular red-brown, external surface and a spongy, grayish-tan cut surface with small black foci. The second was an ovoid, soft mass with an external surface which was smooth, yellowish brown and focally hemorrhagic, and with a cut surface which was peripherally circumscribed, yellowish white, and focally hemorrhagic and necrotic.

Light Microscopic Findings (Recurrent Tumor)

Multiple histologic sections of both specimens (figure 5) demonstrated a malignant mesodermal neoplasm having a highly cellular and variable morphologic pattern. In some areas, the tumor was composed of somewhat plump, spindle-shaped cells arranged in short fascicles in a storiform pattern. These spindle-shaped cells resembled fibroblasts with non-vacuolated eosinophilic cytoplasm and oval somewhat vesicular nuclei. In other areas, the neoplasm was remarkably pleomorphic with haphazardly arranged spindle cells intermingled with malignant giant cells. The giant cells had non-vacuolated, deeply eosinophilic, cytoplasm and multiple irregular nuclei. A considerable chronic inflammatory component was present. Frozen sections stained with oil red 0 were negative for lipid.

These findings were interpreted as a malignant mesodermal neoplasm which had morphologic features characteristic of malignant fibrous histiocytoma but which in actuality probably represented a dedifferentiated form of liposarcoma.

Electron Microscopic Findings (Recurrent Tumor)

An electron microscopic study (figure 6) demonstrated a dense proliferation of mesenchymal cells comparable in shape to those seen light microscopically with nuclei (rarely multiple) having round to moderately irregular shape, peripheral heterochromatin, and occasional moderately prominent nucleoli. The cytoplasm had a moderate to large amount of rough endoplasmic reticulum, the cisterns of which were occasionally dilated and contained proteinaceous material. Also
present in the cytoplasm were scattered polyribosomes, microfilaments, relatively few mitochondria, occasional lysosomes, and rare non-membrane-bound electron-lucent vacuoles, possibly containing lipid. These cells variably appeared histiocytic, fibroblastic, myofibroblastic or undifferentiated, depending upon the prominence of structures such as rough endoplasmic reticulum, lysosomes, microfilaments, peripheral dense bodies, and cytoplasmic projections. The small amount of stroma in this cellular proliferation was predominantly composed of collagen fibers.

**Discussion**

A review of the literature indicates that primary liposarcoma of the pleura is a rare occurrence. Including the present case, there appear to have been only six reported cases\(^1,9,11,13,41\) (table I). None of the previous five case reports acknowl-
Figure 5. Recurrent tumor composed of malignant spindle cells with focal storiform pattern, chronic inflammatory cells, and pleomorphic giant cells. Inset of pleomorphic giant cells (Hematoxylin and eosin stain. ×100, inset ×400.)

Figure 6. Electron micrograph of recurrent tumor showing portions of two cells with histiocytic, fibroblastic and myofibroblastic features, including prominent rough endoplasmic reticulum (focally distended), scattered lysosomes, microfilaments, peripheral densities, and cytoplasmic projections. Collagenous stroma is adjacent. (×6860.)
Reported Cases of Primary Pleural Liposarcoma

<table>
<thead>
<tr>
<th>Case</th>
<th>Year</th>
<th>Author</th>
<th>Age</th>
<th>Sex</th>
<th>Site</th>
<th>Size</th>
<th>Type</th>
<th>Therapy</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1942</td>
<td>Ackerman et al (3)</td>
<td>50</td>
<td>F</td>
<td>Left</td>
<td>1000 g</td>
<td>Well diff. and pleomorphic</td>
<td>None</td>
<td>Death 1 1/2 yrs.</td>
</tr>
<tr>
<td>2</td>
<td>1967</td>
<td>Gupta et al (13)</td>
<td>51</td>
<td>M</td>
<td>Right</td>
<td>21x12x8 cm, 900 g</td>
<td>Poorly diff.</td>
<td>Thoracentesis</td>
<td>Death 1 yr.</td>
</tr>
<tr>
<td>3</td>
<td>1974</td>
<td>D'Ambrosia (9)</td>
<td>52</td>
<td>M</td>
<td>Left</td>
<td>3.5x2x2 cm, recurrence 20x15x8 cm, 1230 g</td>
<td>Myxoid</td>
<td>Resection x 2, radiation</td>
<td>Recurrence 4 1/2 yrs.</td>
</tr>
<tr>
<td>4</td>
<td>1983</td>
<td>Wouters et al (41)</td>
<td>19</td>
<td>M</td>
<td>Left</td>
<td>22x12x10 cm, 1040 g, 25x25x18 cm, 2160 g, recurrence 5.5x3.5x1 cm, 0x5.5x2 cm</td>
<td>Pleomorphic and well diff.</td>
<td>Resection x 2</td>
<td>Recurrence as MFH 2 yrs.; clinical recurrence 3 yrs.</td>
</tr>
<tr>
<td>5</td>
<td>1985</td>
<td>Evans (11)</td>
<td>61</td>
<td>M</td>
<td>Left</td>
<td>Encasing most of left lung x 4.5 cm</td>
<td>Myxoid &amp; pleomorphic</td>
<td>None</td>
<td>Death 2 Days</td>
</tr>
<tr>
<td>6</td>
<td>1987</td>
<td>McGregor et al</td>
<td>54</td>
<td>M</td>
<td>Right</td>
<td>22x12x10 cm, 1040 g, 25x25x18 cm, 2160 g, recurrence 5.5x3.5x1 cm, 0x5.5x2 cm</td>
<td>Pleomorphic and well diff.</td>
<td>Resection x 2</td>
<td>Recurrence as MFH 2 yrs.; clinical recurrence 3 yrs.</td>
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edged the existence of any other reported cases. In our review, it was determined that five-sixths of these cases involved males, and most were in the early 50's in age, comparable to statistics regarding liposarcomas of all sites. All four tumors with recorded size were large, weighing 900 g or more, as might be expected for a neoplasm with relatively late symptomatology growing within a cavity such as the thorax. All histologic types (well-differentiated, myxoid and pleomorphic) were represented, except for the round cell liposarcoma. All five cases with follow-up information either recurred following resection or resulted in death. Cases of intrathoracic liposarcoma, which were apparently secondary from other primary sites, were excluded from this review.

The histogenesis of pleural liposarcomas is uncertain; presumably, they arise from subpleural primitive mesenchymal cells or possibly from the subpleural adipose tissue frequently present in the costal region and less often other regions of the parietal and visceral pleura. This is also the presumed origin for the approximately 200 reported cases of intrathoracic lipomas. Liposarcomas of the other non-pleural, intrathoracic sites are also quite infrequent. Primary liposarcoma of the lung is almost as rare as that of the pleura, with apparently only seven cases having been reported. Only three cases of primary liposarcoma of the pericardium appear to have been reported and two cases of liposarcoma of the interatrial septum have been described. Liposarcomas in other mediastinal sites are more common, however, and at least 55 cases have been reported to date. The reason for this distribution and overall relative infrequency of intrathoracic liposarcoma is uncertain, but it is likely related in part to the relatively small amount of adipose tissue normally present in these regions.

One highly interesting aspect of the present case is that two years after excision it recurred as a neoplasm with histologic features characteristic of malignant fibrous histiocytoma. Such a pheno-
non has been observed by previous investigators. In one study of 52 recurrences in 11 cases of liposarcoma, three cases demonstrated areas in the recurrences with histological features characteristic of malignant fibrous histiocytoma. Similar findings were reported in another comparable study of 20 cases of recurrent liposarcoma. The recurrences in these cases with features of malignant fibrous histiocytoma, however, were accompanied by recurrent tumor with areas histologically characteristic of liposarcoma. In the present case, multiple sections of the recurrent neoplasm consistently demonstrated histologic features characteristic of malignant fibrous histiocytoma. Presumably this represents a dedifferentiation of the original liposarcoma. Such a case as this emphasizes the need for great care prior to rendering a diagnosis of malignant fibrous histiocytoma. Furthermore, this polymorphic differentiation supports the concept that liposarcoma is derived from pleuripotential primitive mesenchymal cells.

Finally, since a recurrent pleural neoplasm characteristic of malignant fibrous histiocytoma was seen in the present case, the frequency of this as a primary diagnosis should be mentioned. To our knowledge there has been only one reported case of primary malignant fibrous histiocytoma of the pleura. Malignant fibrous histiocytoma of the lung, however, appears to be more frequent, with approximately 15 cases having been reported to date.

References


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