Expectoration of Metastatic Endobronchial Rhabdomyosarcoma: A Case Report and Brief Review of the Literature

Larisa M. Lehmer, MA,* Bruce D. Ragsdale, MD,* Ronald E. Rocha, MD,† and Harry F. Corbett, MD‡

Abstract: A 63-year-old male spontaneously expectorated a small piece of solid tissue histologically verified as an endobronchial extension of a pulmonary metastasis of high-grade sarcoma. The primary tumor excised from the thigh 18 months before had been diagnosed as a malignant fibrous histiocytoma. The tumor fragment was reactive for desmin, MyoD1, and myogenin, favoring the alternative diagnosis of high-grade rhabdomyosarcoma.

Key Words: expectorated sarcoma, endobronchial tumor, rhabdomyosarcoma, MyoD1, myogenin

(Clin Palm Med 2011;18:305–308)

Expectoration of endobronchial tumor is a rarely documented phenomenon. As of 2008, <30 cases had been published. Published tumor types include primary lung neoplasms including bronchogenic carcinomas, carcinoid tumors, and sarcomas, but these are outnumbered by the portions of metastatic tumors that have been coughed up. To our knowledge, only 1 case of an expectorated tumor as a result of metastatic malignant fibrous histiocytoma (MFH) has been reported.1 In the spirit of the times to mitigate the use of the term MFH,2 the immunohistochemical profile of the present myogenous tumor favors differentiation, probably rhabdomyosarcoma (RMS), rather than relegating it to a heterogeneous repository of pleomorphic, poorly differentiated sarcomas known as MFH.3

CASE REPORT

A 63-year-old bedridden male with a history of multiple sclerosis, a sarcoma resected from soft tissue of the right thigh 21 months before, and nonhealing ulcer in the thigh surgical site, had a coughing episode during which a 2.9 × 1.5 × 1.0-cm portion of gray-tan, slightly hemorrhagic, apparent soft tissue was expectorated. Published tumor types include primary lung neoplasms including bronchogenic carcinomas, carcinoid tumors, and sarcomas, but these are outnumbered by the portions of metastatic tumors that have been coughed up. To our knowledge, only 1 case of an expectorated tumor as a result of metastatic malignant fibrous histiocytoma (MFH) has been reported.1 In the spirit of the times to mitigate the use of the term MFH, the immunohistochemical profile of the present myogenous tumor favors differentiation, probably rhabdomyosarcoma (RMS), rather than relegating it to a heterogeneous repository of pleomorphic, poorly differentiated sarcomas known as MFH.

A base-line chest radiograph appeared clear (Fig. 2A), whereas a film taken 6 months later showed opacification of the left lung base and increased density over the left mid-lung field indicating a rather rapid progression of metastatic tumor from which the expectorated fragment originated (Fig. 2B). Computed tomography (CT) findings, taken on a Phillips Brilliance 64 detector FH scanner, showed a small-to-moderate layering effusion and collapse/consolidation of the left lower lobe (Fig. 3). The soft tissue density observed in the left main bronchus (Fig. 3, arrow) is most likely the residual pedicle origin of the expectorated tumor fragment.

Diagnosis of the original thigh sarcoma was made from a Tru-Cut needle biopsy of the lesion. An 8 × 5-cm mass noticed 6 months earlier in the soft tissue of the patient’s posterolateral thigh was independent of bone. The high-grade, predominantly spindle cell tumor had a small component of admixed cells with markedly pleomorphic nuclei and frequent mitoses, some of which were atypical. The tumor was unreactive for a limited panel of immunohistochemical reagents including desmin and was therefore reported as MFH. Nineteen days later, a 29.4 × 14.5 × 11.9-cm mass excision specimen was removed containing a 10.5 × 8.0-cm neoplastic mass that was mostly a 5.5 × 5.2-cm hemorrhagic cavity with a 4.8 × 4.5-cm solid, fleshy, yellow-tan solid component extending focally to the deep margin without demonstrable vascular invasion. The patient underwent radiation therapy 3 months after surgery and aside from persistent ulceration, the site remained quiescent. No chemotherapy was administered at the patient’s request. The expectorated fragment was produced 18 months after excision of the thigh tumor.

The patient passed away 45 days after expectoration of the tumor fragment.

Special Laboratory Work

Although the expectorated tumor is consistent with MFH, the current nomenclature prefers to subtype high-grade sarcomas according to any line of differentiation that can be identified with ancillary studies such as immunohistochemistry or molecular studies. Although lacking cross-striations (Fig. 4), even in a phosphotungstic acid hematoxylin stain, and unreactive for smooth muscle actin and calponin, the expectorated tumor fragment was reactive for markers of muscle differentiation, MyoD1 and myogenin, which is a sufficient basis for classifying the expectorated tumor as a high-grade pleomorphic rhabdomyosarcoma (PRMS) (Table 1). Positive reactions for RMS-specific MyoD1 and myogenin rule out leiomyosarcoma, Ewing sarcoma/peripheral primitive neuroectodermal tumors, and other soft tissue sarcomas.4 The MyoD1 family is a superfamily of transcription factors that regulates the cell lineage-specific proliferation of striated muscle. Myogenin and MyoD1 activate their own transcription and that of other basic helix-loop helix proteins working in concert with the retinoblastoma gene to regulate

From the *Western Dermatopathology; †Central Coast Pathology Consultants; and ‡Radiology Associates of San Luis Obispo, San Luis Obispo, CA.
The authors declare that they have nothing to disclose.
Address correspondence to: Larisa M. Lehmer, MA, 3701S, Higuera Street, #200, San Luis Obispo, CA 93401. E-mail: llehmer@ecpathology.com.
Copyright © 2011 by Lippincott Williams & Wilkins
ISSN: 1068-0640/11/1806-0305
DOI: 10.1097/CPM.0b013e318234d532
exodus from the cell cycle and initiation of striated muscle differentiation. Both MyoD1 and myogenin are strictly localized to cellular nuclei; hence, background cytoplasmic labeling, which has been a consistent problem with antibodies to MyoD1 especially, must be ignored as a spurious pattern of staining.

DISCUSSION

Expectoration of tumor fragments, an extremely rare phenomenon, was originally described by Mackenzie in 1886. These fragments tend to be larger than standard biopsy specimens and may readily lend themselves to diagnostic studies, despite the lack of immediate tissue fixation.

Of endobronchial tumors expectorated, the majority are metastases to the lung, for example, 11 of 16 (69%) reported by Kelley et al. Type and quantity among the 16 were: 8 renal cell carcinoma, 2 melanoma, 2 colonic adenocarcinoma, and 1 osteosarcoma. The remaining cases (31%) were primary lung tumors.

Radiologic identification of endobronchial tumors has been found to be more accurate through CT than chest radiograph as characteristic nodular opacities are more readily visualized in this method. There is a mounting consensus that a chest radiograph alone is not a reliable method for the detection of endobronchial tumor components. In fact, radiographic findings in patients with endobronchial/ endotra-

cheal metastases are quite variable. CT facilitates detection of endobronchial neoplasms, including metastatic lesions. Some studies do not even mention the use of chest radiographs and only use CT or proton emission tomography images to track the course of the disease.

Based on history, this is not deemed one of the very rare bronchopulmonary sarcomas. Of the bronchopulmonary sarcomas, leiomyosarcoma and fibrosarcoma are the most frequent histologic types. Histologically, the fascicular arrangement of spindle-shaped cells (Fig. 1) is reminiscent of leiomyosarcoma. The absence of smooth muscle markers combined with presence of MyoD1 and myogenin reactivity (Fig. 4) indicate RMS as confirmed by a series of 57 adult-type (pleomorphic) RMS, which contained no cross-striations in cytoplasm but reported positive for myogenin. Although the study found that the majority of cases had <10% cells labeled with myogenin, this reactivity distinguished them from leiomyosarcoma. Smooth muscle actin positivity and desmin negativity are consistent with a poorly differentiated leiomyosarcoma, but myogenin positivity is sufficient to rule out this diagnosis. The morphologically similar high-grade sarcoma resected from the thigh and satellite nodules in the chest film and CT study favor metastatic disease in the lung rather than a primary lung sarcoma. The 8 cm size of the thigh mass reported in this case is characteristic of PRMS lesions, which tend to be large (>10 cm), almost always arising in adults aged above 45 years with a predilection for males. Another line of

FIGURE 1. A, Moderate pleomorphism characterizes a pale-staining population of oval tumor cells, with interposed spindle cells with darkly eosinophilic cytoplasm (hematoxylin and eosin; × 400). B, Cytoplasm of some tumor cells stains red with Masson trichrome, as expected with smooth muscle differentiation (Masson trichrome; × 400).

FIGURE 2. A, Clear chest radiograph 6 months before expectoration event. B, Retrocardiac density in chest radiograph 1 week after endobronchial tumor expectoration.
evidence pointing to PRMS is that it most commonly arises in the skeletal muscle of the extremities with 36% of cases originating in the thigh (n = 95). The lung was found to be the most common site of RMS metastasis (100% of cases that metastasized, 36% of total cases) and the average time to metastasize was 15 months. PRMS, like other pleomorphic sarcomas, is clinically aggressive with a poor survival rate. The morbidity rate ranges from 70% to 88% with up to 70% of patients passing away in the first 8 months after diagnosis.

The term “malignant fibrous histiocytoma” was coined by Ozzello et al in 1960s to encompass pleomorphic soft tissue sarcomas presumably derived from histiocytes that are capable of fibroblastic transformation. More recent clinicopathologic, ultrastructural, and immunohistochemical investigations have shown that the majority of MFH cases are not derived from histiocytic “facultative fibroblasts” and that most can be subclassified on the basis of a specific line of differentiation. Cell marker studies revealed a lack of histiocyte surface antigens in MFH tumors definitively proving that they are not a true histiocytic neoplasm. As of 2002, the World Health Organization has defined MFH as the residual “small group of undifferentiated pleomorphic sarcomas with no definable line of differentiation.” Although pleomorphic sarcomas are known to express both desmin and muscle-specific actin, and may be considered in the differential diagnosis, they do not express other specific skeletal muscle markers such as MyoD1, fast skeletal muscle myosin, myf4, or myoglobin; such expression requires that the diagnosis be refined. Owing to the vague, heterogeneous nature of the term, the use of the diagnosis “MFH” should be minimized.

There may be several reasons why tumor expectoration seems to be a rare event. First, patients may fail to notice, acknowledge, or report such events; they merely discard the expectorated tissue. Second, clinicians may ignore such specimens even when they are submitted, presuming them to be phlegm or blood clot. Finally, underreporting in the medical literature and search parameter bias are additional factors that may frustrate the determination of the true frequency of these events. It has been suggested that patients at high risk of developing metastatic lung tumors should be advised to save any apparent expectorated tissue as it may be the first indication of tumor dissemination.

<table>
<thead>
<tr>
<th>IHC Stain</th>
<th>Clone</th>
<th>Dilution</th>
<th>Origin</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desmin</td>
<td>D33</td>
<td>1:80</td>
<td>Dako,</td>
<td>Focally positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Glostrup, Denmark</td>
<td></td>
</tr>
<tr>
<td>S100</td>
<td>Polyclonal</td>
<td>10 μg/mL</td>
<td>1:50</td>
<td>Negative</td>
</tr>
<tr>
<td>CD31</td>
<td>JC70A</td>
<td></td>
<td>Dako</td>
<td>Focally positive</td>
</tr>
<tr>
<td>Mart-1</td>
<td>A103</td>
<td>1:25</td>
<td>Ventana, AZ</td>
<td>Positive only in background blood vessels</td>
</tr>
<tr>
<td>Myogenin</td>
<td>F5D</td>
<td>Predilute</td>
<td>Dako</td>
<td>Negative</td>
</tr>
<tr>
<td>MyoD1</td>
<td>5.8A</td>
<td>Predilute</td>
<td>Ventana</td>
<td>Positive</td>
</tr>
<tr>
<td>Keratin</td>
<td>B22.1</td>
<td>1:100</td>
<td>Cell Marque, CA</td>
<td>Negative</td>
</tr>
<tr>
<td>Keratin</td>
<td>Cam5.2</td>
<td>1:100</td>
<td>Dako</td>
<td>Negative</td>
</tr>
<tr>
<td>Keratin</td>
<td>23BE12</td>
<td>1:100</td>
<td>Dako</td>
<td>Negative</td>
</tr>
<tr>
<td>Keratin</td>
<td>5/6</td>
<td>D5/16B4</td>
<td>1:50</td>
<td>Dako</td>
</tr>
<tr>
<td>Keratin</td>
<td>7</td>
<td>OV-TL</td>
<td>1:400</td>
<td>Dako</td>
</tr>
<tr>
<td>Keratin</td>
<td>20</td>
<td>Ks20.8</td>
<td>1:100</td>
<td>Dako</td>
</tr>
<tr>
<td>CD 56</td>
<td>123C3.D5</td>
<td>1:25</td>
<td>Cell Marque</td>
<td>Negative</td>
</tr>
</tbody>
</table>

The immunoperoxidase stain(s) used in this case are adequately controlled, with positive controls being positive and negative controls being negative. HMW indicates high molecular weight; IHC, immunohistochemical.
REFERENCES


