Pleomorphic Leiomyosarcoma of the Adrenal Gland

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Primary leiomyosarcomas arising in the adrenal gland are exceedingly rare, with only 3 cases reported in the literature. We present the clinical, morphologic, and immunohistochemical features of a pleomorphic leiomyosarcoma, a variant of leiomyosarcoma that has not been described in the adrenal gland. A 63-year-old man presented with a 1-year history of enlarging right upper quadrant mass and pulmonary nodule. A diagnosis of metastatic pulmonary carcinoma to the adrenal gland was rendered on a needle biopsy specimen. Preoperative chemotherapy reduced only the pulmonary mass but not the adrenal mass, which continued to enlarge. Documented by computed tomography and confirmed at surgery, the tumor had completely replaced the right adrenal gland, invading into both the posterior aspect of the right liver and the superior pole of the right kidney. Histologic sections showed a diffuse proliferation of pleomorphic, large, and polygonal neoplastic cells with prominent nucleoli. Many bizarre mitotic figures were present. The neoplastic cells were strongly positive for desmin, calponin, and vimentin. Approximately 80% of the neoplastic cells were positive for the proliferation marker Ki-67. They were negative for smooth muscle actin, muscle-specific actin, myoglobin, myogenin, CD117, cytokeratins, carcinoembryonic antigen, epithelial membrane antigen, chromogranin, CD34, CD31, S100 protein, and HMB-45.

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rimary mesenchymal neoplasms of the adrenal gland are rare, with vascular tumors predominating, most likely due to the vascularity of the adrenal gland.1,2 Malignant mesenchymal tumors can arise in the adrenal gland, including rare cases of angiosarcoma, leiomyosarcoma, and malignant peripheral nerve sheath tumors.3-5 The primary smooth muscle neoplasms of the adrenal gland are believed to have originated from the muscular layers of large and small veins of the adrenal gland. Only 3 cases of primary leiomyosarcoma of the adrenal gland have been reported, and they are of the conventional type.3-5 To the best of our knowledge, we present herein the first case of pleomorphic leiomyosarcoma, a variant of leiomyosarcoma that has not been described in the adrenal gland.

REPORT OF A CASE

A 63-year-old man presented with a 1-year history of enlarging right upper quadrant mass. Computed tomography revealed the mass to be in the region of the adrenal gland. The tumor invaded into the upper pole of the right kidney and the posterior aspect of the right hepatic lobe. A pulmonary mass was also detected. A computed tomography-guided biopsy of the mass was performed, and a histologic diagnosis of metastatic pulmonary carcinoma to the adrenal gland was rendered. The patient received preoperative chemotherapy (paclitaxel), resulting in considerable reduction of the size of the lung mass; however, the adrenal mass continued to enlarge. A composite resection was attempted, which included a right hepatic lobectomy, cholecystectomy, right adrenalectomy with a large tumor, and right radical nephrectomy. The patient died shortly after surgery. An autopsy was not performed.

Gross Findings

A large (25 × 12 × 12-cm), hemorrhagic, multinodular mass was seen completely replacing the right adrenal gland with no residual normal tissue identified (Figures 1 and 2). The tumor invaded into the right lobe of the liver and the upper pole of the right kidney. The tumor was well demarcated from both the hepatic and renal parenchyma by a thick fibrous capsule.

Histologic Findings

Histologic sections showed a diffuse proliferation of pleomorphic, neoplastic cells (Figure 3). The cells were large and polygonal and had prominent nucleoli. In areas, pleomorphic neoplastic cells and bizarre mitotic figures were noted (Figure 4). Perivascular growth of tumor cells and large irregular zones of necrosis were present. Typical features of smooth muscle tumors, such as spindled neoplastic cells with cigar-shaped nuclei arranged in fascicles, were not seen.

Immunohistochemical Findings

The neoplastic cells were strongly positive for desmin (Figure 5), calponin (Figure 6), neuron-specific enolase, and vimentin. They were negative for smooth muscle actin, muscle-specific actin, myoglobin, myogenin, CD117, cytokeratins (AE1/AE3), carcinoembryonic antigen, epithelial membrane antigen, chromogranin, CD34, CD31, S100 protein, and HMB-45. Ki-67 labeled approximately 80% of the neoplastic cells.

MATERIALS AND METHODS

Four-micrometer-thick sections were cut from the paraffin blocks and stained with hematoxylin-eosin. Additional paraffin sections of selected blocks were obtained for immunohistochemical studies, which were performed on an automated immunostainer (Ventana, Biotek System, Tucson, Ariz) using the standard avidin-biotin peroxidase complex technique and the heat-induced epitope retrieval buffer. The following primary antibodies were used: alpha smooth muscle actin (1A4, 1:400; Dako Corporation, Carpinteria, Calif), muscle-specific actin (HHF-35, 1:200; Biomeda

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Figure 1. A multinodular tan mass surrounded by thick fibrous capsule is seen adjacent to the kidney.

Figure 2. The tumor invades into the right hepatic lobes.

Figure 3. A diffuse proliferation of pleomorphic neoplastic cells (hematoxylin-eosin, original magnification ×100).

Figure 4. Bizarre neoplastic cells and abnormal mitotic figures (hematoxylin-eosin, original magnification ×100).

Figure 5. Strong desmin immunoreactivity by the neoplastic cells (desmin immunoperoxidase, original magnification ×100).

Figure 6. Strong calponin immunoreactivity by the neoplastic cells (calponin immunoperoxidase, original magnification ×100).

Corporation, Foster City, Calif), calponin (CALP, 1:150; Dako), desmin (D33, 1:50; Dako), myoglobin (1:12000; Dako), myogenin (FD5, 1:50; Dako), Ki-67 (MIB-1, 1:75; Zymed Laboratories, South San Francisco, Calif), CD117 (c-Kit, 1:400; Santa Cruz Biotechnology, Santa Cruz, Calif), AE1/AE3 (1:50; Zymed Laboratories), CD31 (Dako), CD34 (QBend, 1:40; Dako), S100 protein (1:1200; Dako), HMB-45 (1:100; Dako), neuron-specific enolase (BBS/NC/VI-H14, 1:4000; Dako), vimentin (1:200; Dako), chromogranin (DAK-A3, 1:700; Dako), epithelial membrane antigen (E29, 1:200; Dako), and carcinoembryonic antigen (1:200; Dako).
COMMENT

Only a few cases of primary smooth muscle neoplasms of the adrenal gland have been reported.3–5 These tumors most likely arise from the smooth muscle wall of the central adrenal vein and its branches.1,2 The clinical pathologic data of these cases and of our case report are summarized in the Table. The ages of the patients range from 30 to 63 years. All the tumors were large, ranging in size from 11 to 25 cm in greatest dimension. Lung or bone metastasis is documented in one case each. It is of interest that one case of leiomyosarcoma of the adrenal gland has been reported in association with Epstein-Barr virus and acquired immunodeficiency syndrome, since leiomyosarcomas are the most common mesenchymal neoplasm in that setting.5

In a poorly differentiated tumor such as ours, immunohistochemical and ultrastructural studies are essential for classification. Conventional leiomyosarcomas, such as the 2 previously reported cases, would invariably show reactivity for smooth muscle markers such as smooth muscle actin and/or muscle-specific actin in 90% to 95% and desmin in 70% to 90% of the cases.3,5,8 In contrast, studies have shown a marked variability in the expression of smooth muscle markers in pleomorphic leiomyosarcomas.9 In a large series by Oda et al,9 37.5% of the pleomorphic leiomyosarcomas of various sites are desmin positive, 46.4% are muscle-specific actin positive, and 50% are smooth muscle actin positive. Although there is a lack of smooth muscle and muscle-specific actin expression, the presence of strong desmin expression throughout a tumor such as ours is indicative of myoid differentiation. In addition, the neoplastic cells are strongly positive for calponin, a 34-kd protein that is involved in the regulation of smooth muscle contraction.10,11 Calponin appears to be restricted to smooth muscle.10,11 Moreover, the lack of myoglobin and myogenin expression by our tumor excludes the possibility of skeletal muscle origin. The proliferative index of our tumor is very high. In a large series of pleomorphic leiomyosarcoma by Oda et al,9 the MIB-1 labeling index was found to be significantly higher than that of ordinary leiomyosarcoma.

The differential diagnosis of our tumor includes metastatic carcinoma, metastatic sarcoma, direct extension into the adrenal gland by a primary retroperitoneal sarcoma, sarcomatoid renal cell carcinoma, malignant fibrous histiocytoma, malignant melanoma, epithelioid angiosarcoma, and pleomorphic rhabdomyosarcoma. A metastatic lesion would likely involve both adrenal glands. The fact that our tumor completely replaces the right adrenal gland and invades into the kidney and the liver favors an adrenal primary rather than a primary retroperitoneal sarcoma. The distinct demarcation of our tumor from the kidney by a thick fibrous capsule, the lack of cytokeratin expression, and the strong desmin positivity exclude the possibility of sarcomatoid renal cell carcinoma. Malignant melanomas would express S100 protein, HMB-45, or both. Epithelioid angiosarcoma would express vascular markers such as CD34 and CD31. Xanthoma cells and a prominent inflammatory infiltrate would be present in malignant fibrous histiocytoma. Pleomorphic rhabdomyosarcoma would have cells with cross-striations, immunostaining for myoglobin and myogenin in addition to desmin, and ultrastructural evidence of skeletal differentiation.

Recently, documentation of therapeutic response to the tyrosine kinase inhibitor STI571 in a patient with a metastatic gastrointestinal stromal tumor raises an important therapeutic implication for tumors expressing CD117.12 However, our tumor is negative for CD117. This is not a surprising result, since expression of CD117 has been found to be limited in a large series of 365 soft tissue sarcomas.13

References