Fine-Needle Aspiration of Renal Angiosarcoma

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• Angiosarcoma of the kidney is an unusual neoplasm, and primary renal angiosarcoma is exceedingly rare, with fewer than 11 well-documented cases reported to date. To our knowledge, no publication to date has correlated the fine-needle aspiration cytologic findings in renal angiosarcoma with the gross, histologic, and immunohistochemical findings. A 50-year-old man presented with a left kidney mass and multiple liver and pulmonary nodules. Computed tomography–guided fine-needle aspiration biopsies of the renal mass and a hepatic nodule were performed and demonstrated malignant spindle cells consistent with angiosarcoma. The diagnosis was confirmed at autopsy through histologic examination and associated ancillary studies. This case presents the fine-needle aspiration cytologic findings in renal angiosarcoma and correlates these findings with the gross pathologic, histologic, and immunohistochemical findings.

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Angiosarcoma involving the kidney usually represents metastasis from a cutaneous or visceral primary lesion. Angiosarcoma primarily arising in the kidney is a very rare neoplasm, with fewer than 11 cases reported in the English literature to date. We present a case of renal angiosarcoma presenting as a large kidney mass with diffuse lung and liver involvement. Furthermore, we correlate the results of fine-needle aspiration cytology with the findings of autopsy, histology and immunohistochemistry. To our knowledge, no similar comprehensive case analysis has been reported previously in the literature.

REPORT OF A CASE

A 50-year-old man with presenting symptoms of flank pain and hemoptysis was found to have a large left kidney mass with multiple liver and pulmonary nodules by computed tomographic scan. The patient's past medical history was significant only for prior head trauma and subsequent subdural hematoma. He had no prior radiation or exposure to vinyl chloride or Thorotrast. The left kidney mass and a liver lesion were sampled by computed tomography–guided fine-needle aspiration cytology and yielded malignant cells. Shortly after diagnosis, the patient developed tumor-associated hemorrhage and liver failure, resulting in his death. A postmortem examination was performed, and the anatomic, histologic, and immunohistochemical findings were correlated with the cytologic findings.

PATHOLOGIC FINDINGS

Radiologic Findings

Multiple diffuse, single, and confluent nodules were present in all lung fields and liver lobes. The left kidney contained the largest single lesion, a prominent, destructive, irregularly enhancing mass.

Cytologic Findings

Methods.—Computed tomography-guided needle aspiration of 1 liver lesion and the left kidney were performed. The smears were fixed in 95% alcohol and stained with the Papanicolaou method. Air-dried slides were also prepared and stained with the Diff-Quik method. Autopsy material was fixed in treated formalin and embedded in paraffin, and hematoxylin-eosin–stained slides were made from each block. Mucin (mucicarmine) and immunohistochemical stains were performed on sections of neoplasm from the kidney and liver. The following antibodies and dilutions were used: cytokeratin cocktail (1:800; Dako Corporation, Carpinteria, Calif), S100 (1:800; Enzo Diagnostics, Inc, Farmingdale, NY), HMB-45 (1:50; Dako), CD34 (1:200; Becton-Dickinson, Mountain View, Calif), factor VIII (1:3200; Dako), chromogranin (1:800; Enzo), vimentin (1:80; Dako), and muscle actin (1:1; Ventana Medical Systems Inc, Tucson, Ariz).

Renal and Hepatic Fine-Needle Aspiration.—Hypocellular to moderately cellular smears were composed of large, plump spindled cells, which were up to 8 times the diameter of surrounding red cells. Cells were primarily single and noncohesive, with rare groups of 2 to 16 cells. Nuclei were eccentric, hyperchromatic, and pleomorphic with prominent nucleoli. Occasional binucleated cells were identified. The cytoplasm, which tapered into the background, was abundant, wispy, and pale. Fine cytoplasmic processes extended from many cells, and rare groups formed primitive vascular structures (Figure 1). The cytoplasm of many cells contained 1 to 3 discrete, "punched-out" vacuoles (Figure 2). These vasoformative lumens sometimes contained fragmented red blood cell by-products that were densely basophilic on Papanicolaou and on Diff-Quik stains (Figure 3). These by-products were lysed by treatment in 5% acetic acid solution. Intracytoplasmic hemosiderin deposition, while present, was minimal. Mitoses were sparse. The malignant cells of the liver and kidney smears were morphologically identical, but the liv-
er aspiration showed greater cellularity. Abundant red blood cells were present in the background. Benign hepatocytes were also present in the liver aspirates, noted by their bland, small, round nuclei and polygonal shape.

**Autopsy Findings**

The external examination was remarkable for jaundice and pedal edema. The internal examination revealed 200 mL bloody ascites and bilateral hemothoraces. The right lung and left lung weighed 1300 g each. The lung parenchyma was dark red and contained multiple isolated and confluent hemorrhagic nodules ranging in size from 1.0 to 3.0 cm. The liver weighed 3000 g and was diffusely replaced by multiple confluent, dark, hemorrhagic nodules infiltrating yellow and green parenchyma. Copious hemorrhage was admixed within and adjacent to the masses. The left kidney weighed 500 g and the right kidney weighed 210 g. The left kidney had a 9 × 9 × 7-cm, red, hemorrhagic cortical mass, which replaced the superior two thirds of the parenchyma and extended into the soft tissue. The right kidney was without macroscopic abnormalities.

**Histologic Findings**

Histologically, the hepatic and pulmonary tumors were composed of anastomosing vascular channels lined by plump malignant spindle cells with hyperchromatic pleomorphic nuclei. The cells contained intracytoplasmic lumens with red cells in various stages of degeneration (Figure 4). The staining of these by-products ranged from red to densely basophilic. There was associated hemorrhage. The renal cortical mass, which represented the largest isolated mass lesion, showed the same histologic process. However, the kidney lesion was associated with more prominent necrosis. Mucicarmine stain, performed on both the renal and hepatic lesions, was negative in the malignant cells. Immunohistochemistry demonstrated a vascular origin for the malignant cells with factor VIII and CD34 positivity. They were additionally positive for vimentin and negative for cytokeratin, actin, and chromogranin. The features were therefore consistent with angiosarcoma.

**COMMENT**

This case illustrates the cytologic findings of renal angiosarcoma with gross and histologic correlation. The ini-

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**Figure 1.** Fine-needle aspiration specimen showing spindle cells with fine cytoplasmic processes and vascular lumen (microacinar) formation (Diff-Quik, original magnification ×200).

**Figure 2.** Fine-needle aspiration specimen showing focally prominent intracytoplasmic vacuoles (Papanicolaou, original magnification ×200).

**Figure 3.** Fine-needle aspiration specimen demonstrating an intracytoplasmic lumen containing fragmented red blood cell by-products, which stained densely basophilic (Papanicolaou, original magnification ×200).

**Figure 4.** Autopsy histologic liver specimen showing discohesive anastomosing vascular channels lined by plump malignant spindle cells. Intracytoplasmic red blood cells and red blood cell by-products in various stages of degeneration are readily apparent (hematoxylin-eosin, original magnification ×100).
tial aspirates demonstrated highly pleomorphic, clearly malignant cells. The kidney aspirate was less cellular, most likely secondary to the greater tumoral necrosis demonstrated on histologic examination. The differential diagnosis of the renal aspirate included primary sarcomatoid renal cell carcinoma and, although statistically less likely, renal angiosarcoma. The cytologic presence of neovascular structures, particularly the presence of intracytoplasmic lumens containing red cell by-products, made us favor the diagnosis of angiosarcoma. The noncohesive nature of the cells with their long, fine cytoplasmic processes was consistent with sarcoma, although renal cell carcinoma may be similarly dispersed. While sarcomatoid renal cell carcinoma is also markedly pleomorphic with spindled or straplike cells, the cytoplasm is generally more dense and well defined. These cell types have been compared to rhabdomyosarcoma and malignant fibrous histiocytoma, respectively.2

Intracytoplasmic vacuoles in renal cell carcinoma tend to be smaller, more numerous, and do not contain dense inclusions. Cytologically, the presence of vasoformative structures, copious blood, and cytoplasmic hemosiderin and the lack of epithelioid areas also support a diagnosis of angiosarcoma. The presence of "erythrophagocytosis," intraluminal red blood cells or their by-products, and intracytoplasmic vascular luminal formation are important cytologic and histologic clues to the diagnosis. Histologic examination highlighted these features and showed the transition of intracytoplasmic red cells through various stages of degeneration. However, immunohistochemistry was necessary to confirm the diagnosis of angiosarcoma, with positive results for vimentin, factor VIII, and CD34, but negative results for keratin.3

The kidney is the likely primary origin of the angiosarcoma, based on the clinical presentation of flank pain coupled with the gross findings of a single large lesion replacing the kidney and multiple metastatic small pulmonary and hepatic lesions. Angiosarcomas of the kidney, whether primary or metastatic, are very rare neoplasms, and to our knowledge only 11 reported cases of renal primaries have appeared in the English literature to date.1 Most angiosarcomas arise in the skin, characteristically on the scalp or face of elderly men.4 Angiosarcoma usually presents with multifocal disease and a poor prognosis.5 Although no known risk factors for renal angiosarcoma have been identified, angiosarcomas arising elsewhere have known predisposing factors,6,7 including exposure to arsenic, Thorotrast, and polyvinyl chloride (hepatic), as well as radiation and posttreatment lymphedema (soft tissue).

The cytologic features of angiosarcomas have been previously described by Liu and Layfield,8 based on a study of 11 cases, and by Boucher et al9 in a study of 15 cases. The originating sites in Liu and Layfield's cases included liver, breast, skin, and soft tissue. The originating sites in the study by Boucher et al included lymph nodes, soft tissue, scalp, bone, pleural fluid, and breast. Neither study included kidney. Boucher et al described vasoformative structures in 10 of their cases, consisting of microacinar structures, arborization of microtissue fragments, intracytoplasmic lumens, and signet ring cells. Our case also demonstrates striking neovascular structures, including intracytoplasmic vacuoles and lumens containing fragmented red blood cell by-products. In addition, intracytoplasmic hemosiderin was identified. These features are consistent with neovascular formation and should be highly suggestive of angiosarcoma.

This report correlates fine-needle aspiration cytologic gross, and histologic findings in renal angiosarcoma. As this entity is quite rare, and the cellularity of fine-needle aspirates is often scarce and somewhat nonspecific, initial considerations included sarcomatoid renal cell carcinoma, poorly differentiated carcinoma, and sarcomas. Conspicuous cytologic atypia, copious blood, and neovascular structures, coupled with clinical and radiologic features, may yield the correct diagnosis. However, histologic and immunohistochemical confirmation is often required to ensure correct interpretation.

References