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Teaching case

Primary renal myxofibrosarcoma

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ABSTRACT

Kidney sarcomas are rare, representing only 1% of malignant renal tumors. We herein report the case of a 70-year-old woman that was admitted for an episode of confusion in relation to hypertensive encephalopathy. Imaging investigations revealed a large mass in the right kidney with extension to the renal hilum. The patient underwent right open radical nephrectomy. The histopathologic study disclosed a 15-cm, myxoid and cellular, pleomorphic tumor with elongated, curvilinear, thin-walled vessels, and focal necrosis that involved the upper and middle segments of the kidney. Immunohistochemically, the tumor cells showed strong positivity for vimentin, bcl2 protein (nuclear staining pattern), CD34, CD99, and alpha-methylacyl coenzyme A racemase. The tumor was diagnosed as myxofibrosarcoma (MFS) grade 2 according to the FNCLCC system. To the best of our knowledge, this is the first report of an MFS arising from the kidney. Thus, MFS is an uncommon soft tissue tumor that can exceptionally arise from the kidney. The differential diagnosis with other myxoid tumors is of vital importance because it includes lesions with subtle differences and extremely variable biological behavior. Radical surgery is the treatment of choice. Long-term follow-up is recommended because of the tumor's capability for local recurrence and distant metastasis.

Introduction

Myxofibrosarcoma (MFS) is an uncommon soft tissue tumor [1], previously known as the myxoid variant of malignant fibrous histiocytoma [35]. It is one of the most common sarcomas in elderly patients, with the majority arising in the subcutaneous tissues of the extremities. The location in the retroperitoneum occurs in less than 3% of cases [26]. The neoplasm is regarded as a malignant fibroblastic lesion with variable myxoid stroma. Histologically, it can be classified into three grades according to the grading system of the French Federation of Cancer Centers Sarcoma group (FNCLCC) [5]. Local recurrence occurs in over 50% of cases. Intermediate (grade 2) and high-grade (grade 3) neoplasms are capable of metastasizing [26].

Primary renal sarcomas in adults are rare tumors, accounting for around 1% of all primary renal malignancies [13,31]. Most of these sarcomas include leiomyosarcoma, osteosarcoma, angiosarcoma, rhabdomyosarcoma, synovial sarcoma, pleomorphic undifferentiated sarcoma, and fibrosarcoma. Leiomyosarcoma is by far the most frequent renal malignant mesenchymal tumor [4,31].

As far as we are aware, a primary MFS of the kidney has not been described. We report herein what is, to the best of our knowledge, the first documented case of this type of renal sarcoma.

Case report

A 70-year-old woman was admitted for an episode of confusion and frontal headache in relation to hypertensive encephalopathy. Her blood pressure was 22/10 mm. Hg. Past medical history was significant for bilateral knee prostheses. Physical examination revealed a palpable painless mass in the right flank and hepatomegaly. Routine blood analysis and biochemical studies were within normal limits. After controlling blood pressure, symptoms disappeared. Abdominal ultrasonography showed a 10.8 cm × 10 cm. solid mass that replaced the upper two thirds of the right kidney. Contrast-enhanced computed tomography (CT) scan of the abdomen and pelvis revealed a heterodense, enhanced, solid mass with well-defined contours whose diameters were 10.6 cm × 9.3 cm × 10.9 cm (Fig. 1A). The mass contacted the

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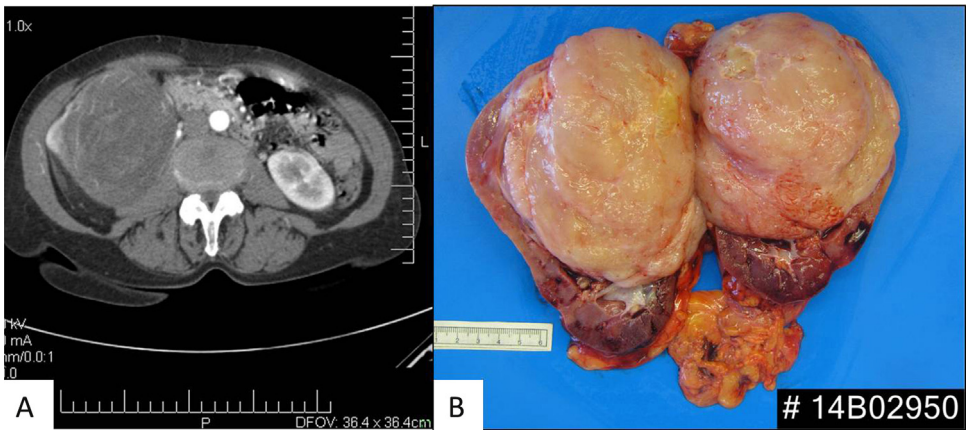

Fig. 1. Myxofibrosarcoma of the right kidney. (A) Contrast-enhanced computed tomography scan shows a solid mass with well-defined contours of the right kidney. (B) Gross view of an unencapsulated, glistening, gelatinous pinkish tumor occupying the upper and middle segments. Areas of necrosis are dull with yellow-green coloration.

parietal peritoneum, the psoas muscle and the perirenal fascia without evidence of invasion. The tumor pushed the right colon forward, and displaced medially the vena cava and the head of the pancreas. The artery and the right renal vein were elongated. The right renal vein was compressed by the tumor, without evidence of infiltrative growth. No enlarged lymph nodes were identified in the mesentery or retroperitoneum. The left kidney showed no alterations. The CT scan of the cranium and thorax showed no abnormalities. The presumptive clinical diagnosis was renal cell carcinoma of the right kidney. The patient underwent open radical right nephrectomy without complications.

A nephrectomy specimen (15 cm × 13 cm × 11 cm, 850 g) with attached ureter (5.5 cm) and perirenal adipose tissue was received. The specimen was bisected to reveal a 12 cm, circumscribed, with pushing margins, and bulging cut surface, unencapsulated tumor occupying the upper and middle segments of the kidney. The neoplasm extended to the renal sinus and the hilum involving the surgical margin.

This tumor showed a pinkish, glistening, gelatinous surface with yellow-green, dull areas of necrosis (Fig. 1B). Microscopic examination revealed a well-delimited, vaguely nodular tumor with varying proportions of myxoid and solid cellular components (Fig. 2A). Myxoid areas were hypocellular and contained spaced spindle cells presenting either a fascicular or a haphazard growth, and elongated, curvilinear capillaries (Fig. 2B). The cells sometimes showed enlarged hyperchromatic atypical nuclei (Fig. 2C). The myxoid areas were randomly arranged and represented 36% of the neoplasm. There was transition from the low-grade myxoid areas to the solid components (Fig. 2A). In cellular, solid areas, the tumor cells formed vague fascicles or showed a patternless growth. Focal areas of necrosis were present (Fig. 2D). A heavy inflammatory infiltrate composed mainly of lymphocytes and plasma cells was evident around some vessels (Fig. 2C). Cytologically, large, spindle, round or stellate, bizarre and sometimes multinucleated giant cells with abundant eosinophilic cytoplasm and hyperchromatic nuclei were commonly found. Neoplastic cells with multiple cytoplasmic mucin-containing vacuoles and nonscalloped nuclei (pseudolipoblasts) were frequently seen (Fig. 3A). These vacuoles were positive for Alcian blue (pH, 2.5) stain (Fig. 3B). Multinucleated giant cells with cytoplasmic vacuolization were also observed (Fig. 3C). The mitotic count mean after counting 60 high power fields (hpf) was 5 mitoses/10 hpf. Fig. 3D shows two mitoses in the same field.

Immunohistochemically, the tumor cells showed strong positivity for vimentin, bcl2 protein (nuclear staining pattern) (Fig. 4A), CD34 (Fig. 4B), CD99 (Fig. 4C), and alpha-methylacyl coenzyme A racemase (AMACR) (Fig. 4D); and negativity for cytokeratin (CK) AE1/AE3, CK19, CK7, PAX8, muscle-specific actin (HHF35), alpha-smooth muscle actin, heavy caldesmon, desmin, myogenin, S100 protein, CD31, CD68 (KP1), MUC4, CDK4, MDM2 and EGFR. About 80% of cells displayed nuclear staining for p53 protein. Ki67 labeled 26% of the neoplastic cells. The tumor was grade 2 within the FNCLCC system (differentiation score 2, mitosis count score 1, necrosis score 1, total score 4).

Fluorescence *in situ* hybridization (FISH) for MDM2 amplification (probe FISH MDM2, 12q15, and CEP Chr12. SureFISH 12q15 MDM2 180kBRD, SureFISH Chr12 CEP 704 kb GR) and for DDIT3 (CHOP) (probe FISH BA DDIT3, 12q13.3 and DDIT3, 12q14.1 SureFISH 12q13.3DDIT3 3, BA 537 kb P5GR and SureFISH 12q14.1 DDIT3 5, BA 498 kb P5RD) were performed. MDM2 pattern showed polysomy with multiple copies of the gen and of the centromere. Amplification was not observed. DDIT3 (CHOP) pattern was normal.

The non-tumor kidney showed hyperplastic arteriolosclerosis.

The patient underwent radiotherapy with good tolerance. The total dose was 58 Gy. Eleven months after intervention, she remained asymptomatic. Physical examination was within normal limits. Thoraco-abdominal CT scan showed no evidence of tumor recurrence.

Discussion

The term MFS highlights the tumor myxoid matrix and implies a fibroblastic origin. Tumor cells do not show histiocytic differentiation. Cytogenetically, MFS is characterized by complex chromosomal aberrations, none of which is specific. This tumor constitutes a distinct clinicopathologic entity [26] included in the WHO classification of soft tissue tumors [27].

Significant morphologic features in the diagnosis of our case include: a vaguely nodular growth pattern; presence of an abundant myxoid matrix; a prominent vascular pattern of elongated curvilinear small capillaries; fusiform, round or stellate tumor cells with indistinct cell margins and a striking inflammatory infiltrate especially around vessels and adjacent tumor cells. Pseudolipoblasts (cells with one large or multiple small cytoplasmic mucin-containing vacuoles) and tumor giant cells with hyperchromatic atypical nuclei and acidophilic cytoplasms were prominent. Tumor differentiation, mitotic activity and focal areas of necrosis qualified our lesion as FNCLCC grade 2 MFS. Mentzel et al. [26] classified the tumor into three grades according to its cellularity and atypia: low, intermediate, and high-grade. Presence of necrosis could qualify our lesion as high-grade. However, as for cellularity and atypia, the lesion is of intermediate grade. Reactivity for CD34