

Renal Angiomyolipoma with Vascular Leiomyomatous Features

- A Case Report -

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Angiomyolipoma is the most common mesenchymal tumor of the kidney. It occurs sporadically and is associated with tuberous sclerosis. It can appear in any organs, but most commonly in the kidney, and it appears slightly more in females. Angiomyolipoma is pathologically composed of three heterogeneous components of blood vessels, smooth muscle cells and fat cells of varying proportion, which occasionally make several unusual histologic variants. We describe a variant of renal angiomyolipoma simulating vascular leiomyoma on routine hematoxylin-eosin stain; prominent thick-walled blood vessels interspersed with proliferation of smooth muscle cells and total absence of fat cells. Perivascular spindle-shaped smooth muscle cells were reactive for smooth muscle actin, desmin and HMB-45 immunostains. This case illustrates vascular leiomyoma-like angiomyolipoma, which was finally diagnosed on the basis of HMB-45 immunostain, and also raises a question about the real existence of renal vascular leiomyoma.

Key Words : Angiomyolipoma-Angiomyoma-Kidney Neoplasms

Angiomyolipoma is the most common mesenchymal renal lesion comprising three mesenchymal components, whereas vascular leiomyoma that seemingly arises from the smooth muscle of blood vessels is common in the skin.¹ Only two cases of renal vascular leiomyomas have been reported.^{2,3} Here, we emphasize the usefulness of HMB-45 immunostain for detecting unusual variants of angiomyolipoma that are undetectable on routine hematoxylin and eosin stain.

CASE REPORT

A 62-year-old woman with a vague abdominal pain she'd had for several years was presented. Gastroduodenal endoscopy revealed gastric cancer at the posterior wall of the antrum. Preoperative abdominal computed tomography (CT) disclosed a 1.3 cm-sized additional bulging mass at the corticomedullary junction of the midportion of the left kidney. On abdominal sonography, the mass showed a slightly increased echogenicity with low inter-

nal echogenicity. Under the impression of synchronous, double primary tumors, subtotal gastrectomy and left simple nephrectomy were performed.

PATHOLOGIC FINDINGS

Resected specimens were fixed in formalin and embedded in paraffin. Representative sections from the gastric lesion and all sections of the renal mass were taken for histologic evaluation. Immunohistochemistry using the avidin-biotin peroxidase complex method was performed. An ulceroinfiltrative tumor of the stomach measured 3 × 2.6 × 2.5 cm. Microscopically, the tumor was of a poorly differentiated adenocarcinoma of a diffuse type, and it extended into the proper muscle layer. Metastasis to 1 out of 25 perigastric lymph nodes was found (T2N1M0). The resected left kidney showed a protruding, oval, cortical mass which measured 1.3 × 1 × 1 cm (Fig. 1). It was well demarcated from the renal parenchyma and the renal calyces were well preserved.

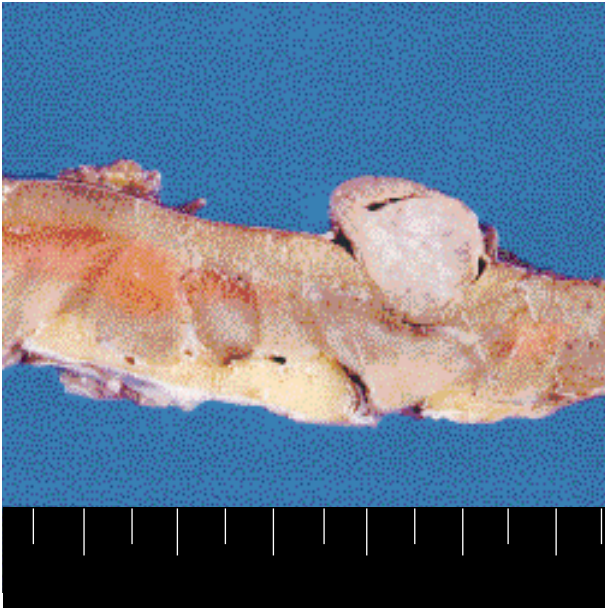


Fig. 1. An oval, well circumscribed, solid protruding mass with whitish tan cut surface is found at the corticomedullary junction of the middle portion of the kidney.

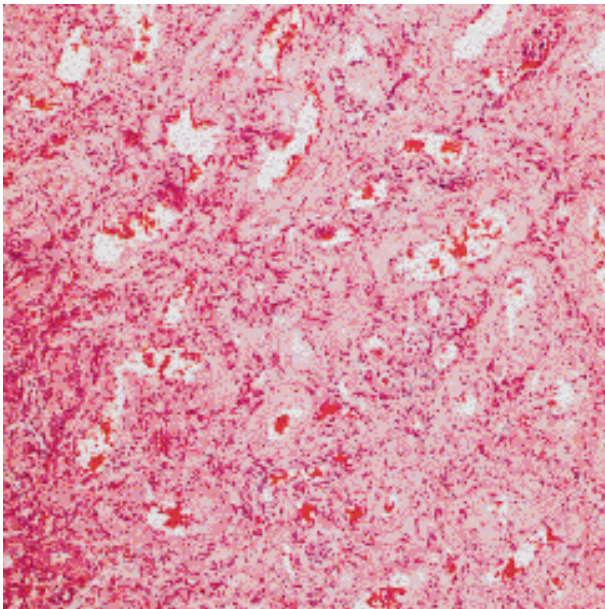


Fig. 2. The lesion consists of thick-walled vessels and intervascular spindle cells.

The cut surface of the tumor was homogeneously brown to tan and focally trabeculated. Microscopically, the tumor was made up of intersecting fascicles of spindle cells blending with thick-walled vessels and most of the vascular lumina were patent (Fig. 2), most of the vessels appeared to be veins and some were stained with van-Gieson elastic stain. Although we examined entire sections

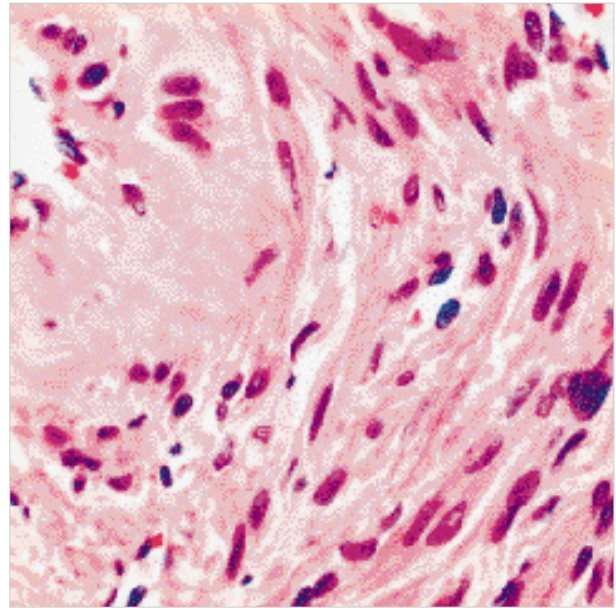


Fig. 3. Spindle-shaped smooth muscle cells blend with thick-walled vessels.

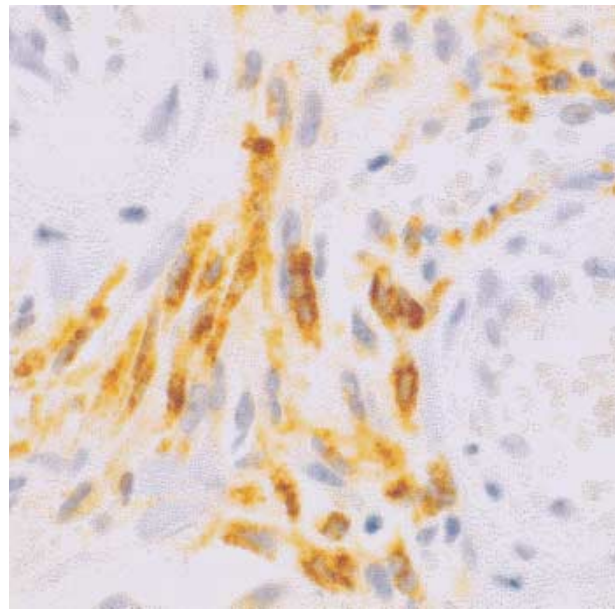


Fig. 4. Spindle cells are strongly positive for HMB-45.

of the renal mass, other components seemed to be absent. Neither cellular atypism nor mitosis was found, and the tumor was initially interpreted as vascular leiomyoma. Some of the spindle cells with lightly eosinophilic and granular cytoplasm were present around the vessels (Fig. 3). Immunohistochemically, these spindle cells were strongly immunoreactive for smooth muscle actin (1A4, 1:100, Dako, Glostrup, Denmark), desmin (D33,

1:100, Dako), progesterone receptor (1:50, Novocastra, Newcastle, U.K.) and estrogen receptor (1:100, Novocastra). Strong immunoreactivity for HMB-45 (gp100 protein, 1:30, Dako) was also detected in some of these spindle cells (Fig. 4). They were negative for S-100 protein (1:1200, Dako) or pancytokeratin (AE1/AE3, 1:80, Zymed, San Francisco, CA, U.S.A.). From these immunohistochemical results, the diagnosis of the renal mass was revised to an angiomyolipoma lacking in fat component.

Clinically, the patient showed no other stigmata of tuberous sclerosis. Four years after the operation, she is alive without recurrence.

DISCUSSION

The main differential diagnosis in the present case was vascular leiomyoma. Spindle cells were strongly immunoreactive for smooth muscle actin and desmin, reflecting a smooth muscle nature. It is important to detect other components of angiomyolipoma, and the diagnosis of angiomyolipoma could not be made simply on hematoxylin and eosin stain. Angiomyolipoma consists of a varying proportion of three distinct components; mature adipose tissue, spindle to epithelioid smooth muscle cells and thick hyalinized vessels.⁴ These smooth muscle cells are known to be reactive for smooth muscle actin and CD 68 as well as HMB-45 melanocyte-specific antibody.^{5,6} Small mesenchymal nodules lacking fat or vascular components, so called "buds" of angiomyolipoma were defined as small foci of renal angiomyolipoma-like proliferation, measuring less than 20 mm in diameter. Among them, nodules of greater than 1.13 mm were positive for HMB-45, while those of less than 1.13 mm were usually negative for HMB-45.⁷ Recent application of immunohistochemistry has considerably widened the spectrum of angiomyolipomas, concerning both its morphological features and its sites of occurrence. Furthermore, capsular or subcapsular renal leiomyomas aberrantly expressing HMB-45 protein have also been reported.⁸ A tiny bud of renal angiomyolipoma probably originates from connective tissue around renal capsular vessels without fat components, and eventually forms angiomyolipoma having three components. These common features of HMB-45 stainability in vascular leiomyomatous angiomyolipoma and capsular leiomyoma might be ascribed to have originated from the same progenitor cell of the renal capsule, because renal leiomyoma of the pelvis showed HMB-45 immunonegativity.⁸ Absence of abnormal or imperfect vessels under light microscopy, however, can distinguish renal leiomy-

omas from angiomyolipomas irrespective of fat tissue.

Angiomyolipoma can arise in extrarenal sites, with the liver being the most common site. Rare additional sites include the spleen, colon, heart, lung, skin, spermatic cord, nasal cavity and retroperitoneal soft tissue, and even in the bone.⁹ Angiomyolipoma appears as variable morphologic spectrum such as the monotypic epithelioid variant, pleomorphic epithelioid variant or lymphangioliomyoma.¹⁰⁻¹² Other unusual forms of angiomyolipoma include the oncocytomatous, lipomatous and leiomyomatous variants, which resemble lipoma or well-differentiated liposarcoma, and leiomyoma or leiomyosarcoma, respectively.¹³ A case of angiomyolipoma with few fat components and marked cystic degeneration which was initially misdiagnosed as cystic renal cell carcinoma has been reported.¹⁴ For specific histologic variants in unusual locations, immunohistochemistry should be performed to arrive at the correct diagnosis, including negative reactivity with anticytokeratin antibodies, positive reaction with antibodies to smooth muscle actin, and consistent expression of melanogenic markers, particularly HMB-45, followed by Melan-A, tyrosinase, and microphthalmia transcription factor.¹⁵

The vascular leiomyomatous variant has not yet been described in renal angiomyolipoma, and we have found only two cases of renal angiomyomas that have been pathologically confirmed.^{2,3} However, it is difficult to establish whether both of the two reported cases are true vascular leiomyomas, because immunohistochemical and histological findings in those papers were incomplete.² Furthermore, inadequate sampling of the tumor in the Heesewijk's case may cause the researcher to miss the presence of adipose tissue. Heesewijk *et al.*² reported that ultrasonography might be helpful in indicating the fat-containing mass of increased echogenicity and that CT is a highly sensitive tool for diagnosing vascular leiomyoma because fat tissue within the lesion appears as a low intensity value. However, radiologic methods cannot fully detect minor proportions of fat tissue. Therefore, angiomyolipoma should be included in the preoperative diagnosis regardless of fat intensity.

In summary, we report a vascular leiomyomatous variant of renal angiomyolipoma that was finally diagnosed after immunohistochemistry. Whenever facing highly vascular renal lesions with thick-walled vessels, it should be conceivable that renal angiomyolipomas might appear as variable proportions of fat, even in the total absence of fat components. All such cases should undergo immunostaining for melanogenic markers to confirm the small buds of angiomyolipoma. In our opinion, the real existence of renal vascular leiomyoma is quite doubtful. Further investigation is necessary.

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