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Clinical challenges and management of primary renal epithelioid angiomyolipoma of duplex kidney with paraneoplastic syndrome

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Abstract

Giant renal epithelioid angiomyolipoma of a duplex kidney has rarely been reported, especially in patients with paraneoplastic syndrome. The present report describes a 33-year-old man of Miao nationality who presented with a 6-month history of intermittent dull pain in the left upper abdomen that occurred after eating. Ultrasonography, intravenous pyelography, and computed tomography revealed a mass lesion localized in the left kidney and connected to the left renal artery. Radical nephrectomy was successfully performed, and the postoperative histopathological examination verified the lesion as epithelioid angiomyolipoma. Inpatient treatment for paraneoplastic syndrome was also performed. The present case is discussed in the context of the patient's clinical presentation and imaging findings, drawing attention to the challenges and management of this condition to assist clinicians in practice.

Keywords

Duplex kidney, renal epithelioid angiomyolipoma, paraneoplastic syndrome, clinical challenge and management, treatment, case report

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Introduction

The first case of renal epithelioid angiomyolipoma (EAML) was reported in 1994.[1] Renal EAML consists of two subtypes: classic and epithelioid.[2] This mesenchymal tumor has malignant potential and exhibits the three components of classic angiomyolipoma, although it is mainly composed of proliferating epithelioid cells. In the clinical setting, renal EAML is not only found in the kidney and liver but also in the retroperitoneal, pelvic, and adrenal tissues. EAML, which belongs to the hemangiopericytoma family of tumors, exhibits aggressive biological behavior. However, primary giant renal EAML of a duplex kidney has not been reported to date, especially in a patient with paraneoplastic syndrome. We herein describe a rare case of giant renal EAML in such a patient who was recently admitted to our hospital. We also discuss the clinical challenges and management of this condition.

Case presentation

A 33-year-old man of Miao nationality presented with a 6-month history of decreased strength and anorexia with no obvious cause. These symptoms recurred with dull pain in the left upper abdomen, which was intermittent and obvious after eating. He was admitted to our department for inpatient treatment. Since the onset of symptoms, his body weight had decreased by 13 kg. Physical examination showed light percussion pain in the left kidney area.

Several imaging examinations were performed. Intravenous urography revealed a huge space-occupying lesion on the left kidney and malformation of a duplex renal pelvis and ureter in the right kidney (Figure 1(a) and (b)). The pelvis and calyces of the left kidney were compressed and deformed. Subsequent B-ultrasound examination revealed a large mass exhibiting non-uniform echo. Although its shape was regular, its boundary with the renal parenchyma was unclear. Additionally, the left ventricular artery and left renal vein were compressed, suggesting the possibility of a left kidney tumor. Abdominal computed tomography (CT) showed a large mass with mixed density in the upper pole of the left kidney, and the CT value of the tumor on the plain scan ranged from −79 to 82. The maximum size in the transverse section of CT was about $15.8 \times 12.3 \times 18.7$ cm, and an area of necrotic liquefaction (uneven enhancement) was observed inside the tumor with a clear boundary (Figure 1 (c) and (e)). In the arterial phase, multiple enhanced vascular shadows were connected to the left renal artery, and the left upper renal calyx was dilated (Figure 1(d) and (f)). A sheet-like shadow with water-like density was observed inside, and adjacent tissue structures were displaced under pressure. No enlarged lymph nodes were found in the abdominal cavity or retroperitoneum.

Routine preoperative blood examination revealed a red blood cell count of 3.53×10^{12}/L, hemoglobin level of 75.00 g/L, red blood cell volume of 26.00%, and platelet count of 918.00×10^{9}/L. In addition, the concentration of neuron-specific enolase, a tumor marker, was 124.2 ng/mL. According to the preoperative examinations, the patient had no contraindications for surgery; the blood coagulation function and the electrocardiography and chest radiography findings revealed no significant abnormalities. Retroperitoneal laparoscopic radical resection of the giant tumor of the left kidney with para-abdominal aortic and renal hilar lymph node dissection was performed. We were prepared for conversion to open surgery depending on the intraoperative situation. During the operation, we unexpectedly found duplex ureters in the left kidney, which had not been depicted on the preoperative imaging examination,

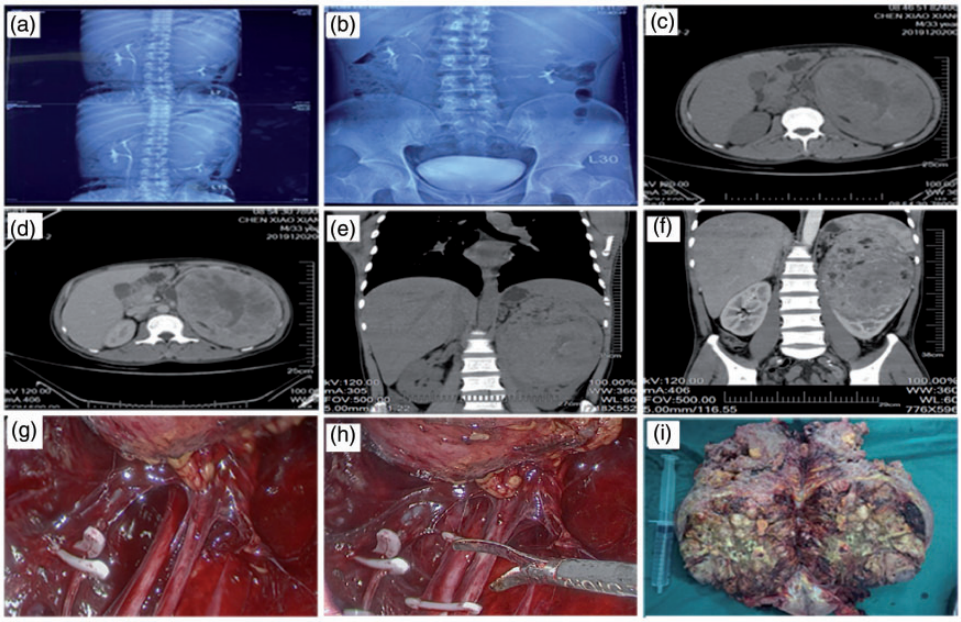

Figure 1. (a and b) Intravenous pyelography examination revealing duplex kidney. (c) Computed tomography scan revealing a large mass with mixed density in the upper pole of the left kidney with a clear boundary. (d) Three-phase enhanced computed tomography scan showing obviously uneven enhancement in the necrotic liquefied area. (e) Coronal plain computed tomography scan. (f) Coronal enhanced computed tomography scan. (g) Finding of a double ureter during the operation. (h) Laparoscopic radical resection of the kidney tumor. (i) The large mass following radical nephrectomy.

and the perirenal fascia was intact without tumor invasion (Figure 1(g), (h)).

A routine blood re-examination the day after surgery revealed a platelet count of 671.00×10^9/L and thrombocytosis level of 0.52% (thrombocytosis was defined as a platelet count of $>300 \times 10^9$/L). On the second postoperative day, the patient developed a sudden disturbance of consciousness with frequent convulsions without an obvious cause, and he exhibited drowsiness and shivering. These abnormalities resolved after symptomatic treatment. On the seventh postoperative day, routine blood examination showed a platelet count of 1012.00×10^9/L and thrombocytosis level of 0.66%; therefore, we advised the patient to take oral aspirin tablets to prevent thrombosis. On the 14th postoperative day, the platelet count was 518.00×10^9/L and the thrombocytosis level was 0.41%. The patient recovered well and was discharged on the 14th postoperative day. On the 23rd postoperative day, a routine blood re-examination showed a platelet count of 390.00×10^9/L and thrombocytosis level of 0.29%. After consideration of these results, we recommended that the patient stop taking aspirin.

A reddish-brown mass of about $19.0 \times 12.0 \times 11.0\,\text{cm}^3$ containing a section with duplex ureters was seen on the left upper kidney during postoperative macroscopic pathologic examination. The cut surface was gray-white and yellow, cauliflower-like, and irregular. Some areas of the section showed hemorrhage and necrosis (Figure 1(i)). Microscopically, the tumor tissue was composed of malformed blood vessels, spindle-shaped smooth muscle

bundles and adipose tissue, and mainly spindle-shaped and polygonal epithelioid cells with abundant eosinophilic granular cytoplasm. Epithelioid-origin ganglionic cells with a large nucleus were observed in some areas. The stroma and nuclear division were easily seen, exhibiting a patchy and stringy arrangement. In some areas, epithelioid-origin ganglion-like cells with a large nucleus could be observed. Anaplasia and mitosis were also easily observed, showing sheet-like and strip-like arrangements. The diagnosis of renal EAML was supported by hematoxylin–eosin staining and immunohistochemical markers (Figure 2(a)), which showed positivity for vimentin, HMB-45, and melan-A; weak positivity for Ki-67 (about 1%–5%); and negativity for epithelial cells (cytokeratin) (Figure 2(b)–(f)). During follow-up after discharge, neither recurrence of the primary lesion nor distant metastasis was found.

Discussion

Renal EAML, a special histological subtype of angiomyolipoma, is a rare mesenchymal tumor with potential malignancy. Its invasive growth, local recurrence, rupture, and metastasis have been described worldwide.[3] Most EAML lesions are located in the kidney, but EAML in the lung, liver, pancreas, bladder, prostate, uterus, ovary, vulva, vagina, and bones has also been reported.[4] Clinically, the age at onset of EAML ranges from 30 to 80 years (average, 49.7 years), and the male-to-female ratio is 9:11.[5] In our patient, a 33-year-old man, the

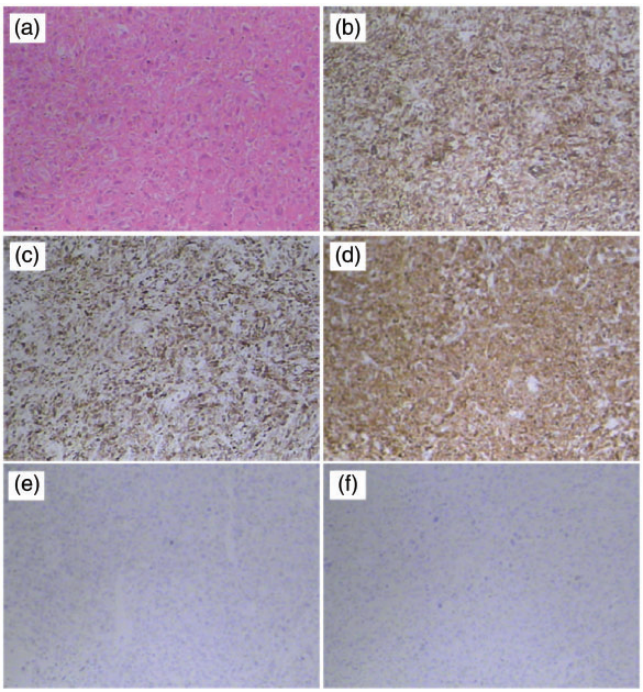

Figure 2. (a) Hematoxylin and eosin staining of the left kidney tumor cells. (b–f) Immunohistochemical staining of the left kidney tumor cells demonstrating positivity for (b) vimentin, (c) the melanocyte marker HMB-45, and (d) the myoid marker melan-A; weak positivity for (e) Ki-67 (about 1%–5%); and negativity for (f) epithelial cells (cytokeratin).

EAML was located in the upper pole of the left kidney.

The etiology of EAML is not yet clear; however, some reports have suggested that it is associated with *p53* mutation and deletion of the *TSC1* and *TSC2* genes.[6,7] Few cases of EAML have been reported, and the clinical symptoms are diverse. If the tumor is complicated with intertumoral malformation, spontaneous rupture of blood vessels may cause sudden back or abdominal pain or even hypotensive shock. In the present case, the patient's gastric body and gastric fundus were compressed by the huge left kidney tumor, resulting in weakness and poor appetite. After summarizing 41 previous cases, Nese et al.[8] found that EAML had five clinical features: the presence of tuberous sclerosis syndrome, tumor necrosis, extrarenal extension or renal vein invasion, carcinoid histology, and a tumor size of >7.7 cm. In the present case, the tumor was relatively larger with necrotic tissue inside and carcinoid tissue in the pathological sections, which is consistent with the above clinical features. However, the tumor occurred in the upper kidney of a duplex kidney. That the tumor only squeezed the lower renal tissue and did not invade the lower renal tissue is considered rare.

EAML is often hypoechoic and shows heterogeneous peak enhancement or pseudocyst formation by ultrasound. Some experts have reported that most cases of EAML manifest as high-density solid lesions on plain scans and a fast-in, slow-out pattern on enhanced CT. The possibility of EAML might be considered when renal tumors are mixed with fatty masses containing large amounts of soft tissue.[9]

If magnetic resonance imaging shows a gradually increasing T1-weighted signal (acute hemorrhage) and low T2-weighted signal (due to the highly cellular nature of the lesion), obvious edge and heterogeneity enhancement can be observed.[10]

Under hematoxylin–eosin staining, EAML in most cases shows proliferation of and vascular invasion by epithelioid cells accompanied by atypia, mitotic activity, necrosis, and hemorrhage. Eosinophilic granular cytoplasm is often abundant in the visual field, and ganglioid-like cells of epithelioid origin are observed in some areas. In most cases, the epithelial cells in EAML tumor tissues are immunohistochemically positive for the melanocyte marker HMB-45 and myoid marker melan-A; weakly positive for E-cadherin and β-catenin; and negative for epithelial cells (cytokeratin), nerve cells (S-100), smooth muscle actin, and desmin.[11,12]

Paraneoplastic syndrome is a set of signs and symptoms that are not caused by direct invasion of a tumor or its metastasis but instead develops secondary to the presumably immune-mediated remote effects of cancer on other systems or organs. Affected patients most commonly present with a high red blood cell sedimentation rate, elevated platelet count, and hormone and immune system abnormalities. In the present case, the high preoperative platelet count might have been caused by the production of interleukin 6 by the tumor cells, stimulating thrombopoietin production in the liver and further induction of megakaryocytes in the bone marrow, finally resulting in thrombocytosis.[13] After the operation, the platelet count gradually returned to normal by anticoagulant therapy (aspirin).

Because of the low incidence of renal EAML in the general population, the treatment methods are not uniform. In the present case, the preoperative examination did not reveal obvious invasion of the surrounding tissues and distant organs. Laparoscopic radical resection of the huge left EAML with conversion to open surgery for tumor removal was performed, and this procedure was combined with abdominal aortic lymph node and renal hilar lymph

node dissection. Modern laparoscopy currently allows radical resection of huge renal tumors while improving the patient's postoperative quality of life and reducing pain. In recent years, the experience level and laparoscopic skills required for huge lesions in an emergency setting have dramatically changed. The beneficial effects of high skill levels are more prominent in an emergency laparoscopy setting. Hence, enhancement of laparoscopic skills is becoming an innovative approach to surgical emergencies.[14]

After regular follow-up in the present case, neither recurrence nor distant organ metastasis was observed at the excision site of the primary lesion. In some patients, however, surgical treatment alone is not curative. Adjuvant treatments such as chemotherapy should also be considered and regularly reviewed.[15,16] Patients who have metastatic EAML or cannot be treated with surgery may be treated with systemic chemotherapy. Some scholars have found that doxorubicin, a chemotherapy drug, has a certain effect on the treatment of renal EAML; however, its long-term effects have not been determined.[17] Additionally, studies have shown that renal EAML is not sensitive to radiotherapy.[18] Kenerson et al.[19] found that the mTOR pathway was abnormally activated during the growth and progression of renal EAML; thus, the application of mTOR inhibitors such as rapamycin, everolimus, and others might lead to tumor reduction. Inoue et al.[20] reported that the MDM2 protein was negative in primary EAML and showed a gradually increasing trend in two patients with metastasis or recurrence. These findings indicate the likelihood of new prognostic factors as treatment targets for EAML.

Conclusions

Renal EAML is a low-grade malignant tumor. Because of its lack of specific clinical symptoms, the findings from a variety of imaging examinations are taken into account, and some patients still need surgical exploration and pathologic examination to attain a definitive diagnosis. Radical surgery may be the main treatment for renal EAML, while chemotherapy and radiotherapy can be used as adjuvant therapies. However, regular follow-up observation is still required after surgery because of the malignant potential of this tumor. Patients with distant metastases may be treated with related chemotherapy and radiotherapy. Further experience with renal EAML is required.

Ethics and consent

This study was based on clinical case, and ethical approval was not required. Written and verbal informed consent was obtained from the patient for publication of this case report and any accompanying images.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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