Epithelioid hemangioendothelioma arising from the kidney
A rare case report
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1. Introduction

Epithelioid hemangioendothelioma (EH) is a rare angiocentric vascular tumor of intermediate biologic behavior with metastatic potential. It was initially grouped along with other hemangiendotheliomas, however due to the aggressive biological behavior, it is now grouped in angiosarcomas according to the current World Health Organization (WHO) classification.\[^{1}\] Hemangioendotheliomas have been reported in various sites, which are most commonly in soft tissues followed by liver, lung, bone, peritoneum, stomach, thyroid, and central nervous system.\[^{2–6}\] Kidney is an extremely rare site, especially for the epithelioid variant. At present, to the best of our knowledge, there are only 4 case reports documenting EH in the kidney.\[^{6–9}\] Obviously, its diagnostic and therapeutic experience remains limited. We aimed to share a case of renal EH from the aspects of clinical, imaging, operative, and pathological findings to provide more information for further study.

2. Case report

2.1. Clinical findings

A 30-year-old woman without family history of malignant tumor was admitted to our hospital with 3-months history of gross hematuria without obvious cause and aggravated for half a month. And this patient had no fever, vomiting, or urinary syndromes. The symptoms were slightly better after being treated with anti-infection treatment. The occasional feeling of discomfort at the waist was unpleasant, so the patient came to our hospital for further treatment. A mass measuring 1.1 cm was noted in the mid pole of the left kidney on computed tomography (CT) images (Fig. 1). Otherwise, she had a history of appendicectomy, and she denied recent weight loss. All other blood analysis including tumor markers and the chest CT completed before surgery showed no abnormalities.

2.2. Imaging findings

Ultrasound examination of abdomen showed a mild separation on the left renal collection system with a range of 35 × 16 mm,
and a low echo mass measuring 14 × 14 mm in the middle upper pelvis. CT scan showed that the left superior partial perfusion of the left kidney was reduced in delayed phase. The local branch of the renal artery was slender and was considered as an inflammatory disease. In the upper left group, the renal calices were partially widened and filled with defects, the diameter was about 1.1 cm. At the upper pole of the left kidney, abdominal magnetic resonance imaging (MRI) showed a nodular shadow with equal signal on T1-weighted images, a long signal on T2-weighted images, and high signal intensity on diffusion-weighted images (DWI) (Fig. 2). According to our imaging findings, it was considered as an inflammatory disease.

2.3. Operative findings

The patient subsequently underwent ureteroscopy and partial left nephrectomy. During operation, a small, soft, and cystic mass measuring about 0.5 cm was identified at the upper pole of the left kidney.
kidney. The intraoperative frozen pathology revealed a renal vascular tumor like lesion in the left renal pelvis with vascular network distribution, and we observed lining cell dysplasia and inflammation, infarction and ulcer (Fig. 3). The patient was uneventful during postoperative course, her postoperative condition was good.

2.4. Pathological findings

Gross examination revealed a gray and red irregular tissue, the size was $1 \times 0.8 \times 0.6$ cm, when opened, the tangent surface was gray red, and with medium texture and locally dirty surface. Histological examination revealed many hemorrhagic necrotic lesions on the surface of the lesion. The proliferative vascular tissue was branched reticulate, the proliferation of endothelial cells was active, and the mucous glue was observed between blood vessels (Fig. 3). No mitoses or necrosis were identified.

Immunohistochemical studies showed CD10: $(0)$, CD31: $(+)$, CD34: $(0)$, D2–40: $(0)$, ERG: $(+)$, ki-67 $(+20\%)$, which may provide a more reliable basis for our diagnosis.$^{[1,6]}$

3. Discussion

EH was reported as a characteristic lesion of soft tissue in 1982.$^{[10]}$ In 2002, the EH was classified as low grade malignant vascular tumor via WHO histologic classification of soft tissue tumor.$^{[11]}$ EH may be discovered in a wide range of age, but it is more common for middle-aged and old people. There is no significant gender difference in the tumor. It can occur at any part of the body, which can be located in the superficial and deep parts, and can also be located in the substantive organs. It occurs in the skin, liver, spleen, lung, kidney, brain, bone, and peritoneum, but it is more common in the limbs and soft tissues, and the main viscera are liver and lung. To the best of our knowledge, the renal EH is an extremely rare case, and there are only 4 cases of primary renal EH reported so far.$^{[6–9]}$ To review the 4 renal EH literatures, 4 patients experienced partial nephrectomy and in good post-operative condition without complications. One of the cases documented that the child patient was reviewed 6 months after surgery and showed no evidence of local recurrence or metastatic disease. No follow-up period and the recently known status of the other 3 cases.

The treatment of EH has no clear standard, and at present, the surgical treatment has been the most common strategy while there are still several differences in treatment effects. Radiotherapy and chemotherapy may also play a role to some extent, but there is no sufficient evidence to support their effects on the treatment of EH. There were 2 EH cases treated by chemotherapy and their clinical symptoms were alleviated.$^{[12,13]}$ Some scholars have suggested that the treatment plan should be individualized, and it is suggested that the cases with positive estrogen and progesterone receptor should be treated with hormone therapy.$^{[13]}$

EH needs to be differentiated from the following diseases.

1. Metastatic carcinoma and malignant melanoma: there are obvious heterotypic and nuclear mitotic figures. There is usually no angiocentric tissue conformation. EH usually has tubular or vacuolated structures that secrete mucus and should be carefully examined for vacuoles containing single red blood cell in the diagnosis. Angiogenic tumors may be indicated. Immunohistochemistry is the most reliable method for identification, positive for metastatic carcinoma epithelium, malignant melanoma HMB45 positive, and no vascular source marker.

2. Angiomyolipoma: due to the great changes of vascular smooth muscle cells in tumors, the bright and empty epithelioid smooth muscle cytoplasm makes it more easily to confuse the vascular components of EH. The main method to avoid misdiagnosis is to take multiple pathological slices and observe carefully. Immunohistochemically, HMB45 positive is helpful for diagnosis.

3. Inflammatory or reactive lesions: EH is sometimes dominated by sclerosing components, and tumor cells are very rare, the
benign reactive lesions of fibrous hyperplasia with extensive collagens are common. When we have similar pathological changes, we should carefully search for strands or loose scattered spindle tumor cells and vacuoles containing single red cells. If necessary, we can exclude them by immunohistochemical examination.

(4) Epithelioid angiosarcoma: the features of epithelioid angiosarcoma are as follows: the specificity of tumor cells is more obvious, the mitosis, tumor size and common hemorrhagic necrosis, common spindle cells in solid areas, and vascular cavities are connected into a network region.

(5) Myxoid chondrosarcoma: the tumor can have lobular and cartilaginous areas, but has no primitive lumen. Immunohistochemical S-100 is positive.

The disease related mortality of EH varies depending on anatomic sites. It is approximately 13% with soft tissue lesion in contrast to 65% and 35% with lung and liver lesions, respectively.[2] Survival data for renal lesion is unclear due to extremely few documented cases. EH is histologically between hemangioma and angiosarcoma, some of the heterotypic characters are not obvious, and others are very heteromorphic, which are easy to find pathological mitosis and necrosis. The effect of radiotherapy and chemotherapy is not clear, surgical resection of the lesion is the best method of treatment so far. In the treatment of renal EH, the literatures consider that partial nephrectomy is the first choice for the treatment and it has been widely accepted. This is especially suitable for EH patients with less than 4cm lesions. The survival rate of the patients is comparable to that of eradicating nephrectomy, and the renal function is retained.[7] For our patient, she experienced partial nephrectomy and was in good post-operative condition without complications. No clinical evidence of local recurrence or metastatic disease was found during 6 months of follow-up clinical and ultrasound examinations. In addition, laboratory tests, including a urine examination, were normal. Our present study reviewed the clinical and biological information of previous cases, which was diagnosed as renal EH and we supplemented more data for further study.

Author contributions
Data curation: Jingjun Wu.
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