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Case Report

Clinicopathologic features of renal epithelioid angiomyolipoma: report of one case and review of literatures

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Abstract: Epithelioid angiomyolipoma (EAML) is a rare renal mesenchymal tumor with malignant potential and is frequently associated with tuberous sclerosis complex (TSC). As metastasis of the tumor cells occur early, EAML is considered a potentially malignant tumor type and intrigues further research on it. Under the microscope, we could find the tumor was composed of atypical polygonal cells sheet mixed with classic angiomyolipoma (AML) components such as blood vessels with notable thick vascular walls, smooth muscle-like cells and adipocytes. Immunohistochemical studies showed that epithelioid cells were focally positive for vimentin, melanocytic markers (HMB-45), myoid markers (α-smooth muscle actin), CD34 and CD68; negative for cytokeratin, epithelial membrane antigen, CD10, and S-100. And the Ki67 index showed approximately 3%. Here, we report the morphological and immunohistochemical features of clinically or histologically malignant renal EAML and discuss its diagnosis, differential diagnosis and the prognosis.

Keywords: Epithelioid, angiomyolipoma, immunohistochemistry, diagnosis

Introduction

Epithelioid angiomyolipoma (EAML) is a rare renal mesenchymal tumor with malignant potential and is frequently associated with tuberous sclerosis complex (TSC) [1]. It is composed of tumor cells arranged in an epithelioid manner. As metastasis of the tumor cells occur early, EAML is considered a potentially malignant tumor type and intrigues further research on it. We do search for EAML between January 2008 and June 2014 and review analysis of its clinical features and pathology results. We have found one case, and report it as followed.

Case report

A 52-year-old man with an unremarkable medical history visited the hospital with persistent low back pain. A enhanced computed tomography (CT) scan revealed a mass: an approximately 2.4 cm × 2.8 cm mass that border was still clear in the lower pole of the left kidney of which location, size and morphology were normal (**Figure 1A**). Around the renal, we could find slightly high density imaging and no metastatic lesions were detected. The radiologic differential diagnosis was that of renal cell carcinoma versus oncocytoma. Radical left nephrectomy was performed. The specimen consisted of a kidney covered by perinephric fat, measuring 9.7 × 6.1 × 6.5 cm, and a segment of ureter measuring 4.8 × 0.4 cm. The renal capsule was intact and smooth. On bivalving the kidney coronally, we could find the lower mass was a 3.0 cm × 4.0 cm brownish and soft tumor replacing two thirds of the lower pole of the renal parenchyma and the tumor was almost circumscribed and located in the lower pole of the kidney. Hemorrhage and necrosis were observed in this mass.

Sections from the mass showed a highly cellular neoplasm comprising predominantly epithelioid cells that are diffuse and show morphological diversity and blood vessels with notable thick vascular walls, smooth muscle-like cells and adipocytes. The tumor predominantly comprised Tumor cells arranged in diffuse sheets, irregular or hemangiopericytoma-like. The epi-

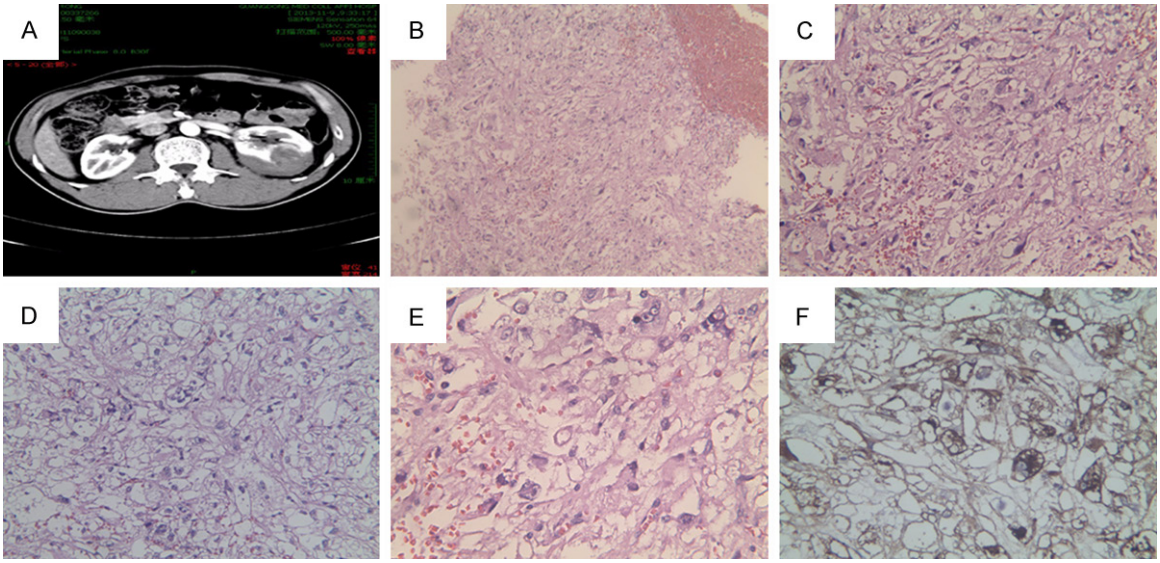

Figure 1. (A) Contrast-enhanced computed tomography scan of the Case showing a 2.4 cm × 2.8 cm mass in the left kidney. Microscopic findings from the Case revealed. (B) Extensive necrosis and hemorrhage and (C), (D) a sheet of epithelioid cells (H.E., original magnification 200×). (E) Polygonal tumor cells with bizarre nuclei and eosinophilic granular cytoplasm (H.E., original magnification 400×). (F) Immunohistochemical staining original magnification 400×. Immunohistochemical staining of tumor cells showed HMB-45 was positive.

thelioid cells were mainly circular, polygonal, slightly spindled in some region. The cytoplasm is abundant and pale eosinophilic, and the nuclear with obvious nucleoli is circular or oval, centered or offset. And the chromatin is coarse. Most regions of tumor cells were atypical in which some multinucleated giant cells existed and we could find a few visible minority. A small amount of local area thick-walled blood vessels and abnormal sinus could be found through extensive coverage. A small part of the region of tumor cells degenerated, necrosis, and the tumor cells scattered in a large number of background comprised eosinophils and lymphocytes (**Figure 1B-E**).

Immunohistochemical studies showed that epithelioid cells were focally positive for Vimentin, melanocytic markers (HMB-45) (**Figure 1F**), myoid markers (α-smooth muscle actin), CD34 and CD68; negative for cytokeratin, epithelial membrane antigen, CD10, and S-100. And the Ki67 index shown positive approximately 3%.

Accordingly, the tumor was diagnosed as renal EAML by the presence of an extensive proliferation of spindled cells with rare epithelioid cells and more frequent necrosis as well as a higher mitotic index. Furthermore, it shows to be associated with a more aggressive clinical course of evolution.

Neither recurrence nor metastasis was clinically identified at the last follow-up visit, 7 months post-surgery.

Discussion

Mai et al [2] reported EAML in 1996 as the first case. The EAML comprised epithelioid cells mixed with classic AML components such as blood vessels and fat. WHO urinary system and male genital tumor classification classified the tumor alone, defined it as a kind of potential malignant mesenchymal tumor. In addition, the renal EAML could be sort out of pure EAML and EAML associated with tuberous sclerosis complex, of which occurred with sporadic or familial tuberous sclerosis and other tumor of body and the proportion of renal EMAL with TSC was significantly higher than the classic type of renal AML [3].

Renal EAML lacked of specific clinical manifestations, when the tumor was small, might have no symptoms, physical examination findings. Only when the tumor was increased to 4 cm, 30% of patients got with low back pain and abdominal discomfort, palpable mass and weakness symptom. Radiographic imaging of renal EAML could have classic performance, but also has its own characteristics. CT findings of EAML had certain characteristic, unlike the

classic AML and showed multiple lesions, the much larger volume and the still clear boundary [4]. However, CT couldn't accurately diagnose EAML, and sometimes was misdiagnosed, so we need other methods of diagnosis and differential diagnosis of EAML, including morphology and immunohistochemistry [5].

Due to component of a large number of epithelial tumor cells, and even a variety of histological changes, especially apparent polymorphism and cellular atypia, we believed that the most important things in the pathological diagnosis of tumor were the followed three points: (i) Perivascular epithelioid cell differentiation: perivascular epithelioid cells showed Sleeve-like arrangement. Round or polygonal tumor cells, large nuclei, prominent nucleoli, visible mitotic figures could be found. Multinucleated tumor cells often appeared. Sometimes we could see hemorrhagic necrosis; (ii) AML classic ingredients: carefully looking for a classic ingredient is helpful for positive diagnosis of renal EAML; (iii) Immunohistochemical features were significant for the diagnosis of EAML such as Vimentin (+), HMB45 (+), SMA (+), CD34 (+), CD68 (+), CD10 (-), EMA (-), S-100 (-), CK (-), Ki-67 (1%-3%).

Since EAML on morphology-based comprised epithelioid cells, and some exhibited adhesion of cancer-like growth pattern, at the mean time there were different degrees of nuclear atypia, mitotic activity and necrosis, the EAML could be easily confused with other malignancies, including characteristic of granule cell of renal cell carcinoma, sarcomatoid renal cell carcinoma and urothelial carcinoma, malignant melanoma and other pure sarcoma. Combination of these histological features, if necessary, and supplemented immune markers, we could accurately identify EAML. Belanger et al [6] retrospectively analysed a group of kidney tumors and found that there were two cases previously diagnosed as sarcomatoid renal cell carcinoma and renal sarcoma tumors were positive for HMB45 and MART-1, and under microscope, these two cases were similar with EAML, but lacking the region of classic renal cell carcinoma and AML. Therefore, Immunohistochemistry (IHC) played an important role in the differential diagnosis of renal EAML. (i) Renal cell carcinoma: epithelial markers CK and EMA were positive, CD10 and Vimentin could be positive, and melanoma markers HMB45, Melan-A and smooth muscle markers SMA were negative; (ii) Leiomyosarcoma: tumor cells Vimentin, SMA, actin and MSA were positive and melanoma markers negative; (iii) Melanoma: HMB45, Melan-A and S-100 protein were positive, Vimentin and CK could be expressed, but did not express smooth muscle cell markers SMA; (iv) Malignant fibrous histiocytoma: tumor cells were positive for Vimentin and CD68, but negative for HMB45 and Melan-A. Currently, in order to accurately identify EAML, Konosu-Fukaya et al [7] reported three cases of renal EAML and shown E-cadherin and β-catenin might be another indicators of IHC results of the renal EAML and indicated the IHC had revealed the activation of mammalian target of rapamycin pathway. In this case, HMB45-positive of melanoma cell markers and SMA-positive were specific immunohistochemical indicators of renal EAML, when the EMA was always negative.

AML was generally believed that almost always benign, but sometimes local infiltration could occur, in rare cases could be fatal. Currently, parameters for the diagnosis and prognosis of malignant renal EAML were not uniform understanding. Delgado et al [8] reported a group EAML, and followed up for 1 to 8 years without recurrence. However, Pea et al [9] had reported three cases EAML, a metastasis occurred in 2 cases and deaths occurred after the diagnosis of 12 to 18 months. Some scholars believe EAML tumor cell atypia, mitotic figures, hemorrhage and necrosis, aggressive growth, vascular invasion, lymph node metastasis and local recurrence were potential indicators of malignancy [10]. Brimo et al. [11] proposed renal EAML has followed three or more indicators of biological behavior that highly represented malignancy: (i) Atypical epithelioid cell ratio ≥ 70%; (ii) Mitotic count ≥ 2/10 HP; (iii) Atypical mitotic; (iv) necrosis. Nese et al [12] shown those five adverse prognostic parameters of renal EAML: concurrent tuberous sclerosis or ordinary type angiomyolipoma; necrosis; tumor size > 7 cm; aggression and/or renal vein invasion: cancer-like growth pattern. Wherein the tumor with less than two parameters of poor prognosis had a low degree of risk of disease progression; presence of 2 to 3 tumor poor prognosis parameters had the "intermediate risk" disease progression; presence of 4 or more tumor poor prognosis parameter was considered as a high risk of disease progression. The patient of this case was followed up for 7 months, and we did not find a positive distant

metastasis. Although it was necessary for closer observation and longer follow-up, we thought it belong potentially malignant tumors. It was noteworthy that all of the pathological examination results further illustrated the potentially malignant nature of EAML ingredients.

In summary, renal EAML with malignant potential was subclinical and currently preoperative diagnosis was done by imaging, while immunohistochemical diagnosis was important postsurgery. We primarily adopted surgical treatment and the prognosis was no unified understanding.

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Disclosure of conflict of interest

None.

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