Original Article

From angiomyolipoma to malignant epithelioid angiomyolipoma of the kidney, a case report with a history of eight years

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Abstract: Epithelioid angiomyolipoma (EAML) is a rare subtype of angiomyolipoma (AML) with potential has malign tendency. Up to now, the biological association between EMAL and typical AML is not well known. In the present study, we reported a case of EMAL arose in AML seven years post AML operation. A 34-year-old man with bilateral kidney AML was operated with an open cytoreductive surgery of both sides. After seven years, the left nephrectomy was performed due to a new neoplasm was found in the left kidney. The pathology diagnosis and immunohistochemical staining suggested the new neoplasm was EAML. Finally the patient developed metastases to liver and retroperitoneum and died 19 months post the last operation. After reviewing the history of the patient, we thought that the EAML might be developed from a little amount of EMAL accompany with AML in the small lesson that was missed by the CT scan. The results revealed that a carefully screening for the epithelioid cells in the typical AML specimen should be made to avoid missing the important EAML.

Keywords: Malignancy, renal angiomyolipoma, histology, immunohistochemistry

Introduction

AML is a well-known rare soft tissue tumor and it is believed to be a benign hamartoma. EAML is a subtype of AML and is potentially malignant arising from the mesenchymal tissue characterized by the epithelioid cells. In recent years, more and more reports showed the invasion of EAML and the organ metastasis in a short time. This special biological behavior arises the importance of re-recognition to this diseases [1, 2].

This report presents a case of bilateral kidney AML at the beginning. After seven years, an EAML was found on the left kidney. Liver metastasis occurs soon after the last operation. This case further proved the debut of the term, “Malignant EAML”.

Case report

In June 2002, a male patient of 34 years old was diagnosed with hyperechoic tumors in both kidneys by the renal echo in a regular medical examination, but presented no clinical symptoms. The contrast-enhanced computed tomography (CT) confirmed a heterogeneous mass occupying the upper and lower portion of the left kidney and the lower middle portion of the right kidney. The fat density could be discernible (Figure 1A). The patient had no history of tuberous sclerosis. The open cytoreductive surgery was performed on the left side and the other side two weeks later. The mass size of both sides is 20.5×8.5×6.5 cm³ (left) and 12.5×10.5×8.5 cm³ (right), respectively.

Pathology examination after the first operation: the size of the tumor in the left kidney was 13×13×6 cm³, and the right was 12×12×3 cm³. The color of the incisal surface was pink-white and the tissue is soft and fragile. Typical fat cells, the thick-walled irregular blood vessel, and the smooth muscle around the blood vessel could be observed under microscopy (Figure 2A). But there were also some epithelioid cells that located in the edge of the tumor and only distributed in less than 1% of total specimen.
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Figure 1. A. The contrast-enhanced computed tomography (CT) of 2002, confirmed the presence of a heterogeneous mass occupying the upper and lower portion of the left kidney and the lower middle portion of the right kidney (arrow). B. The contrast-enhanced computed tomography (CT) of 2009, confirmed the presence of a heterogeneous mass occupying the lower portion of the left kidney (arrow).

Figure 2. A. Microscopically (2002), The typical fat cells, the thick-walled irregular blood vessel and the smooth muscle around the blood vessel are observed. The shape of most smooth muscle is fusiform. But there are also some epithelioid cells (hematoxylin & eosin, 400×). B. Microscopically (2009), Most of the hyperplastic epithelioid cells arranged in nest and foliated shape around the blood vessels can be seen under microscopy (hematoxylin & eosin, 400×). C. Immunohistochemically, the tumor cells show strong HMB-45 cytoplasmic reaction (ABC method, 400×). D. Immunohistochemically, the tumor cells show strong Melan-A cytoplasmic reaction (ABC method, 400×) (+).
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There were eosinophil granules in the endochy-lema. Immunohistochemistry showed positive results of SMA and HMB45 proteins.

On February 2009 during the routine follow-up, seven years post operation, the renal echo showed a heterogeneously hypoechoic tumor in the lower pole of the left kidney. CT confirmed the presence of a heterogeneous mass occupying the lower portion of the left kidney. Because no fat density was discernible, we suspected he suffer from malignant tumor (Figure 1B). The open surgery was performed again because the renal cell carcinoma (RCC) cannot be excluded. Intraoperative frozen cytology found that most epithelioid cells looked more like the RCC. The partial nephrectomy was difficult to perform because of the previous open surgery and the total nephrectomy had to be done.

Pathology examination post the second operation: the tumor located in the inferior pole of kidney with a size of 10×9.5×7.5 cm³. The renal capsule and the fatty renal capsule were penetrated. The thickness of the tumor’s capsule wall was 0.2-0.5 cm. There were some dark red and yellow-white hemorrhage and necrosis. Most of the hyperplastic epithelioid cells arranged in nest, around the blood vessels with a shape of foliated under microscopy (Figure 2B). Another character of the tumor was that the cells near the kidney tissue were well differentiation and only the smooth muscle cells were a bit of atypia. The main body of the tumor and the tissue infiltration out of the lipid vesicle were full of the epithelioid cells. Immunohistochemical results showed that Vimentin, SMA, HMB45 (Figure 2C), Melan-A (Figure 2D), and P53 were positive while MSA and CK were negative. In addition, the Ki-67 index was 20%.

On January 2010, a quickly enlarged mass in the right upper abdominal was detected that caused dull pain of the right upper quadrant of the abdomen. The CT scan indicated it was liver metastatic carcinoma. The patient became marasmus and anorexia. A palpable mass was found in the right upper quadrant of the abdomen. The CT scan showed a 13×13 cm² tumor in the right liver and most lymph nodes were found around the abdominal Aorta. The patient was treated with oral Sorafenib for half year, however, on obvious improvement was observed and the tumor in the liver was still growing. Finally the patient was disease-specific death on September 2010.

Discussion

AML is a histologically complex mesenchymal tumor with the proliferation of thick-walled blood vessels, adipose tissue, and smooth muscle-like cells. The kidney is the most common primary organ for AML. AML is believed to be a benign hamartoma. EAML is a rare form of AML characterized by the proliferation of predominant epithelioid cells [3]. It is predominantly found in kidney, liver, pancreas, pelvic cavity, ovary, and bone. It’s a kind of neoplasms from mesenchymal tissue with potential malignancy and has huge amounts of hyperplasia epithelial cells. EAML is closely related with AML and both of them belong to neoplasms with perivascular epithelioid cell differentiation (PEComas) [4]. PEComas comprise AML, capsuleoma, or microhamartoma in kidney, clear cell sugar tumor of the lung (CSST), extrapulmonary ‘sugar’ tumor, clear cell epithelioid tumor in falciform ligament/round ligament and a group of lesions arising at various visceral and soft-tissue sites, which are morphologically and immunophenotypically similar. Almost all of these tumors show immunoreactivity for both melanocytic (HMB-45 and/or melanin A) and smooth muscle (actin and/or desmin) markers [5].

The image character of EAML is high density in plain CT scan and uneven enhancement in enhancement CT. The tumor is always big with complete envelope. Some local lymph nodes or other organs metastasis may be found [6]. The patient is diagnosed to be EMAL at the first visiting. But the CT scan showed it a typical manifest of AML because there was only small part of EMAL in the edge of AML. The CT scan in February 2009 showed that the original AML did not grow after the first operation whereas there was a new plasma at the lower polar of the left kidney. This new plasma showed typical CT scan characters of EAML. So we thought that the CT scan can only reveal the big and typical EAML but not the EAML accompany with AML, especially when the scale of EAML is too small to be seen by the CT scan. This reminds the pathology doctor to search carefully for the epithelioid cells in the typical AML specimen so that the important EAML diagnosis would not be missed.
A great quantity of the proliferative epithelioid cells abundant of granular hyalomitome is the pathology character of the EAML. Immunohistochemical staining study showed that the EAML occupies positive result on melanocytes marker such as HMB45 and Melan A but negative result on the epithelial cells marker such as CK and EMA. The expression of the smooth muscle marker just like the SMA and MSA is different. Martignoni [7] defined EAML as a tumor containing no fat, thick-wall blood vessel, flakiness arranged and with the expression of melanocytes marker. But some studies thought that the typical AML areas can exist in EAML [8]. In this case, epithelium cells comprise the main tumor body whereas the typical AML areas can be seen near the kidney. The pathological sections made in 7 years ago were reviewed. It was found the tumor was well differentiated and the epithelioid cells were found in the area with the percentage of less than 1% of the whole tumor periphery. According to the clinic history of the patient, it was presumed that the part of epithelioid cells grew faster in the primary tumor, and occupied the main part of the periphery area. This might be related with the invasion capacity of the tumor which needs to be elucidated.

Several cases of renal EAML metastasize to lung or liver with a mortality rate of 35%-40% [9]. Before the metastasis, renal EAML is more likely to be a kind of latent malignant disease. Folpe and coworkers [10] distinguished the PEComa into 3 types (benign lesion, latent malignant lesion and malignant lesion) according to the following standards: Tumor size exceed 5 cm or not, infiltrative growth or not, nuclear heteromorphism, cellular necrosis, karyokinesis exceed 1/50 HP or not, and tumor cells’ clinical biological behavior. Ki-67 and P53 are also useful for differential diagnosis of benign or malignant renal AML. As to the case we reported, it was malignant according to Folpe’s classifications because the immunohistochemical stain characteristics were P53 (+), Ki-67 index 20%. The metastasis was founded 11 months post the second operation and this supports the criteria of Folpe’s classifications.

Surgical procedure is the first treatment choice of EAML. The usage of adriamycin, cyclophosphamide, ifosfamide and other adjuvant chemotherapy were also be reported but their effects were not so optimistic [11]. In our case, the oral sorafenib was given to the patient but it seems to be useless.

In conclusion, the diagnosis of AML cases is easy. But we must pay more attention to the EAML. The CT scan can only find the typical EAML tumor. The pathology doctor should also search for the epithelioid cells carefully in the typical AML specimen so that the important EAML would not be missed.

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Disclosure of conflict of interest

None.

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