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Case Report

Malignant perivascular epithelioid cell tumor of the kidney with rare pulmonary and ileum metastases

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Abstract: Aims: To report one case of malignant perivascular epithelioid cell tumor (PEComa) of the kidney with rare pulmonary and ileum metastases and analyze its clinicopathological features. Methods: We analyzed the clinicopathological features of one case of malignant PEComa of the kidney with pulmonary and ileum metastases. Immunohistochemistry staining was performed. Results: The patient was a 48-year-old man with a renal mass approximately 14 cm × 11 cm × 8 cm in size. Microscopically, the tumor was mainly composed of polygonal epithelioid cells with dense eosinophilic cytoplasm and round nuclei with small nucleoli. Focal tumor cells showed pleomorphism with multinucleated giant cells and prominent nucleoli. The tumor cells nests were surrounded by thick-walled irregular blood vessels. Focal fat cells were found within the tumor. Hemorrhage and coagulative necrosis were also present. The tumor cells were positive for vimentin, HMB45, and Melan-A, and focally positive for SMA and S-100 protein. After 5 years and 5.6 years of nephrectomy, the tumor metastasized to the right lung and ileum, respectively. Conclusion: We first reported one case of malignant PEComa of the kidney with pulmonary and ileum metastases. Metastatic PEComa of the lung and ileum should differentiate from primary carcinoma, metastatic carcinoma, malignant melanoma, and gastrointestinal stromal tumor.

Keywords: Perivascular epithelioid cell tumor, kidney, metastasis, lung, ileum

Introduction

Perivascular epithelioid cell tumors (PEComas) are composed of epithelioid cells with clear to eosinophilic cytoplasm, perivascular distribution, and usually express melanocytic and myogenic markers [1]. PEComa may arise in variety of sites including retroperitoneum, abdominopelvic region, uterus, uterine cervix, vagina, gastrointestinal tract, kidney, liver, bladder, prostate, soft tissue, skin, and bone [2-6]. Malignant PEComa is rare and associates aggressive clinical course and metastasis. The most common metastatic sites are the liver, lymph nodes, lungs, and bone. Herein, we first reported one case of malignant PEComa of the kidney with pulmonary and ileum metastases.

Case presentation

Clinical findings

The patient was a 48-year-old man. He complained abdominal pain for 6 months and blood in urine twice and consulted our hospital in March 2008. Computer tomography (CT) scan showed a mass with the maximum diameter of 14 cm in the right kidney. There was no evidence of tuberous sclerosis complex in the patient or his family. The patient received a radical right nephrectomy. The postoperative course was uneventful and no adjuvant therapy was given for the patient.

In October 2013, the patient presented with dry cough and chest distress for 1 month. CT scan showed a mass approximately 6 cm in diameter in the right lower lung and hilar node enlargement. The mass was suspected of "peripheral lung cancer" and the right lower pneumonectomy was performed.

In April 2014, the patient presented with blood in stool for one month. Enteroscopy and CT examination demonstrated a mass about 6 cm in diameter in the ileum. He received an ileum resection with the mass.

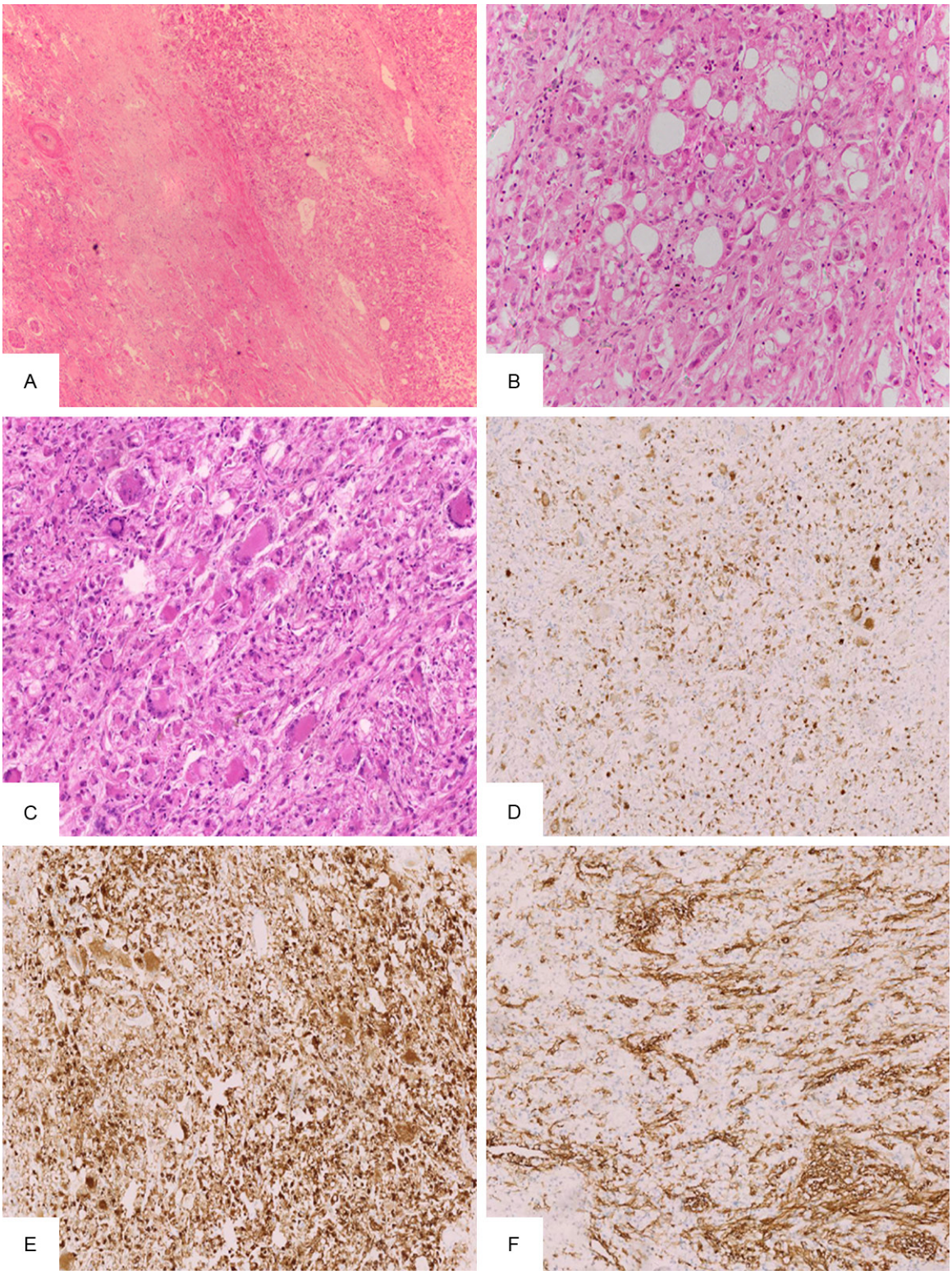

Figure 1. Malignant PEComa of the kidney. (A) There was clear border between tumor tissues (right side) and kidney (left side), HE × 40; (B) Tumor cells was mainly composed of polygonal epithelioid cells with dense eosinophilic cytoplasm and round nuclei with small nucleoli. Focal fat cells were found within the tumor, HE × 100; (C) Focal tumor cells showed pleomorphism with multinucleated giant cells and prominent nucleoli, HE × 200; (D-F) Tumor cells were positive for HMB45 (D), Melan-A (E), and SMA (F) by immunohistochemistry staining. IHC × 200.

Pathological features

Grossly, the tumor located in right kidney, right lower lung and ileum was well-circumscribed and 14 cm × 11 cm × 8 cm, 6.5 cm × 5 cm × 3 cm, and 5.8 cm × 5 cm × 4 cm in greatest diameter, respectively. On the cut surface, the tumors from 3 sites were grayish and brownish with vague boundary. Hemorrhage and necrosis were consistently observed in such 3 tumors.

Microscopically, the tumor in kidney showed a nested architecture and was mainly composed of polygonal epithelioid cells with dense eosinophilic cytoplasm and round nuclei with small nucleoli. There were spindle tumor cells in some area. Focal tumor cells showed pleomorphism with multinucleated giant cells and prominent nucleoli. The tumor cells nests were surrounded by thick-walled irregular blood vessels. Focal fat cells were found within the tumor. Hemorrhage and coagulative necrosis were also present. Mitotic figures were not found. There was no evidence of tumor cells invasion of renal capsule, blood vessel and lymph node. The tumor cells were positive for vimentin, HMB45, and Melan-A, and focally positive for SMA and S-100 protein, Ki-67 expression was about 1% of tumor cells. However, tumor cells were negative for CK, EMA, and CD10 by immunohistochemistry staining (**Figure 1**). Based on these findings, we made a diagnosis of malignant PEComa of the right kidney.

The tumor in the lung was mulifocality with vague boundary. There was the residual alveolar epithelium within the tumor. The tumor cells were arranged in nests or trabeculae and composed of epithelioid cells with abundant eosinophilic cytoplasm and round nuclei with prominent nucleoli. Mitotic figures were about 12/10 HPF. Atypical mitosis could be easily found. No fat cells and thick-walled irregular blood vessels were found within the tumor. Hemorrhage and tumor necrosis were also present. Immunohistochemistry staining showed that tumor cells were positive for vimentin, HMB45, and Melan-A, focally positive for SMA. P53 and Ki-67 expression was approximately 60% and 30% of tumor cells, respectively (**Figure 2**). However, tumor cells were negative for CK, EMA, CK5/6, CK7, CEA, P63, TTF-1, desmin, CD56, CgA, Syn, NSE, S-100 protein, Hepatocyte, and CD10. The hilar node enlargement was reactive hyperplasia of lymph node.

The tumor in ileum was mainly located within the submucosa and muscular layer and infiltrated the mucosa of ileum. The tumor cells showed remarkable atypia with polygonal epithelioid cells with abundant eosinophilic cytoplasm and round nuclei with prominent nucleoli. Numerous tumor cells showed pleomorphism with mononuclear or multinucleated giant cells. Mitotic figures were about 10/10HPF and atypical mitosis was easily found. As similar to pulmonary tumor, no fat cells and thick-walled blood vessels were observed within the tumor. Tumor cells were positive for vimentin, HMB45, and Melan-A (**Figure 3**), focally positive for SMA. Ki-67 expression was approximately 20% of tumor cells. However, tumor cells were negative for CK, CD117, DOG-1, CD34, and S-100 protein by immunohistochemistry staining.

Based on the clinical history and pathological findings, the patient was diagnosed as malignant PEComa of the right kidney with right lower pulmonary and ileum metastases. The patient underwent a radical right nephrectomy, the right lower pneumonectomy, and ileum resection without any radiology and/or chemotherapy. The patient was alive without evidence of disease for 148 months since PEComa of the kidney was surgical treated.

Discussion

PEComas are a family of rare mesenchymal neoplasms, including angiomyolipoma, clear-cell “sugar” tumor of the lung and extrapulmonary sites, lymphangioleiomyomatosis, clear-cell myomelanocytic tumor of the falciform ligament/ligamentum teres, and clear-cell tumors at various other anatomic sites [1].

The criteria for malignancy in PEComas have not been established. In 2002 WHO of tumors of soft tissue and bone [7], PEComas displaying any combination of infiltrative growth, marked hypercellularity, nuclear enlargement and hyperchromasia, high mitotic activity, atypical mitotic figures, and coagulative necrosis should be regarded as malignant. In 2005, Folpe et al. reviewed 26 cases of PEComas from soft tissue and gynecologic origin and observed a significant association between tumor size >5 cm,

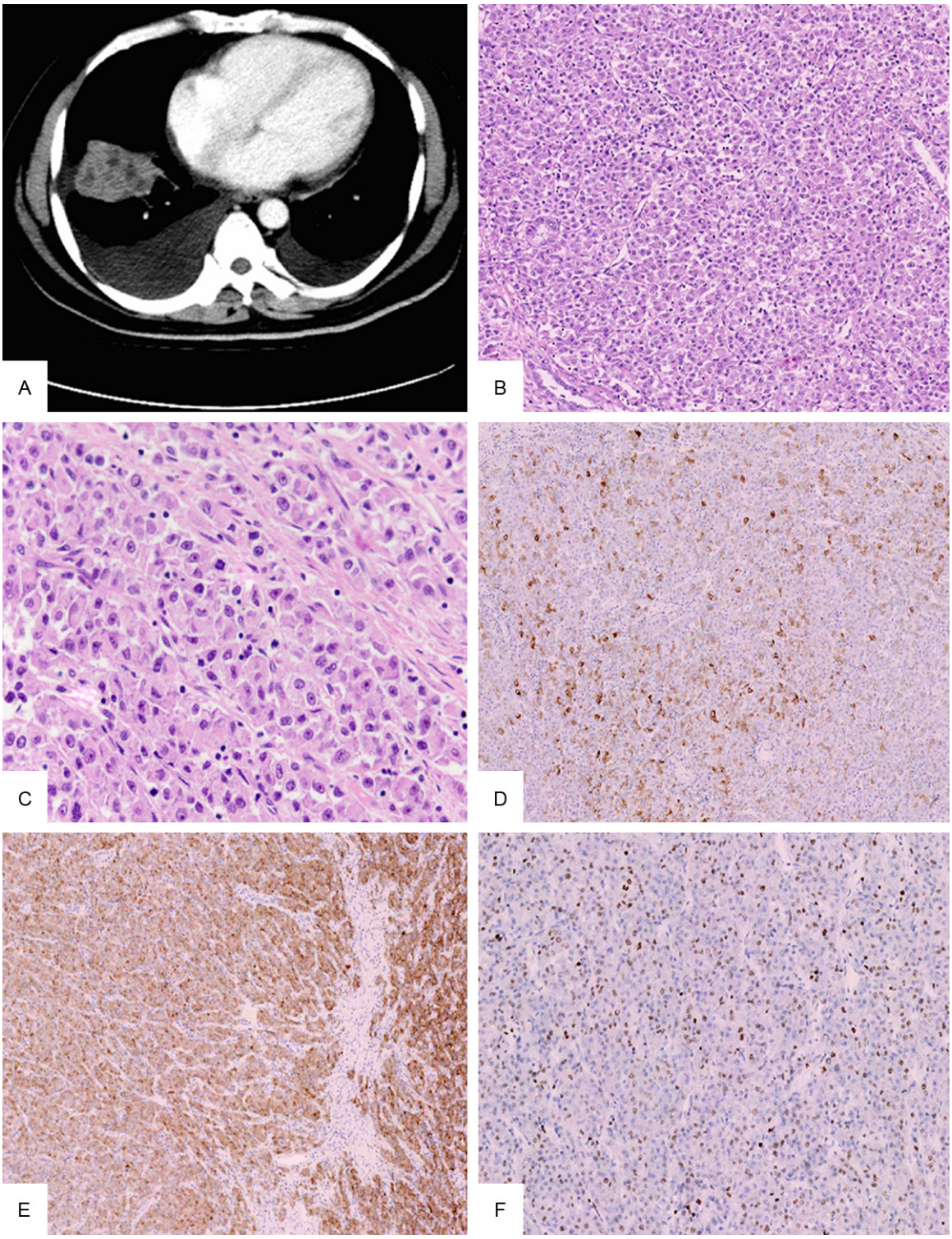

Figure 2. Metastatic PEComa in the lung. (A) CT showed a mass approximately 6 cm in diameter in the right lower lung and hilar node enlargement; (B) There was the residual alveolar epithelium within the tumor. The tumor cells were arranged in nests or trabeculae, HE × 100; (C) Tumor cells were composed of epithelioid cells with abundant eosinophilic cytoplasm and round nuclei with prominent nucleoli. Atypical mitosis could be found, HE×200; (D, E) Tumor cells were positive for HMB45 (D) and Melan-A (E) by immunohistochemistry staining. IHC × 200; (F) Ki-67 expression was about 30% of tumor cells by immunohistochemistry staining. IHC × 200.

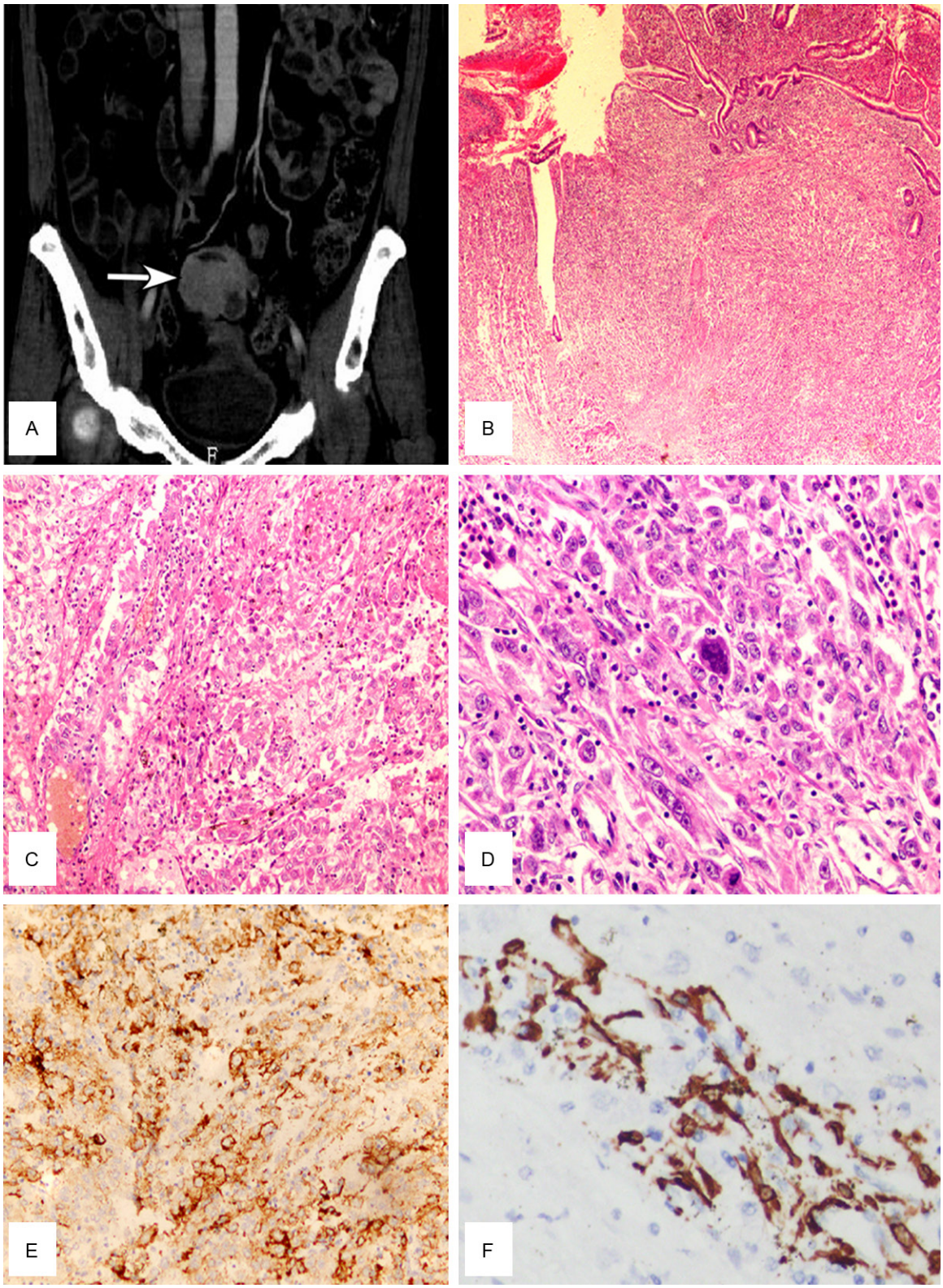

Figure 3. Metastatic PEComa in ileum. (A) CT demonstrated a mass about 6 cm in diameter in the ileum. (B) The tumor in ileum was mainly located within the submucosa and muscular layer and infiltrated the mucosa of ileum, HE × 40; (C) The tumor cells showed remarkable atypia with polygonal epithelioid cells with abundant eosinophilic cytoplasm and round nuclei with prominent nucleoli, HE × 100; (D) Tumor cells showed pleomorphism with mononuclear or multinucleated giant cells, HE × 200; (E, F) Tumor cells were positive for HMB45 (E) and Melan-A (F) by immunohistochemistry staining. IHC × 200.

infiltrative growth pattern, high nuclear grade, necrosis, and mitotic activity >1/50 HPF and subsequent aggressive clinical behavior of PEComa. Recurrence and/or metastasis of PEComa in their series was strongly associated tumor size > median size (8 cm), mitotic activity greater than 1/50 HPF, and necrosis. They conclude that PEComas of soft tissue and gynecologic origin may be classified as "benign", "of uncertain malignant potential", or "malignant". Small PEComas without any worrisome histologic features are most likely benign. PEComas with nuclear pleomorphism alone ("symplastic") and large PEComas without other worrisome features have uncertain malignant potential. PEComas with two or more worrisome histological features should be considered malignant [6]. Hornick and Fletcher suggest that PEComas that show marked pleomorphism and nuclear atypia (sometimes resembling a pleomorphic myogenic sarcoma) also have the potential to behave in a malignant fashion [8]. Fadare has reviewed 41 previously reported uterine PEComas and reported a mitotic count of >1/10 HPF and/or coagulative necrosis are features for the definite potential for aggressive behavior of PEComa [5]. In 2013 WHO of tumors of soft tissue and bone, malignant PEComas are characterized by mitotic activity, necrosis, marked nuclear atypia, and pleomorphism [1]. So based on the above criteria, we made a diagnosis of our current case as malignant PEComa of the kidney because of tumor size >5 cm (14 cm in diameter), necrosis, marked nuclear atypia, and pleomorphism.

Malignant PEComas associates recurrence and/or metastasis. The common metastatic sites are the liver, lymph nodes, lung, and bone. Primary PEComa of small intestine is rare [9, 10]. To our knowledge, our current case was the first report of metastatic PEComa in ileum except for the lung. In addition, metastatic PEComa in the lung and ileum showed much more atypia including a number of mitotic figures, atypical mitosis, prominent nucleoli and tumor necrosis compared with primary tumor of the kidney. Fat cells and thick-walled blood vessels, which present in primary PEComa of the kidney, were not found in metastatic PEComa of the lung and ileum. Ki-67 expression was 30% and 20% of metastatic PEComa in lung and ileum, respectively compared with 1% of primary PEComa of the kidney. This finding suggests that metastatic PEComas have more aggressive clinical course than primary tumor. As for the differential diagnosis, the primary malignant PEcoma of the kidney should differentiate from renal cell carcinoma and malignant melanoma. Metastatic PEComa in the lung should differentiate from pulmonary carcinoma, metastatic carcinoma, and malignant melanoma. Metastatic PEComa in ileum should differentiate from gastrointestinal stromal tumor, malignant melanoma, and carcinoma.

Some PEComas are associated with tuberous sclerosis complex gene mutations causing upregulation of mTOR [4, 11]. So targeting mTOR might be a novel treatment strategy for malignant PEComas [11-13].

Disclosure of conflict of interest

None.

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