A Solitary Metastatic Lung Tumor Slow-Growing with Late Onset from Renal Epithelioid Angiomyolipoma

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We report the case of a 46-year-old Japanese woman with a past medical history of right nephrectomy for a sarcomatoid renal cell carcinoma 14 years earlier. A pulmonary nodule was detected in the left upper lobe 7 years after nephrectomy and it had grown slowly for 6 years. We performed wedge resection for the tumor because we suspected that the nodule was metastasis from the renal tumor. But the nodule was diagnosed as epithelioid angiomyolipoma since the nodule was positive for HMB-45 and negative for epithelial markers and S-100 protein by immunohistochemical analysis. Therefore her disease was revised as a solitary pulmonary metastasis from renal epithelioid angiomyolipoma. Epithelioid angiomyolipoma is a potential malignant mesenchymal tumor because the tumor recurs or metastasizes, and progresses rapidly on one-third of the cases. This case is the first report that the disease was stable for a long time after late recurrence caused.

Keywords: renal epithelioid angiomyolipoma, pulmonary metastasis

Introduction

Epithelioid angiomyolipoma (EAML) is a subtype of angiomyolipoma (AML) which is classified as a member of the perivascular epithelioid clear cell tumor family (PEComa) composed by lymphangioleiomyoma and clear cell “sugar” tumor. Renal EAML is known to be a potential malignant tumor because the disease causes local recurrence and distant metastasis frequently.1) In previous reports, the disease progression was relatively rapid and many cases resulted in death within 2 years after recurrence or metastasis.2–4) Therefore, a case with late recurrence more than 5 years after resection of primary tumor and with long term stable condition after metastasis is rare. We report a case on which renal EAML recurred in the left lung 7 years after initial renal surgery and the pulmonary metastasis grew slowly for 6 years prior to metastasectomy.

Case Report

A 46-year-old woman, who had undergone right radical nephrectomy for a diagnosis of renal sarcomatoid 14 years earlier, was referred to our division for treatment of a pulmonary nodule. The follow-up computed tomography (CT) performed 7 years earlier demonstrated a solitary nodule (5 mm in diameter) of the left upper lobe (Fig. 1A). Since she had encephalopathy with paralysis and aphasia due to pulmonary embolism occurred just after renal surgery, she did not want to receive any treatment. Therefore, she was observed with no active intervention for 6 years. The nodule grew to 20 mm in diameter slowly until this referral (Fig. 1B). We performed wedge...
resection in the left upper lobe one year earlier because the nodule was suspected as a pulmonary metastasis from renal sarcomatoid tumor.

On gross pathological examination, the specimen contained a circumscribed 2.0 × 1.5 × 2.5 cm nodule with necrosis and hemorrhage (Fig. 2). Microscopically, there was a sheet of pleomorphic large atypical cells with round to polygonal nucleoli and abundant acidophilic cytoplasm (Fig. 3A and 3B). By immunohistochemical assays, the tumor cells were positive for human melanoma black (HMB)-45 (Fig. 3C), while the staining for AE1/AE3 and S-100 protein were negative (Fig. 3D). The diagnosis of epithelioid angiomyolipoma (EAML) was made pathologically. The morphologic feature of the renal tumor was similar to that of the pulmonary lesion. The renal tumor was also positive for HMB-45 and was negative for AE1/AE3. The corrected diagnosis of the renal EAML with a pulmonary metastasis was made.

The postoperative course was uneventful and no adjuvant therapy was given for patient. There is no evidence of disease recurrence one year after the operation.

Discussion

EAML, a potentially malignant tumor composed of predominant epithelioid cells with minimal or no adipose tissue, is closely related to AML. AML is a common, benign, renal mesenchymal tumor in patients presenting with tuberous sclerosis complex (TSC). AML is composed of adipose tissue, epithelioid smooth muscle cells, and abnormal blood vessels. Approximately 50% of patients with EAML have a history of TSC. AML and EAML can occur in lymph node, liver, spleen, lung, uterus, heart, bone, brain, or retroperitoneum in extrarenal sites.

EAML, unlike AML, has the paucity of adipose tissue and atypia such as pleomorphic cell and nuclear fission. Therefore EAML is often misdiagnosed radiographically, histologically, or both, as RCC, oncocytoma, leiomyomas or leiomyosarcomas. By immunohistochemical assay, EAML is positive for melanocytic markers such as HMB-45, melan-a protein and melanoma antigen recognized by t cells 1 (MART-1), tryosinase and microphthalmia transcription factor but negative for epithelial markers and S-100 protein.

The optimal treatment for EAML is unclear. Surgical resection is the first choice for primary lesion and metastatic lesion, because there are few reports of the effective radiation therapy and chemotherapy. Recently, inhibitor of mammalian target of rapamycin complex 1 (mTORC1), functions as a serine/threonine kinase and plays regulating protein translation and protein, is reported as an effective treatment option. It is because, in AML and TSC patients, mTORC1 is inappropriately activated due to disruption of tuberous sclerosis complex 1 and 2 genes which regulate mTORC1.

Among patients with EAML, approximately one third of cases show local recurrence or distant metastasis to lymph node, liver, lung, bone, pancreas, adrenal gland,
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mediastinum, or retroperitoneum. In almost all cases of recurrence and metastasis, disease progressed within 2 years after initial renal surgery that resulted in death.2–4) Therefore, the cases which had recurrence or metastasis more than 5 years after renal surgery are rare. The factors related to the prognosis of renal EAML are discussed in some studies. Brimo, et al. suggested that ≥70% epithelioid cells, ≥2 mitotic figures per 10 HPF, atypical mitotic figures, and necrosis as pathological features of malignancy.3) Nase, et al. suggested that tumor necrosis, primary tumor size >7 cm, nuclear atypia, renal vein invasion and mitotic activity have been associated with recurrence, metastasis and death due to disease.4) Also Takahashi, et al. and Faraji, et al. suggested the possibility of primary tumor size as a predictor of malignancy.14,15) In the present case, primary renal EAML had the size more than 7 cm, necrosis, more than 70% epithelioid cell, nuclear atypia and renal vein invasion without atypical mitoses and mitotic activity. In spite of these adverse prognostic factors, this case of renal EAML had a 7-year disease-free interval prior to metastatic recurrence and the metastatic pulmonary tumor grew slowly for 6 years without systemic spread.

When renal EAML metastasizes to the lung, the pulmonary lesions are likely to be multiple or accompanied by simultaneous metastases to other organs in previous reports. Thereby, they described metastasectomy just for histological diagnosis in some reports. To the best of our knowledge, this is the first report of pulmonary metastasectomy for recurrent renal EAML with intention of cure.

Conclusion

EAML is potential malignant tumor and is often misdiagnosed as other renal tumor due to its histological and radiographical features. Local recurrence and distant metastasis after resection of primary EAML tumor frequently happen and mostly progress rapidly. But in some cases, disease may progress slowly even after recurrence like the present case. Atypical mitoses and mitotic activity in epithelioid cells may be related to malignant behavior of EAML. The data collection of the future cases diagnosed precisely as EAML is necessary to determine with more certainty which clinical and pathological features affects the disease progression.
Disclosure Statement

None of the authors has any financial or other potential conflict of interest.

References


