Renal Perivascular Epithelioid Cell Tumor with Lymph Nodes Metastasis: A Case Report and Literature Review

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Case report

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Abstract

**Background:** Perivascular epithelioid cell tumor (PEComa) is a mesenchymal tumor that originated from perivascular epithelioid cells. Angiomyolipoma (AML) is a common benign PEComa, composed of blood vessels, smooth muscle and mature adipose tissue. Epithelioid angiomyolipoma (EAML) is a rare subtype of AML that has the potential to be malignant.

**Case presentation:** The patient was a 42-year-old woman admitted to the hospital for her left low back swelling. The computed tomography angiography (CTA) revealed a 6.3*5.5*6.7cm cystic-solid tumor in the intermediate kidney. Then we performed a left nephrectomy. Postoperative pathology showed that the tumor was angiomyolipoma (PEComa) with necrotic formation and was 6cm*6cm*5.5cm in size. Additionally, lymph nodes involved (4/17) were observed in the left renal hilum. Immunohistochemistry staining indicated that tumor cells focally expressed MelanA and HMB45. No evidence of disease progression at the six-month follow-up after surgery.

**Conclusions:** Lymph nodes involvement in renal PEComa was rare and was regarded as a type of metastasis. Lymph nodes metastasis might indicate a poor prognosis.

**Background**

Perivascular epithelioid cell tumor (PEComa) was first described in 1943, and it is a mesenchymal tumor that originated from perivascular epithelioid cells with the immunohistochemical characteristics of smooth muscle and melanocytes [1]. PEComa has been described in various anatomical locations. The liver, pancreas, uterus and kidney are frequently involved [2]. Additionally, the PEComa family includes angiomyolipoma (AML), pulmonary clear cell ‘tumor, lymphangiomymomatosis and soft-tissue clear cell myomelanocytic tumors, as well as other extremely rare malignancies [3]. Although the majority of PEComas have benign clinical characteristics, a small part of them have aggressive features and can evolve into distant metastases. At present, surgery is the primary technique of treating local diseases, and there is no universally accepted standard for postoperative adjuvant therapy [4]. Notably, mTOR inhibitors have been reported to be used in the treatment of advanced PEComa [5]. Here, we present a patient who suffered from malignant renal PEComa with renal hilum lymph nodes metastasis.

**Case Presentation**

The patient was a 42-year-old woman admitted to the hospital for 15 days because of left lumbus pain, but no positive signs were identified in the physical examination. She did not complain of hematuria, urinary tract irritation symptom, or dysuria and no abnormality was identified in laboratory examination. There was no history of tuberous sclerosis complex (TSC).

The computed tomography angiography (CTA) revealed a 6.3*5.5*6.7cm cystic-solid tumor in left kidney’s middle and lower pole, with an obvious enhancement of solid components measuring approximately 1.8*1.7cm and a patchy hemorrhagic focus. The boundary of the mass is still visible. Then the left nephrectomy was performed, revealing several enlarged lymph nodes in the renal hilum, followed by renal hilar lymph node dissection. A solid mass with a clear border of approximately 6 cm was evident in the renal hilum, containing hemorrhagic and necrosis tissue.

"It is diagnosed as PEComa with necrotic formation, and tumor size was 6cm*6cm*5.5cm," according to postoperative pathology. Additionally, the lymph nodes involved (4/17) were seen in the left renal hilum. Besides, we observed that epithelioid component comprised around 30% of total. And the heterogeneity of some cells is evident, as evidenced by large and deep nucleus staining and an increase in the nuclear to cytoplasmic ratio. Necrosis was observed within the tumor. Immunohistochemistry staining showed that tumor cells expressed MelanA, Vimentin, SMA, and CD24 and were focally positive for HMB45 and CD10. Ki67 expression was detected in roughly 20% of tumor cells. However, tumor cells lacked Pax-8, S-100, and CK-pan expression. Within the six months follow-up post-operation, no disease recurrence and progression were identified.

**Discussion**

Angiomyolipoma (AML) is a common subtype of PEComa. It is composed of curved thick-walled blood vessels, smooth muscle, and adipocytes in varying proportions. And about 80–90% of renal AML occurs sporadically, usually isolated and unilateral [6, 7]. Some studies [8] have pointed out that AML is a common disease associated with tuberous sclerosis. Typical AML is a benign mesenchymal tumor. However, part of EAML tends to be malignant. EAML is extremely rare, accounting for about 5% of AML surgically removed [9]. Mai et al initially reported that renal AML with epithelioid morphology and its relation to AML [10] in 1996. Over 100 cases of EAML have been reported to date; however, the majority of them have benign results. At present, the pathogenesis of EAML is not clear, and there are no objective diagnostic criteria. We have recently treated a female patient who had been diagnosed as renal PEComa with lymph node involvement.

Nalan et al [11] considered the EAML as a malignant tumor after evaluating the characteristics of numerous cases. Previous studies [11, 12] revealed that 20–30% of EAML patients developed metastasis and recurrence, with the liver, lung, and peritoneum being the most frequently implicated locations. However, the definition of the proportion of epithelioid components in EAML is not defined explicitly. Based on the literature review, the proportion of epithelioid cells ranged between 10% and 100%, and studies indicated that more than 20% of epithelioid components are associated with recurrence and metastasis. The malignant risk seems to grow in direct proportion to the percentage of epithelioid components [13, 14]. At present, rigorous diagnostic criteria for malignant renal PEComa has not been established. Pure et al [11] discovered that tumors linked with associated TSC, size > 7cm, necrosis, infiltrative growth, or vascular invasion were associated with disease progression. In our case, around 30% of the cells are epithelioid, and the heterogeneity of some cells is pronounced. As a result, this patient should be continuously monitored.
Interestingly, there is no conclusive evidence that multiple AMLs are metastatic. Some researchers considered that multiple AMLs are polycentric in origin and that may be caused by the congenital presence of cell precursors in numerous locations [7] [15]. Tallarigo et al [16] considered that lymph nodes with regional or multiple involvements demonstrated multifocal development patterns rather than metastases. At present, there is no detailed research on the postoperative adjuvant therapy and prognostic factors of renal PEComa patient with lymph node involvement. Hence, we reviewed reported cases from 2001 to 2021. As illustrated in Table 1, 16 cases of PEComa with lymph node involvement have been recorded. Among them, 43.8% (7/16) of patients experienced local recurrence or metastasis. The most common metastatic organs were the liver and lung. Besides, 6 out of 7 patients died, with a median PFS of 16 months. As shown, metastasis to lymph node may indicated a poor prognosis. However, we can only evaluate patients with lymph node metastasis retrospectively when they are reported and cannot combine them for additional analysis.

Table 1

| Cases | Age | Sex | TSC | Location of metastasis | Metastasis at the time of diagnosis | Recurrence | Location of metastasis | Tumor Size (cm) | Epithelioid cells | Number of Mitosis/50 HPF | Renal vein involvement | Follow up | PFS (mo) |
|-------|-----|-----|-----|------------------------|-----------------------------------|------------|------------------------|-----------------|------------------|----------------------|------------------------|-----------|---------|
| 1     | 21  | M   | Yes | Both                   | Liver, spleen, peritoneum; retroperitoneal lymph nodes | No         | 0.5–17                | > 90%           | NA               | No                   | NA                     | Died      | NA      |
| 2     | 78  | F   | NA  | Left                   | Lung, bone, regional lymph node    | No         | 12.5                  | NA              | NA               | NA                   | Died                   | NA        | 16      |
| 3     | 31  | F   | Yes | Both                   | Retroperitoneal lymph nodes        | No         | 1–10                  | < 50%           | NA               | Yes                   | Alive                  | NA        | 24      |
| 4     | 48  | F   | No  | Right                  | Retroperitoneal lymph nodes        | Yes        | Liver, lung           | 13              | NA               | Yes                   | Died                   | 16        | 12      |
| 5     | 14  | M   | Yes | NA                     | Lymph nodes                        | No         | 11                    | NA              | 1                | NA                   | Alive                  | 24        |         |
| 6     | 25  | F   | No  | NA                     | Lymph nodes                        | Yes        | Peritoneal, liver, lung | 8               | NA               | 2                    | NA                     | Died      | 12      |
| 7     | 67  | M   | No  | NA                     | Lymph nodes                        | No         | 15                    | NA              | 2                | NA                   | NA                     | NA        | NA      |
| 8     | 58  | M   | No  | NA                     | Lymph nodes                        | Yes        | Liver                 | 37              | NA               | 0                    | NA                     | Died      | 24      |
| 9     | 55  | F   | No  | NA                     | Lymph nodes                        | Yes        | Extensive metastatic  | 12.8            | NA               | 4                    | NA                     | Died      | 12      |
| 10    | 11  | F   | No  | Left                   | Lymph nodes                        | No         | 10.5                  | NA              | NA               | NA                   | Died                   | seve mon  |         |
| 11    | NA  | NA  | NA  | NA                     | Lymph nodes                        | No         | NA                    | NA              | NA               | NA                   | Alive                  | 36        |         |
| 12    | 71  | F   | NA  | NA                     | Retroperitoneal lymph nodes        | No         | 9                     | 10%             | 1/10HPF          | No                   | Alive                  | 54        |         |
| 13    | 59  | M   | NA  | NA                     | Retroperitoneal lymph nodes        | Yes        | Retroperitoneal recurrence | 16             | 100%            | 2/10HPF              | Yes                    | Alive      | 40      |
| 14    | NA  | NA  | NA  | NA                     | Renal hilus and para-aortic Lymph nodes | Yes        | Hepatic, lung         | NA              | > 90%            | NA                   | NA                     | Died      | 17      |
| 15    | NA  | NA  | NA  | NA                     | Renal hilus lymph nodes            | Yes        | Local recurrence      | NA              | > 90%            | NA                   | NA                     | Died      | 14      |
| 16    | 42  | F   | NA  | Left                   | Lymph nodes                        | No         | 6.7                   | 30%             | NA               | No                   | Alive                  | 4         |         |

Liu et al [17] analyzed the CT scan characteristics of EAMLs and discovered a tendency for super-attenuation on pre-contrast CT with or without fat components, as well as a dynamic enhancement-mode from rapid wash-in to slow wash-out. PEComa, mainly composed of epithelial cells, could be misdiagnosed as renal clear cell carcinoma if HMB45 and Melan-A are negative. HMB-45 and Melan A are the most sensitive immunohistochemical markers in PEComa [18]. In addition, renal PEComa should be distinguished from pleomorphic rhabdomyosarcoma, malignant melanoma, alveolar soft part sarcoma, etc. Currently, tumor excision with negative tumor margins is still the recommended treatment strategy.

Many research indicated that malignant PEComa was associated with mutations in the TFE3 and P53 genes [19, 20]. Besides, activation of mTOR was related to the malignant potential of PEComa, for which mTOR inhibitors might be beneficial [4, 5]. Thus, a multi-modal therapy strategy for PEComa with malignant potential should be explored. However, there are few publications discussing the options and efficacy of postoperative adjuvant therapy, indicating an urgent require for further research.

Conclusions
Lymph nodes involvement in renal PEComa was rare. Through the literature review, we believe that renal PEComa with lymph node involvement is a type of metastasis, which indicates the malignant potential of PEComa, and lymph node metastasis may indicate a poor prognosis. At present, patients with renal PEComa usually receive surgical treatment, but there is no standard postoperative adjuvant treatment, for such patients, postoperative adjuvant treatment may be beneficial to their prognosis.

Abbreviations

AML
Angiomyolipoma
CT
Computed tomography

Declarations

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Research Ethics Committee of The First Affiliated Hospital of Nanjing Medical University and with the 1964 Helsinki declaration and its later amendments. ALL written informed consent to participate in the study was obtained from the patient.

Consent for publication

All subjects have written informed consent; All presentations of case reports have consent for publication.

Availability of data and material

All data generated or analyzed during this study are included in this article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

LC: made substantial contributions to the conception, design of the work, acquisition, analysis, interpretation of data and has drafted the work. QC: made substantial contributions to the interpretation of data and has substantially revised it. HH: made substantial contributions to the data collection. QW,BY: made substantial contributions to the picture editing. JZ,KL,JH: made substantial contributions to the patient treatment and care. HY,JL,DF,PL,PL: made substantial contributions to the manuscript revision. XY,QL: made substantial contributions to the conception, design of the work, analysis. All authors read and approved the final manuscript.

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Figure 1

CT image of the patients' abdominal organs. A, several enlarged lymph nodes were also noted (white arrow). B, a cystic-solid mass of 6.3*5.5*6.7cm was seen in the middle and lower pole of the left kidney with a noticeable enhancement of solid components and a patchy hemorrhagic focus. C and D, the solid components and blood supply of the tumor can be well observed. CT = computed tomography.

Figure 2

Histochemical and immunohistochemical features of the kidney. A, The typical PEComa area. B, Tumor cells with epithelioid appearance. C, Local necrotic area within the tumor. D, Lymph node metastasis ×40. E, Tumor cells were strongly positive for MelanA. E, Tumor cells were strongly positive for SMA.
Figure 3

A mass with a clear boundary of approximately 6 cm in the renal hilum, as were 1.5 cm solid components including hemorrhagic and necrosis tissue.