

Perirenal Perivascular Epithelioid Cell Tumor (PEcoma) with Pulmonary Micro Invasive Adenocarcinoma: A Case Report and Literature Review

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Abstract: Perivascular epithelioid cell tumor (PEcoma) is a rare type of mesenchymal neoplasm, which occurs most commonly in uterus and gastrointestinal tract. PEcoma with perirenal manifestation is an extremely rare entity. To the best of our knowledge, only four cases have been reported up to now. In this case, we reported a patient with both a pulmonary mass and a perirenal mass. Two resections were performed successively and postoperative pathology suggested pulmonary micro invasive adenocarcinoma (MIA) and perirenal PEcoma. This is the first case of perirenal PEcoma with pulmonary MIA. Combining the present case and prior literature, we summarized the crucial role of immunohistochemistry in the diagnosis and consider that complete operation might be conducive to patients with perirenal PEcoma that presents a benign phenotype, regardless of complications with other tumors.

Keywords: perivascular epithelioid cell tumor, pulmonary micro invasive adenocarcinoma, case report

Introduction

Perivascular epithelioid cell tumor (PEcoma), first described by Zamboni et al. in 1996,¹ is a rare type of mesenchymal neoplasm. In 2007, the World Health Organization (WHO) formally defined it as “a kind of mesenchymal tumors composed of histologically and immunohistochemically distinctive perivascular epithelioid cells”.² According to the distinctive morphology and expression of myomelanocytic markers, the PEcoma family mainly includes angiomyolipoma (AML), clear cell “sugar” tumor of the lung (CCST), lymphangiomyomatosis (LAM), and a number of unusual visceral, intraabdominal, soft tissue and bone tumors.³ PEcoma most commonly occurs in the uterus (including uterine and cervix uteri)⁴ and gastrointestinal tract.⁵ Perirenal manifestation is an extremely rare entity. To the best of our knowledge, only four cases have been reported up to now,⁶⁻⁹ among which only one case study⁶ described a case in which the perirenal PEcoma coexisted with malignant gastroenteric tumors. No certain origin and uniform histological pattern has been detected yet.¹⁰ The treatment of PEcoma remains controversial; complete resection is the mainstay of treatment while chemotherapy and immunotherapy are also applied in some cases.

In this study we report the first case of perirenal PEcoma with pulmonary micro invasive adenocarcinoma (MIA)¹¹ and discuss the diagnosis and treatment of the perirenal PEcoma.

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Case Report

The study was approved by the Ethics Committee of Tongji hospital, Tongji Medical College, Huazhong University of Science and Technology, China. Written informed consent for publication of the details was obtained from the patient.

A 43-year-old man presented to the department of thoracic surgery with a 13×4 mm nodule in the right upper lung detected by computed tomography (CT) during examination (Figure 1A). This patient had no clinical symptoms and no history of smoking. Tumor marker tests showed that the level of anti-CAGE antibody was slightly elevated (8.8 U/mL, normally ≤ 7.2 U/L), which is

commonly thought to be a lung cancer-associated auto-antibody. Furthermore, a perirenal mass, 18×28 mm in size, close to the hilum of the left kidney was found through abdominal magnetic resonance imaging (MRI) (Figure 1B). Positron emission tomography-computed tomography (PET-CT) showed lesions in both the lung and the renal hilum (Figure 2A and B), which suggested neoplastic lesions. Since the main complaint of the patient was the pulmonary neoplasm, firstly he was scheduled for sublobectomy of right upper lung tip by video-assisted thoracic surgery (VATS). The postoperative pathology indicated that the lung nodule was microinvasive lung adenocarcinoma (Supplementary Figure 1A and B).

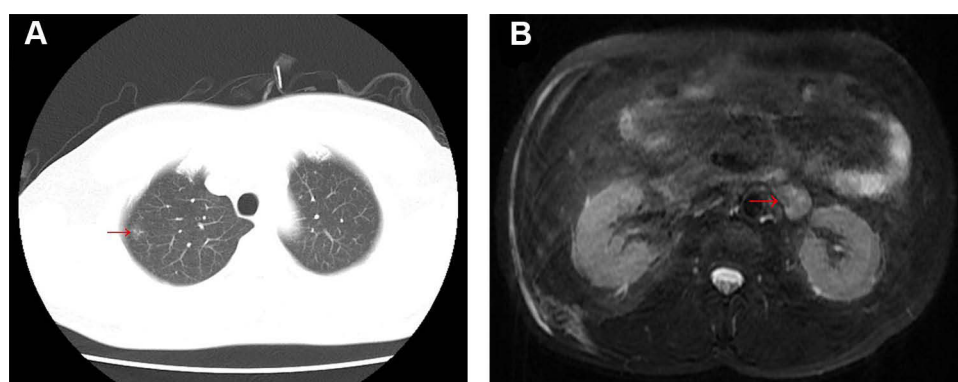


Figure 1 (A) Chest CT detected a 13×4 mm nodule in the right upper lung; (B) abdominal MRI revealed a perirenal tumor, 18×28 mm in size, close to the hilum of the left kidney.

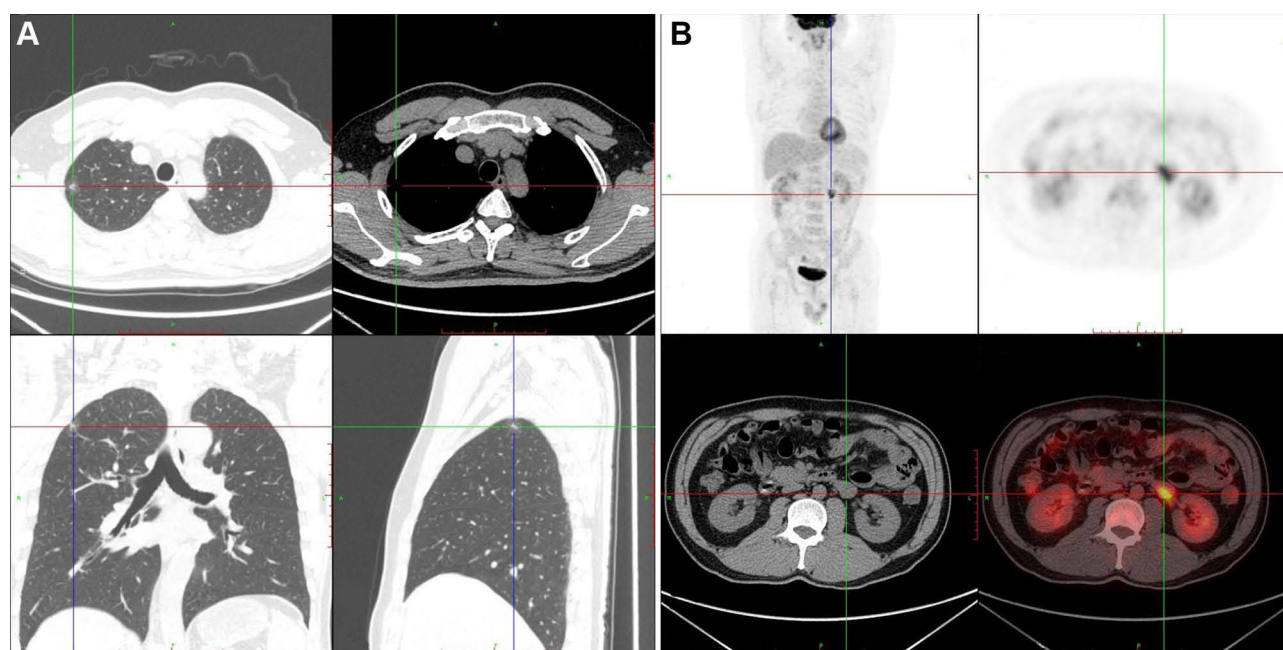


Figure 2 Positron emission tomography (PET)-CT whole body imaging. (A) A 15×10 mm shadow with ground glass density in the upper right lung was detected; (B) a neoplastic lesion with hypermetabolism close to the left renal hilum was shown.

Furthermore, immunohistochemical stains showed that this lesion was C-MET (+) and ROS1 (+) ([Supplementary Figure 1C and D](#)). Considering the patient's physical condition, he went home for two months after the first operation and was then admitted to our hospital for retroperitoneal neoplasm. Abdominal enhanced CT suggested a 22×30 mm mass inferior to the left renal vein with enhancement but no sign of local and vascular invasion. Hormone tests showed normal levels of renin, aldosterone, cortisol and epinephrine. To further define the nature of the mass, endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) was performed and the histopathology of the biopsy showed tumor cells. Subsequently, laparotomy was conducted and the postoperative period was uneventful. Macroscopically, the perirenal tumor consisted of a grayish yellow fragile tissue fragment measuring 40×20×10 mm. Histologically, the tumor was composed of cells with eosinophilic cytoplasm

with moderate epithelioid appearance ([Supplementary Figure 2A–D](#)). No prominent nuclear polymorphism was shown in most cells. Further immunohistochemical stains were performed on the perirenal lesion and showed that the lesion was positive for Melan-A, cluster differentiation (CD)56 and TFE3, while negative for HMB45, CgA, Syn, S-100 and SOX10. In addition, Ki67 was present in approximately 1% of tumor cells ([Figure 3](#)). The histological examination and immunohistochemical stains fulfilled the criteria for the diagnosis of benign PEComa. Finally, the patient was identified as a benign perirenal PEComa coexisting with micro invasive lung adenocarcinoma (T1aN0M0R0). The patient was discharged on the 10th postoperative day.

Discussion

Since the first case of PEComa reported in 1996, cases involving various anatomic locations have been reported,

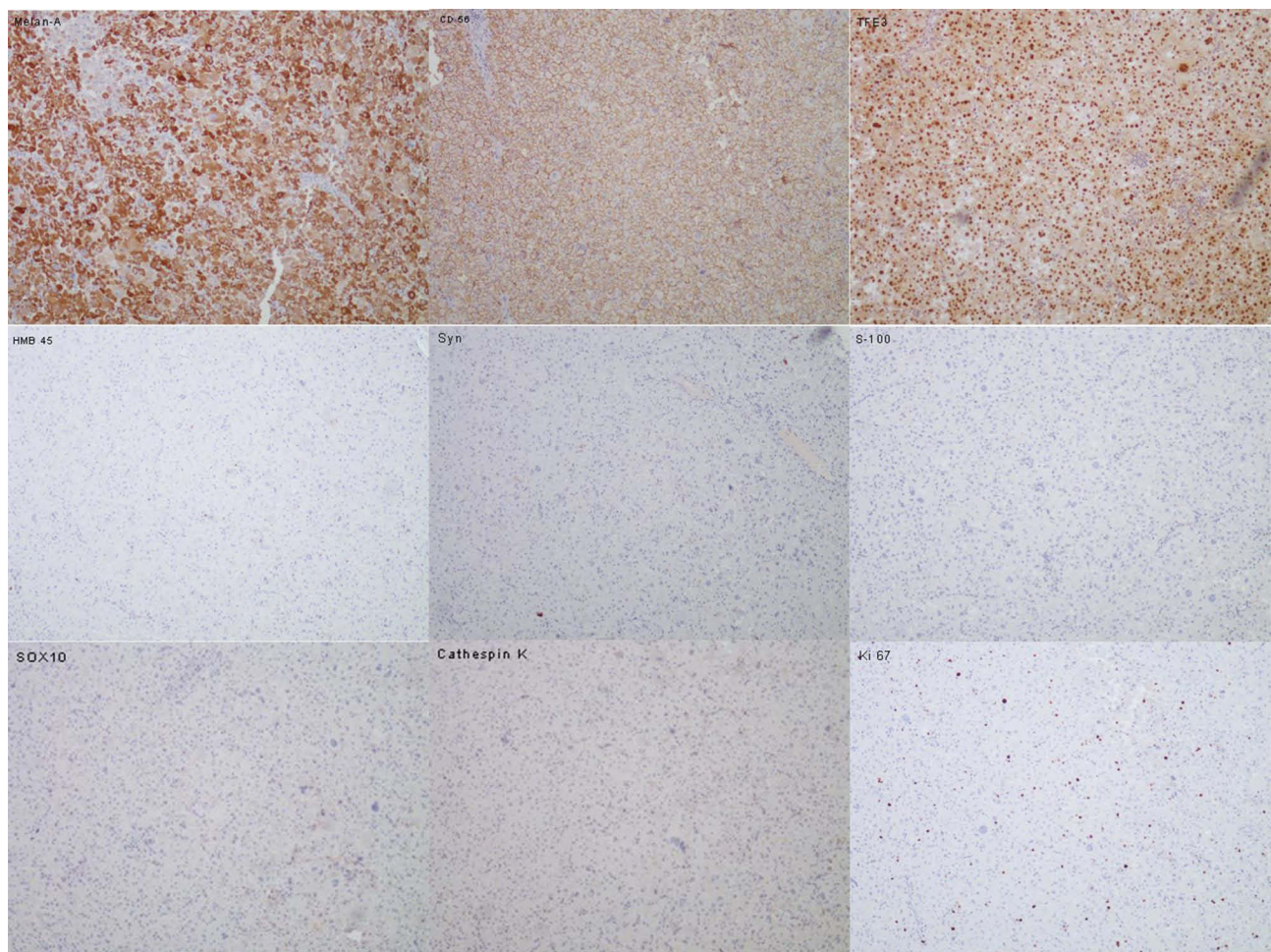


Figure 3 Immunohistochemistry of the perirenal mass showed positive for Melan-A, cluster differentiation (CD)56, and TFE3, while negative for HMB45, Syn, S-100 and SOX10. Ki67 was present in approximately 1% of tumor cells.

such as gastrointestinal tract,⁴ kidney,¹² pancreas,¹³ liver,¹⁴ ovary,¹⁵ uterus⁵ and so on.^{16,17} According to the recent systematic reviews,^{10,15} the most commonly affected organs were uterus (including uterine and cervix uteri) and colon, with approximately 65 and 20 cases reported online, respectively. Perirenal PEComa are extremely rare, to date, only four cases have been reported and our case is the fifth one (Table 1). Besides, this case is the second case of perirenal PEComa complicated with other primary tumor. Demographically, perirenal PEComa mainly occurs in middle-aged and elderly women while our case involved a middle-aged man. No certain location preference and morphological features were found.

The PEComa coexpresses melanocytic and muscle markers characteristically. Immunohistochemistry plays a vital role in the diagnosis. According to a systematic review in 2020,¹⁸ HMB45, a specific marker for PEComa, abundantly clear to eosinophilic granular cytoplasm, is 99% positive in PEComa and has been utilized to support the diagnosis of PEComa at multiple sites.¹⁹ The positive rate of Melan-A, which is recognized as an antigen on melanoma cells by cytotoxic T-lymphocytes, varied from 13% to 88% in PEComa.¹⁸ In addition, MTF, HMSA-1,²⁰ smooth muscle actin (SMA), desmin²¹ and CathepsinK²² were successively reported to be potential markers in the diagnosis of the PEComa, yet no consensus has been reached. CD56 (+) supported the origins of neural tissue while S100 were usually negative in PEComa.²³ Consistent with data shown in Table 1, immunoactivity for HMB45 was most commonly demonstrated, present in 4/5 cases. Notably, our case showed positive expression for Melan-A while negative expression for HMB45 in perirenal lesion. Combining HMB45-negative cases occurring in other locations,^{10,23} more studies are still needed to reveal the certain pattern of the immunohistochemical features of PEComa.

In this case, the patient was admitted to the hospital due to pulmonary nodules considered as adenocarcinoma and the perirenal mass was found by further examination. Since kidney is one of metastasis sites of lung adenocarcinoma, and lung is a common metastatic organ of many malignant tumors, including primary malignant tumors in the kidney, we could not distinguish whether the perirenal neoplasm was a metastatic tumor or a primary tumor through image tests including enhanced CT and PET-CT. Finally, pathology of the pulmonary mass suggested MIA (<0.6 cm invasion), and immunohistochemistry stains suggested that the perirenal neoplasm was not the metastasis of pulmonary MIA but

the primary PEComa. Similar to the other case,⁷ as most PEComa show no specific symptoms, the distinction between one primary tumor with metastatic sites and concomitantly primary tumors was difficult when imaging detected multiple lesions. On this occasion, the acquisition of specimens in multiple lesions is crucial for the diagnosis and the selection of the treatment. It is essential for pathologists to know the lesion to avoid misdiagnosis.

As a rare mesenchymal soft tissue neoplasm, no consensus has been reached on the treatment of PEComa. The classification and treatment of PEComa were significantly associated with six factors, including tumor size, infiltrative growth pattern, high nuclear grade cellularity, mitotic rate, necrosis and vascular invasion.³ However, considering the limited data, we could not conclude a similar classification targeted to the perirenal or retroperitoneal PEComa. In our case, the patient had no clinical symptoms and most of the other auxiliary examinations were normal. Besides, tumor size (40x20x10 mm) was consistent with the characteristics of benign tumor and no sign of progression was detected after the complete resection. Combined with the pathologic results, we confirmed that the perirenal PEComa was a benign lesion. Similarly, three other patients with perirenal PEComa with no obvious clinical symptoms, tumor size ≤ 10 cm and postoperative pathology suggesting no obvious nuclear heterogeneity, showed different degrees of improvement after the prompt surgery, which indicates that small tumor size, high nuclear grade and high cellularity are benign manifestations. Complete operation might be conducive to patients with perirenal PEComa that presents a benign phenotype, regardless of complications with other tumors. On the other hand, for patients with PEComa that shows malignant phenotype without resectability, both mTOR inhibitor and chemotherapy might not considerably improve the survival rate.⁷

Conclusion

To conclude, perirenal PEComa is a rare entity with no certain pathologic features and immunohistochemistry might play a crucial role in diagnosis. The acquisition of specimens in multiple lesions is vital to the distinction between one primary tumor with metastatic sites and concomitantly primary tumors. We hope that this case may contribute to an improved understanding of this disease and ultimately to avoid clinical misdiagnosis, missed diagnosis and treatment delay. Considering the limitations of the data, more studies are needed to provide new and comprehensive evidence for the diagnosis and treatment of PEComa.

Table I Characteristics of Prior Cases of Perirenal Perivascular Epithelioid Cell Tumor (PEComa)

| Study (Publication Year) | Gender | Age | Region | Tumor Location | Tumor Size (cm) | Pathology | Immunohistochemical Study | Coexisting Tumor | Resectability | Other Treatments | Prognosis |
|---------------------------------------|--------|-----|---------|--|-------------------|---|--|---|---------------|---------------------------------|---|
| Sven Gunia (2005) ⁴ | 57 | F | Germany | Below the left perinephric capsule with a tongue-like growth pattern towards the hilus of the kidney | 5.3 x 5.0 x 3.0 | Composed of epithelioid cells and spindle cells | HMB-45(+), Melan A(+), CD99(+), Ki67(+)<1% | NR | Yes | NA | No evidence of any local recurrence or of any distant metastases at the 8-month post-surgical follow-up No local recurrence or distant metastases at the 8-month post-surgical follow-up |
| Shotaro Nakanishi (2014) ⁵ | 51 | F | Japan | In the right perirenal space and multiple liver metastases | 20.0 x 16.0 x 9.0 | Composed of lightly eosinophilic cytoplasm, round to slightly ovoid nuclei, and small nucleoli | HMB-45(+), Melan-A (+) | NR | No | mTOR inhibitor and temsirolimus | Die Died about five months after the start of molecular targeted therapy |
| Christos V Gkizas (2015) ⁶ | 44 | F | Greece | In close proximity to the left renal capsule | 6.0 x 7.0 x 10.0 | Composed of spindle and epithelioid cells | Vimentin(+), desmin(+), SMA(+), HMB45(+), CD56(+), CD99(+), NSE (+) | NR | Yes | NA | Uneventful recovery |
| Marian Danilewicz (2017) ⁷ | 66 | F | Poland | Close to the superior pole of the right kidney | 1.5 x 1.0 x 0.6 | Composed of polygonal clear cells or cells with eosinophilic cytoplasm with moderate epithelioid appearance | HMB-45 (+), vimentin (+), focally desmin (+), Ki-67 (+) (8%), CD10(-), S-100 (-) | Mucinous gallbladder cancer and pancreatic head tumor | Yes | NA | Uneventful recovery |
| Present case | | | | | | | | | | | |
| Zhaoxun Li (2021) | 43 | M | China | Close to the hilum of the left kidney | 4.0 x 2.0 x 1.0 | Composed of cells with eosinophilic cytoplasm with moderate epithelioid appearance | Melan A (+), CD56(+), TFE3(+), HMB45(-), SMA (-), desmin(-), S-100(-), SOX10(-), Ki-67(+)=1% | Pulmonary micro invasive adenocarcinoma | Yes | NA | Uneventful recovery |

Abbreviations: F, female; M, male; NR, not reported; NA, no application; CD, cluster differentiation.

Author Contributions

All authors contributed to data analysis, drafting or revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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