CASE REPORT PEER REVIEWED | OPEN ACCESS

Perivascular epithelioid cell tumor of the lung with focal pigment production

Sowmini Medavaram, Trishala Agrawal, Gail Prado, Maya Shah

ABSTRACT

Introduction: Perivascular epithelioid cell (PEC) tumors, also (PEComas), are rare mesenchymal tumors defined by the presence of perivascular epithelioid cells that express muscle and melanocytic markers and have no known normal tissue counterparts. These include wide range of tumors like angiomyolipoma (AML), lymphangioleiomyomatosis (LAM) and clear cell "sugar" tumor of the lung (CCST). These are associated with tuberous sclerosis. The PEComa with pigment production is rare and it can be a diagnostic challenge to distinguish it from malignant melanoma. The immunoprofile of the tumor with strong human melanocytic black-45 (HMB-45) expression and the absence of other melanocytic markers like S-100 and SOX-10 suggests the diagnosis of PEComa.

Case Report: We report a 34-year-old female with past medical history of hypothyroidism who presented with right upper back pain for past six months. Chest X-ray performed at that time revealed a lung mass. Computed tomography scan of chest showed a multi-lobular 3.4x2.2 cm soft tissue mass in the right lower lobe. Bronchoscopy was non-diagnostic. Computed tomography guided biopsy revealed atypical spindle cells strongly positive for HMB-45 and vimentin, negative for melanoma markers like S100. She eventually underwent a VATS procedure with complete resection of the tumor. Pathology of the lung mass confirmed the same.

Conclusion: Pigmented PEComas are rare and difficult to distinguish from malignant melanoma. Findings of atypical spindle cell neoplasm with focal pigment production which is positive for HMB-45 and negative for S-100 stain makes PEComa more likely. Pigmented PEComas of the lung have not been reported so far to our knowledge.

Keywords: PEComa of lung, Pigmented PEComa, HMB-45, Perivascular epithelioid

How to cite this article

Medavaram S, Agrawal T, Prado G, Shah M. Perivascular epithelioid cell tumor of the lung with focal pigment production. J Case Rep Images Pathol 2016;2:10–14.

Article ID: 100007Z11SM2016

****

doi:10.5348/Z11-2016-7-CR-3

Sowmini Medavaram[1], Trishala Agrawal[2], Gail Prado[3], Maya Shah[4]

Affiliations: [1]MD, Internal Medicine Resident, Newark Beth Israel Medical Center, Newark, NJ; [2]MD, Hematology/Oncology fellow, Newark Beth Israel Medical Center, Newark, NJ; [3]MD, Pathology Resident, Newark Beth Israel Medical Center, Newark, NJ; [4]MD, Hematology/ Oncology Attending, Assistant Program Director of Fellowship, Newark Beth Israel Medical Center, Newark, NJ.

Corresponding Author: Sowmini Medavaram, MD, 3111 Bristol Station Ct, Carteret, NJ-07008; Email: Sowmini. medavaram@gmail. com

Received: 05 January 2016
Accepted: 05 February 2016
Published: 29 March 2016

INTRODUCTION

Perivascular Epithelioid Cell (PEC) tumors, also PEComas, are rare mesenchymal tumors defined by the presence of perivascular epithelioid cells that express muscle and melanocytic markers and have no known normal tissue counterparts [1]. Angiomyolipoma (AML), clear cell "sugar" tumor (CCST) of the lung,

lymphangioleiomyomatosis (LAM), clear cell melanocytic tumor of the falciform ligament/ligamentum teres, and rare clear cell tumors of other anatomical sites, such as the liver, uterus, vulva, rectum, urinary bladder, abdominal wall and pancreas are tumors which have both muscle and melanocytic markers which fall in the category of PEComa [2–4]. These tumors are usually associated with tuberous sclerosis complex with female predominance, especially AML and LAM [5]. Pigmented PEComas are rare and difficult to differentiate from metastatic melanoma. The pigmented PEComa, unlike the typical PEComa, occurs in females without tuberous sclerosis [5]. So far only 10 reported cases of pigmented PEComas of the kidney and one in liver have been reported [6, 7]. The immunoprofile of the tumor with strong human melanocytic black-45 (HMB-45) expression and the absence of other melanocytic markers like S-100 and SOX-10 suggest the diagnosis of PEComa [7]. To the best our knowledge, this is the first reported PEComa of the lung with pigment production.

CASE REPORT

A 34-year-old female with a medical history of hypothyroidism presented with a lung mass on chest X-ray performed to evaluate chronic right upper back pain present for last six months. Physical examination and laboratory results were unremarkable. A previous chest X-ray done two years ago on a routine visit to her primary care doctor has shown a smaller lesion but was not followed-up until she became symptomatic. Computed tomography scan of chest confirmed a multi-lobular 3.4x2.2 cm soft tissue mass in the right lower lobe (Figure 1). Bronchoscopy with biopsy was negative for malignant cells and microorganisms. Computed tomography guided biopsy revealed atypical spindle cells strongly positive for HMB-45 and vimentin expression, negative for S100, SOX-10, cytokeratin, CD20, LCA, CD15, desmin and SMA. PET scan confirmed uptake of FDG in the right lung mass with no other pulmonary, mediastinal, cervical, intra or retro abdominal foci of increased uptake. Lymph nodes were unremarkable in all regions. She had wedge resection of the right upper lobe mass through video assisted thoracoscopic surgery (VATS). Grossly it was 3.5x2.5x 2.0 cm bulging dome shaped mass. There were no postoperative complications and the patient was discharged seven days after the surgery. A thorough gynecological examination did not reveal any pathology.

Pathology:

Macroscopic findings after VATS showed right upper lobe of the lung measuring 9.0x8.5x 6.0 cm and weighing 64 grams. Along the hilum was a bulging dome shaped mass measuring 3.5x2.5x2.0 cm. On section, the mass consisted of friable soft gray-white tissue. The pleural surface was smooth and showed moderate congestion.

Light microscopic examination revealed a relatively well defined sub-pleural densely cellular mass composed of sheets and short fascicles of tumor cells with scattered lymphoid aggregates. The predominant tumor cell population was ovoid to spindle, with a moderate amount of pale eosinophilic cytoplasm, vesicular chromatin and tumor giant cells, as well as cells containing fine brown intracytoplasmic pigment (Figure 2). It had conspicuous intratumoral lymphoid infiltrate with numerous eosinophils. Mitotic figures were scattered throughout the specimen with an average of 2 mitoses per 2 square mm. Focal necrosis was seen.

Immunohistochemical stains were positive for HMB 45 (Figure 3), focally for Melan-A (Figure 4), vimentin (Figure 5) and negative for S-100 (Figure 6) and SOX-10. Ki-67 immunostain was positive in 5% of the tumor

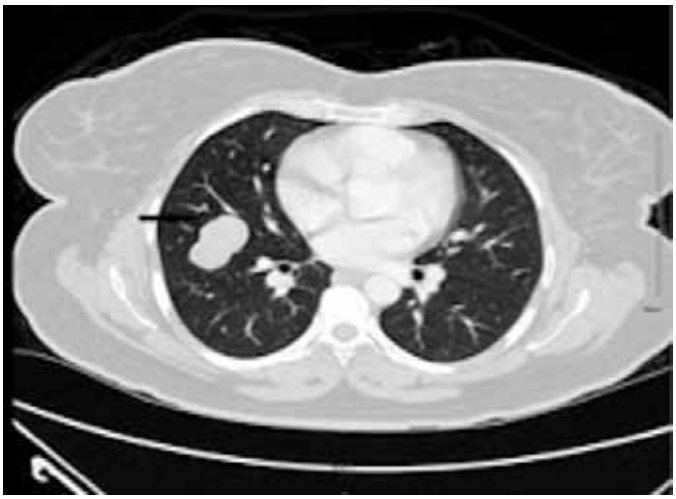

Figure 1: Computed tomography scan of chest showing multi-lobular 3.4x2.2 cm soft tissue mass in the right lower lobe. It has well defined margins and does not contain macroscopic calcification.

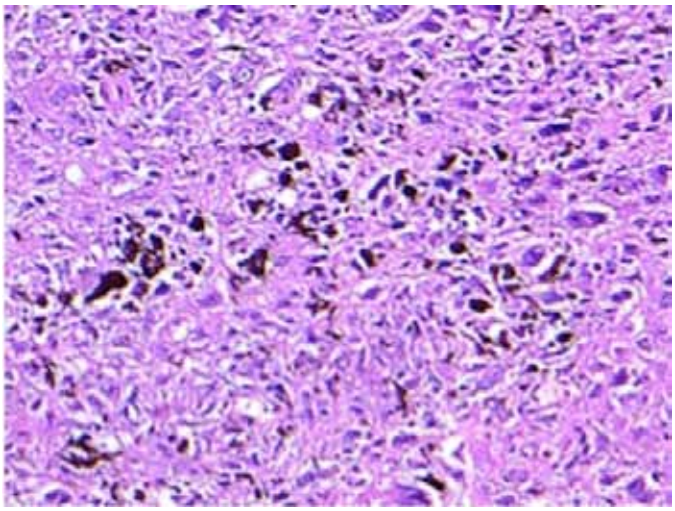

Figure 2: Light microscopy reveals sheets and nests of spindle cells, and thin-walled blood vessels. The malignant cells have eosinophilic cytoplasm, and pleomorphic nuclei with vesicular chromatin and visible nucleoli. Also numerous cells contain brown intracytoplasmic pigmentation. Scattered abnormal mitotic figures are also seen averaging 2 mitoses per 2 mm^2.

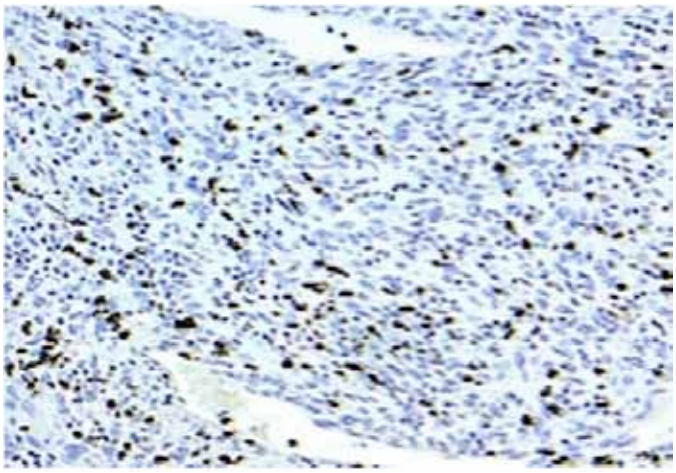

Figure 3: HMB-45 positive stain.

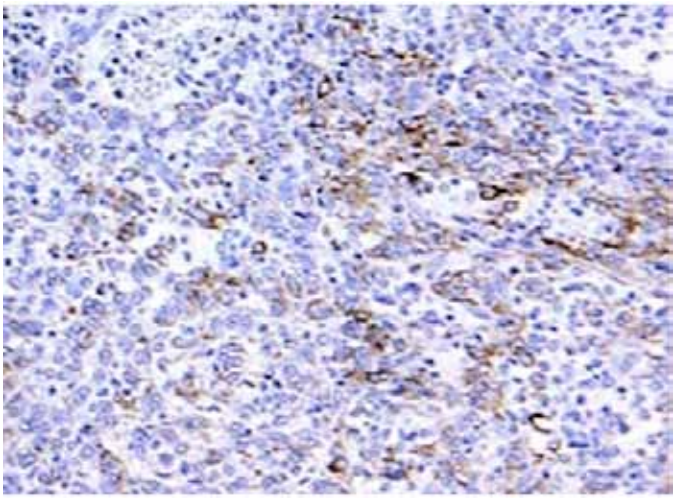

Figure 4: Melan-A focally positive.

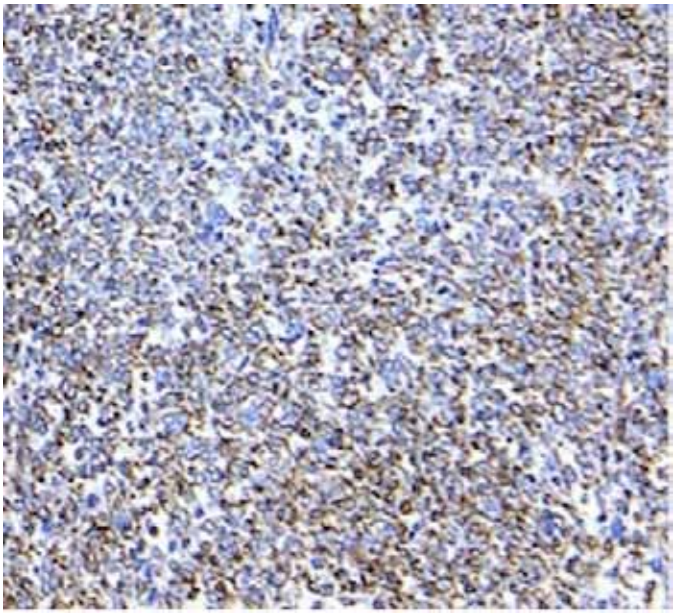

Figure 5: Vimentin positive.

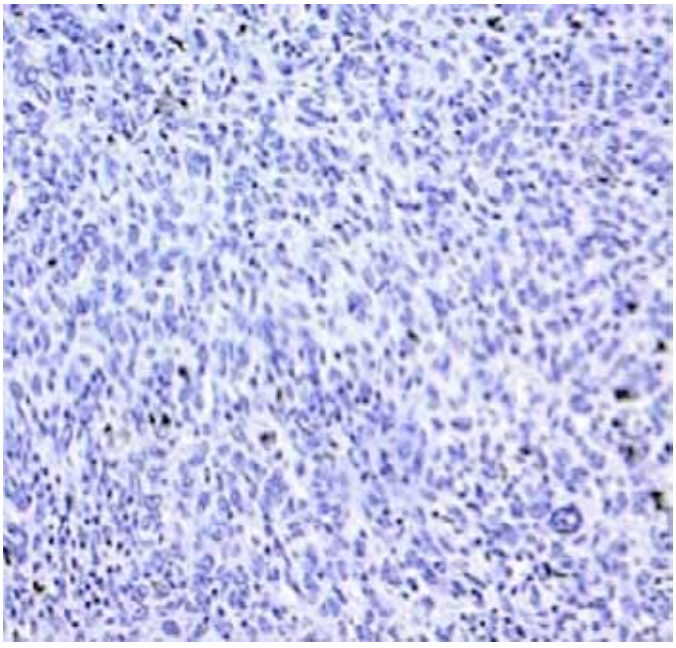

Figure 6: S-100 negative.

cells. Remaining immunohistochemical stains are shown below in the Table 1. Table 2 shows immunostains which help in differentiating between Pigmented PEComas and malignant melanoma.

Table 1: Immunohistochemical stains performed on the tissue from the lung

Vimentin (+)	CK 7 (-)
Melan-A (focally +)	CK 20 (-)
HMB-45 (focally +)	CD 43 (-)
S-100 (-)	CD 138 (-)
Calretinin (focally +)	PAX-5 (-)
Desmin (-)	PAX-8 (-)
CD34 (-)	CD 30 (-)
TTF-1 (-)	ALK (-)
CD117 (-)	ER (-)
CK (-)	Low Ki-67 < 5%
Sox-10 (-)	Iron (-)

Table 2: Immunostains which help in differentiating between Pigmented PEComas and malignant melanoma.

Pigmented PEComa	Malignant Melanoma
S-100 negative	S-100 strongly positive
HMB-45 focally positive	HMB-45 strongly positive
Melan-A focally positive	Melan-A strongly positive
SOX-10 negative	SOX-10 positive
Vimentin positive	Vimentin positive

DISCUSSION

Typically PEComas of the lung are characterized by the presence of epithelioid or spindle cells with clear or granular eosinophilic cytoplasm. These tumors are also known as clear cell 'sugar' tumor of the lung (CCTL) as the PAS stain shows glycogen granules in the cytoplasm of these clear cells [8, 9].

Typically, CCTL is a rare benign pulmonary neoplasm which can occur in any age group (8–73 years) with slight female preponderance [9]. Most lesions are solitary, asymptomatic, located within the peripheral lung and pose a significant diagnostic problem. Only few develop symptoms like breathlessness, back pain, chest pain, fever and hemoptysis [9].

Macroscopically, CCTL appear as well circumscribed, peripheral nodules usually less than 3 cm in diameter and cut surface is without evidence of hemorrhage, necrosis, cavitation or calcification. Histologically, they consist of mitotically inactive round or oval cells with clear or granular eosinophilic cytoplasm and distinct cell borders, with characteristic intervening thin-walled sinusoidal vessels [9].

Though most of these tumors are benign, malignant behavior is occasionally reported. The degree of malignancy is highly variable in PEComas. The size of the tumor and the mitotic rate seem to be the most reliable prognostic factors associated with recurrence after surgical resection [10]. Our patient had tumor <5 cm, mitotic rate of 2 mitoses per 50 hpf and absence of necrosis which makes the PEComa benign as per the modified Folpe's criteria [10]. Repeat CT scan of chest done six months later showed no evidence of recurrence of the tumor.

CONCLUSION

In summary, our patient had atypical spindle cell neoplasm with focal pigment production positive for HMB-45 and negative for S-100 and SOX-10 immunostains. The differential diagnosis included metastatic melanoma and PEComa. While it is unusual for melanoma to be negative for both S-100 and SOX-10, it remained a diagnostic consideration as the tumor had melanin pigment and HMB-45 staining. However, the presence of atypical spindle shaped cells with an immunostain positive for vimentin and HMB-45 made PEComa more likely. Our case is distinguished by the presence of the melanin pigment which is unusual in PEComa. The final morphologic and immunohistochemical findings are most consistent with a tumor with perivascular epithelioid cell differentiation (PEComa).

****

Author Contributions

Sowmini Medavaram – Conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Critical revision of the article, Final approval of the version to be published

Trishala Agrawal – Conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Critical revision of the article, Final approval of the version to be published

Gail Prado – Conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Critical revision of the article, Final approval of the version to be published

Maya Shah – Conception and design, Acquisition of data, Analysis and interpretation of data, Critical revision of the article, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

Copyright

REFERENCES

1. Folpe AL. In: World Health Organization Classification of Tumors. Pathology and genetics of tumors of soft tissue and bone. Fletcher CDM, Unni KK, Mertens F eds. Neoplasms with perivascular epithelioid cell differentiation (PEComa). Lyon, France: IARC Press; 2002. p. 221–2.
2. Vang R, Kempson RL. Perivascular epithelioid cell tumor ('PEComa') of the uterus: a subset of HMB-45-positive epithelioid mesenchymal neoplasms with an uncertain relationship to pure smooth muscle tumors. Am J Surg Pathol 2002 Jan;26(1):1–13.
3. Tazelaar HD, Batts KP, Srigley JR. Primary extrapulmonary sugar tumor (PEST): a report of four cases. Mod Pathol 2001 Jun;14(6):615–22.
4. Folpe AL, Goodman ZD, Ishak KG, et al. Clear cell myomelanocytic tumor of the falciform ligament/ligamentum teres: a novel member of the perivascular epithelioid clear cell family of tumors with a predilection for children and young adults. Am J Surg Pathol 2000 Sep;24(9):1239–46.
5. Eble JN, Sauter G, Epstein JI, Sesterhenn IA. eds. World Health Organi¬zation classification of tumors: pathology and genetics of tumors of the urinary system and male genital organs. Lyon: IARC Press; 2004.
6. Chang H, Jung W, Kang Y, Jung WY. Pigmented perivascular epithelioid cell tumor (PEComa) of the kidney: a case report and review of the literature. Korean J Pathol 2012 Oct;46(5):499–502.

7. Patra S, Vij M, Kota V, Kancherla R, Rela M. Pigmented perivascular epithelioid cell tumor of the liver: report of a rare case with brief review of literature. J Cancer Res Ther 2013 Apr-Jun;9(2):305–7.
8. Martignoni G, Pea M, Reghellin D, Zamboni G, Bonetti F. PEComas: the past, the present and the future. Virchows Arch 2008 Feb;452(2):119–32.
9. Wang GX, Zhang D, Diao XW, Wen L. Clear cell tumor of the lung: a case report and literature review. World J Surg Oncol 2013 Oct 1;11:247.
10. Bleeker JS, Quevedo JF, Folpe AL. "Malignant" perivascular epithelioid cell neoplasm: risk stratification and treatment strategies. Sarcoma 2012;2012:541626.