



Case Report

Malignant Gastric PEComa: A Rare Malignancy

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Abstract

Introduction: Perivascular epithelioid cell tumor (PEComa) is characterized by its perivascular location and spindle appearance of tumor cells with clear to lightly granular eosinophilic cytoplasm and a round-to-oval centrally located nucleus. Immunohistochemically, nearly all PEComas show reactivity for melanocytic (HMB-45 and/or melan-A) and smooth muscle (actin and/or desmin) markers. Malignant gastric PEComa is extremely rare and only 3 cases have been reported to best of our knowledge. We report a 4th case of malignant gastric PEComa.

Case presentation: We are presenting a case of a 48 year-old Caucasian female who presented to the emergency department with complaint of abdominal pain for 3-4 weeks associated with intermittent nausea and vomiting. CT Abdomen/Pelvis with contrast showed a mass at the greater curvature of the distal stomach. Patient underwent resection of the mass and pathology result was consistent with malignant PEComa.

Conclusion: PEComas are a family of rare mesenchymal tumors, composed of histologically and immunohistochemically distinctive perivascular epithelioid cells. These tumors co-express, the muscle and melanotic markers. Surgical resection is the best treatment option. Most commonly, they arise in the retroperitoneum and colon is most the common site followed by small intestine in the GI tract.

Keywords: PEComa; mTOR inhibitors; Malignancy

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Consent: Consent was taken from the patient for publication of this case report.

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Introduction

In 2002, the WHO defined PEComas as “mesenchymal tumors composed of histologically and immunohistochemically distinctive perivascular epithelioid cells” [1]. The cells are typically arranged around blood vessels and appear to form the vessel wall, often infiltrating the smooth muscle of small- to medium-sized vessels. Periluminal cells are usually epithelioid and the more peripheral cells are spindle shape. PEComas constitute a genetically diverse group that includes neoplasms harboring TFE3 gene rearrangements and TSC2 mutations, indicating alternative tumorigenic pathways.

Case Presentation

The patient is a 48 years old caucasian female with past medical history of GERD, morbid obesity and gastric bypass surgery. She presented to the emergency room with complaints of epigastric pain associated with intermittent nausea and vomiting for few weeks. She did not report weight loss, decreased appetite or changes in bowel habits. She denied any history of smoking, alcohol or drug abuse and no known family history of malignancy.

Physical examination was unremarkable, except for positive epigastric tenderness on deep palpation. CBC showed mild anemia with hemoglobin of 11.5 gm/dl, WBC count and platelets within normal limits. Comprehensive metabolic panel was unremarkable. Anemia work up was not suggestive of nutritional deficiency. CT of the abdomen and pelvis with contrast showed a mass at the greater curvature of stomach and suggestive of malignancy. Patient was admitted to the hospital, Endoscopy was done and was negative for any mass, ulcer or tumor. CT chest was negative for lung metastasis. Patient underwent exploratory laparotomy, a mass was found to greater curvature of stomach and resection of the distal part of stomach was done.

Pathology showed mass from greater curvature of stomach involved sub mucosa, muscularis propria and subserosal tissue, but no involvement of gastric mucosa. Tumor size was 11.5/8.7/7.6 cm, approximately 20 mitosis/10 HPF with necrosis present in at least 1% of the tumor. Histopathology showed, mesenchymal proliferation with spindle cells, with granular cytoplasm and some fibrillary areas at high power. Mesenchymal proliferation was suggestive of GIST, but C-kit and DOG1 immunostains were negative. CD34 was also totally negative. Differential diagnoses were melanoma, leiomyosarcoma and PEComa. Immunostains supported the diagnosis of PEComa in the context that, the lesion clearly had myxoid features (SMA and calponin positive) and was also positive melan-A and TEF3. HMB45 stain was negative, which can be negative in 10-20% of PEComas. Ki-67 was 25%.

The diagnosis was malignant PEComa in the presence of the morphological (spindles cells, high number of mitoses, atypical mitoses, nuclear pleomorphism) and immunohistochemical findings. Four lymph nodes taken during surgery were negative for metastasis.

Patient recovered from surgery and was discharged to a rehab facility after a few days. No adjuvant treatment was recommended.

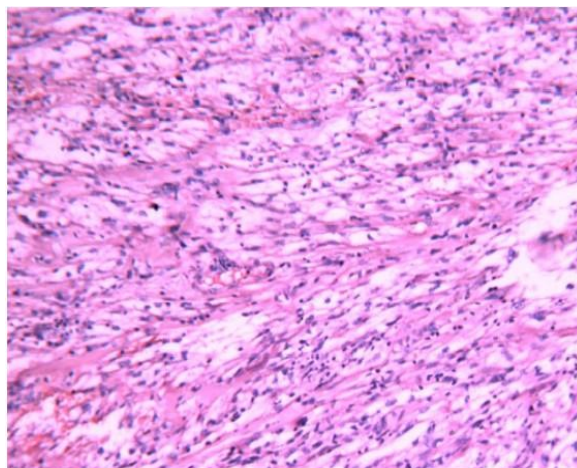


Figure 1 Histopathology positive for spindle cells

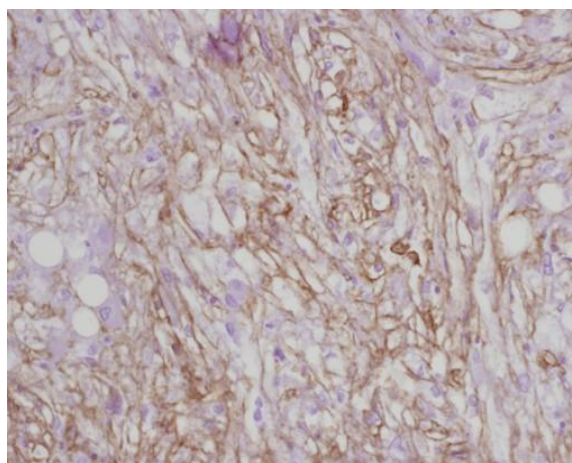


Figure 2 IHC positive for SMA7

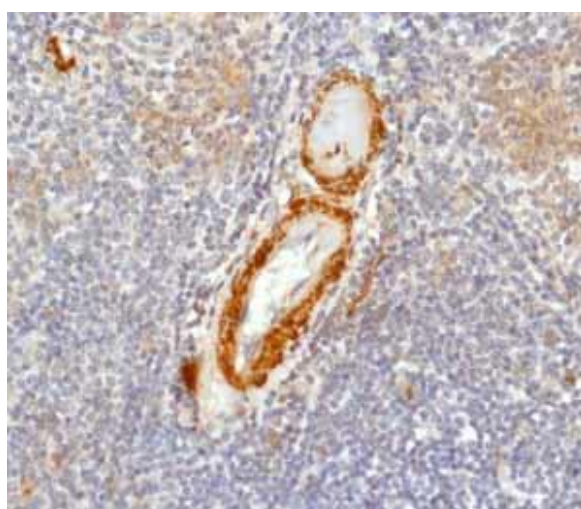


Figure 3 IHC positive for calponin

Discussion

Bonetti et al were the first group to propose the concept of a PEComa family of tumors derived from perivascular epithelial cells (PECs), which include clear-cell “sugar” tumors and lymphangiomyomatosis of the lung. PEComa is a rare tumor, which result from the proliferation of PECs. The normal tissue counterpart of PECs is unknown.

Typically these tumors are composed of epithelioid to spindle cells, with a clear to granular cytoplasm, a round to oval, centrally located nucleus and an inconspicuous nucleolus [2, 3]. Immunohistochemical analysis is the only way to establish the diagnosis of PEComa. Nearly all PEComas show reactivity for melanocytic (HMB-45 and/or Melan-A), smooth muscle (actin and/or desmin) markers and negative staining for cytokeratin and S100 protein [4,5]. Typical perivascular location is the consistent feature of these tumors.

PEComas have unpredictable biological behavior and may be subdivided into benign, malignant and tumors with uncertain malignant potential. The natural history of this condition is not well documented, which make this entity an unpredictable malignancy. There are no strict criteria established yet to distinguish between benign, malignant and tumors of uncertain malignant potential. Majority of PEComas are benign in nature and have a better prognosis. Their natural history can be very aggressive, leading to multiple metastases and death as expected with a high-grade sarcoma.

PEComas may arise in variety of locations including retroperitoneum, uterus, uterine cervix, vagina, gastrointestinal tract, kidney, liver, bladder, prostate, soft tissue, skin, and bone [6-10]. It is estimated that the mean survival time of patients with malignant PEComas affecting the terminal ileum & caecum is 28 months, mesentery and colon is 27 months and 38 months, respectively.

Based on the data from well-documented malignant PEComas, WHO guidelines suggest that PEComas should be considered as malignant when they display infiltrative growth, marked hypercellularity, nuclear enlargement, hyperchromasia, high mitotic activity, atypical mitotic figures and coagulative necrosis. The presence of marked nuclear atypia, diffuse pleomorphism, high mitotic activity, necrosis, infiltrative growth pattern and tumor size > 5 cm are the strongest predictors of malignant behavior.

GIST, metastatic melanoma, leiomyoma, angiomyolipoma (AML), leiomyosarcoma, paragangliomas, neuroendocrine tumors, other epithelial tumors with clear cell features and epithelioid smooth muscle tumors, are the main differential diagnosis. Perivascular arrangement of epithelioid cells is the characteristic feature of PEComas, which is not seen in other tumors.

Numerous cases of PEComa (particularly classic AML) may occur sporadically or in association with the tuberous sclerosis complex (TSC) [11]. These tumors appear to be associated with specific genetic alterations of the TSC, including the loss of TSC1 (chromosome 9q34) or TSC2 (chromosome 16p13.3) genes [12]

CT/MRI scans are not sufficiently sensitive enough to establish the diagnosis, with the exception of classic AML with macroscopic fat, since PEComas demonstrate a wide spectrum of imaging findings; their imaging characteristics are nonspecific and preoperative diagnosis is difficult using radiological criteria alone [13]. The diagnosis can only be confirmed by histological analysis of the tumor after resection.

Optimal treatment is not well established because of paucity of this entity. Surgery is the most recommended primary treatment while adjuvant therapy is generally reserved for high-risk cases. No effective medical treatment has been reported for patients with advanced disease. A retrospective analysis done by Benson and colleagues showed, the response to mTOR inhibitors (Sirolimus and Temsirolimus) in

10 patients of PEComas [14]. Wagner *et al* [15] have previously identified that inhibition of mammalian target of rapamycin complex 1, which is pathologically activated by loss of the TSC1/TSC2, is a rational mechanistic target for the development of novel PEComa treatment strategies. Adjuvant treatment with mTOR inhibitors can be considered in high risks patients after surgery and patients with metastasis disease.

Conclusion

PEComas belongs to the family of rare mesenchymal tumors, which can arise in any location of body and diagnosis is confirmed following histological analysis of the tumor after resection. No effective treatment is available for metastatic disease and surgical resection is the primary treatment for localized disease.

Consent

We confirm that the patient has given the informed consents for case report to be published.

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