

PECOMA – A Histological Surprise

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Abstract: Introduction: Perivascular epithelioid cell tumor (PEComa) is rare neoplasm arising from mesenchymal cells with distinctive histologic, immunohistochemistry and clinical characteristics. It probably arises through activation of the mTOR signaling pathway. Malignant PEComa are extremely rare with very few cases being reported in literature. They occur at various anatomic sites in the body and have distinctive clinical presentation and variable prognosis. Presentation Of Case: We present a case of 39 yr old male patient who presented with anemia and palpable abdominal mass. He had previous history of two laprotomies for abdominal mass histologically suspected of GIST. He was evaluated with regular blood investigations, bone marrow examination and CECT Abdomen. Laprotomy was done and a tumor was found arising from the previous anastomotic site and transverse mesocolon. Clinically suspected as recurrent/malignant GIST, tumor was excised and sent for histopathology examination. At histopathology tumor sections showed perivascular pattern of spindle shaped epithelioid cells with atypia, high mitotic figures, and necrosis. IHC marking was positive for HMB45, SMA, Melan-A, Desmin, and immunonegative for S-100, ckit and DOG-1. Thus confirming the diagnosis of Malignant PEComa and patient kept on follow up. Discussion: The earliest description of PEComa date back to 1943 when they were first described as an abnormal myoblast found in section specimen of renal angiomyolipoma. PEComa are rare tumors with variable presentation. There have been around 100 reported cases of PEComa with around 55 being malignant. Malignant PEComas of GIT are even rarer with few cases reported. They have an aggressive course with mean life time of around 30months. Conclusion: Malignant PEComas are very rare tumors with aggressive course and no known effective treatment. The information we have are from various case series and reports. The article is to sensitize the occurrence of this tumor in case of histologically proven GIST, its clinical and histologic diagnostic difficulties and probable treatment options.

Keywords: PEComa, HMB45, SMA, DESMIN, Malignant PEComa, Colon, Recurrent GIST

1. Introduction

Perivascular epithelioid cell tumor (PEComa) is an extremely rare neoplasm that appears to arise most commonly at visceral (especially gastrointestinal and uterine), retroperitoneal and abdomino pelvic sites. Malignant PEComa exist but are very rarely found and reported.

In 1991 Bonnetti et al. found characteristic cell type in three mesenchymal lesions angiomyolipoma, sugar tumor of lung and lymphangiomyomatosis and named the cell Perivascular epithelioid cell. They also noted characteristic morphologic, ultrastructural and immunophenotypic features. Initially the term was used to describe characteristic cells found in sugar tumor of lung. Zamboni et al. in 1996 employed the term to include lesions outside lung which showed similar features of sugar tumor in lung and noted possibility of similar tumors existing at many anatomical sites in body. To date PEComa have been described in many anatomic sites like liver, heart, rectum, breast, uterus, abdominal wall, and pancreas.

PEComas are generally benign lesions with variable presentation and prognosis is usually good. Malignant PEComas are extremely rare and may have local and distal metastasis. To date there have been only fifty five cases of malignant PEComa reported in literature with very few being reported from gastrointestinal tract. PEComa of mesentery exceedingly rare with only 6 cases being reported in literature.

Immunohistochemically, nearly all PEComa are immunoreactive for both smooth muscle (actin/desmin) and melanocytic (HMB45/melanA) markers. There are no

anatomical or physiological counterparts to these cells. However possible deviation from undifferentiated neural crest cells and molecular alteration from myoblastic smooth muscle origin or evolution from pericytic origin has been described. Also noted is the typical perivascular location with spindle and epithelioid shape.

2. Case

We present the case of a thirty nine year old male patient who presented to casualty with severe anemia and breathlessness. On detailed history taking he had two laprotomies and bowel resection anastomosis for abdominal mass histologically and immunohistochemically proven to be GIST of small bowel. He was given packed cell transfusions and symptomatic treatment in ICU setting. He was evaluated with regular blood counts and CECT of abdomen. Blood counts showed severe thrombocytosis with platelet counts at 7 lakhs and CECT abdomen showed cavitory mass lesion in transverse colon and mesentery overlying the previous anastomotic site with lymph nodes. Initial working diagnosis was made as recurrent/malignant GIST with suspected myeloproliferative disorder. Bone marrow examination revealed normal study. JAK2 and BCR ABL mutation study was negative. In hospital course patient improved symptomatically but anemia failed to improve with persistent low hemoglobin. Patient was taken up laprotomy. Intraop large lesion size of 15x20cms was found in the previous anastomotic site involving adjacent transverse colon and mesentery. Tumor was freed of adhesions from previous surgery and excised in toto with ileo-transverse anastomosis. Specimen was sent for histopathology examination.

Histopathology examination showed spindle and epithelioid cells. not typical of GIST and showed predominantly perivascular pattern with nuclear atypia. There were many mitotic figures, and areas of necrosis. No lymph nodes were found. CD 117 marker was done which is negative in the present tumor. And hence HMB 45, smooth muscle actin A, Melan-A, Desmin, and TFE-3 markers were which are positive. Based on histologic features and IHC markers a diagnosis of malignant PEComa was made.

Postop patient recovered well with orals starting on 4th postop day and drain removed 6th postop day. Patient was mobilized and physiotherapy given and discharged on 9th postop day. He was kept on weekly follow up for two weeks and there after monthly follow up. At 2 month patient is asymptomatic and follow up scans showed no recurrence. Patient was advised 3 monthly follow ups.

3. Histological Section

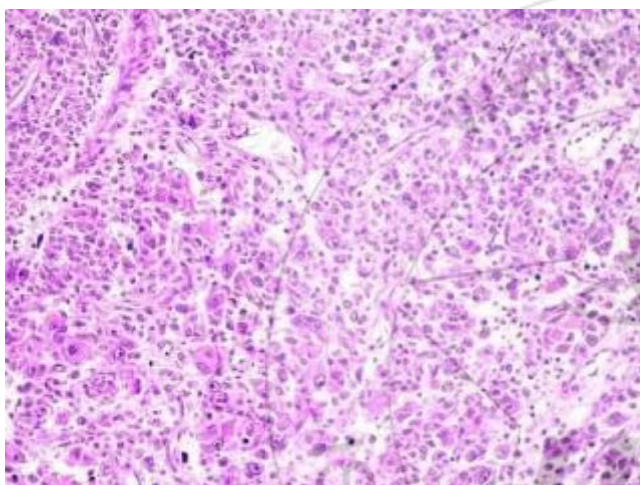


Figure 1: H & E Stain x 100 : Histological picture shows epithelioid tumor cells arranged around blood vessels in perivascular pattern

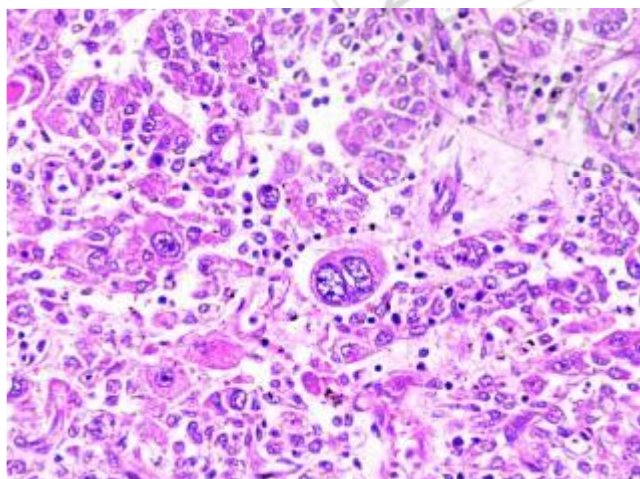


Figure 2: H & E Stain x 200 : Epithelioid tumor cells with eosinophilic cytoplasm and bizarre nuclei and prominent nucleoli

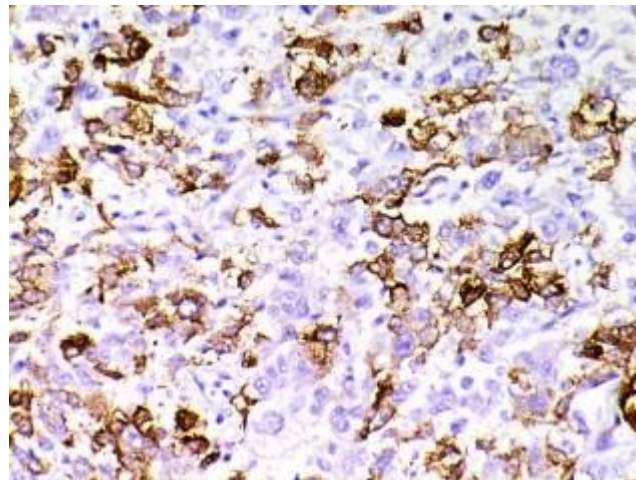


Figure 3: IHC – HMB 45 : Cytoplasm of tumor cells are positive for HMB 45 marker

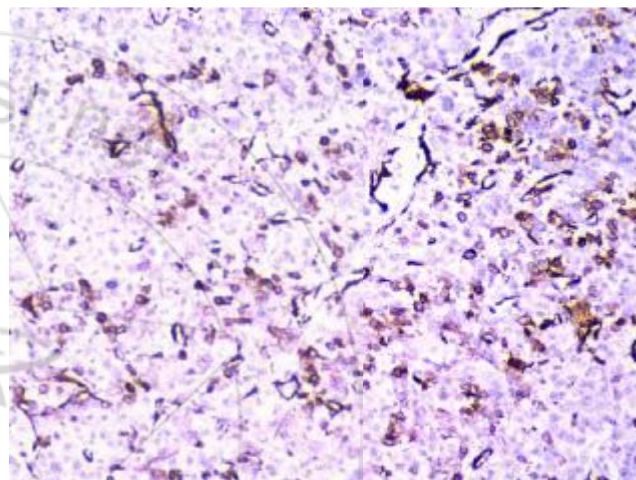
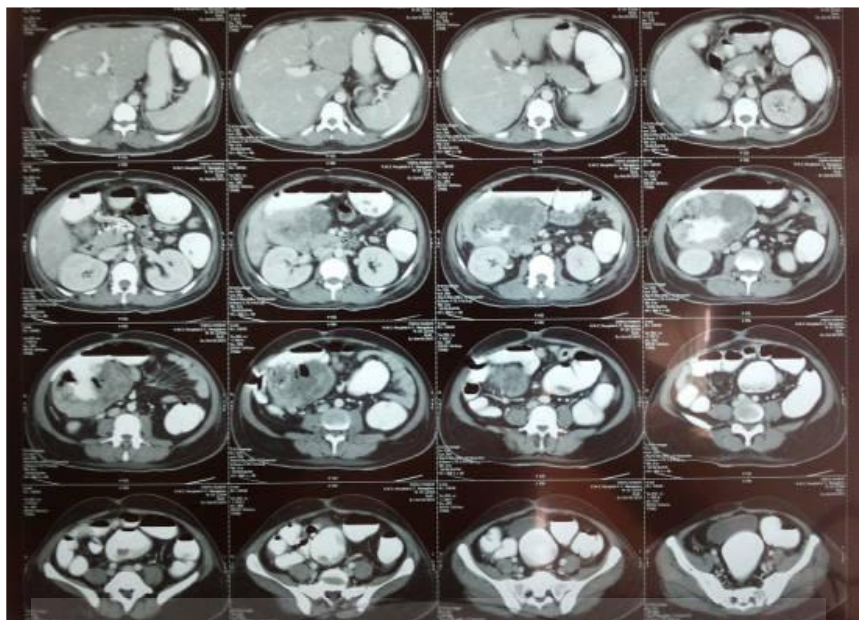


Figure 4: IHC – SMA : Cytoplasm of tumor cells are positive for SMA

CECT Picture showing well defined growth arising from transverse colon mesentery with necrotic central area and loss of fat planes with surrounding structures. Few mesenteric lymph nodes also noted



4. Discussion

PEComa or Perivascular epithelioid cell tumors are a family of related mesenchymal neoplasms composed of histologically and immunohistochemically distinctive perivascular epithelioid cells that include angioliipoma, lymphangiomyomatosis, clear cell tumor of the lung and a group of rare visceral and retroperitoneal abdominopelvic tumors. They were first described as abnormal myoblast in a case of renal angiomyolipoma in 1943. A subset of PEComas exhibit malignant behavior with either locally invasive recurrence as in our case or distal metastasis. There are approximately 100 reported cases of PEComa of which around 55 are malignant and only 6 are reported in GIT.

PEComa may be benign, uncertain malignant or malignant. Due to the rarity of cases and less commonly being reported criteria, prognosis and course of malignant PEComa have not been made and are being revised internationally with more number of cases being reported. The bulk of known information is from case reports and case series.

Folpe and colleagues have suggested 6 criteria for malignancy in PEComa : tumor size greater than 5cm, mitotic count of more than 1 per 50 high power fields, vascular invasion, infiltrative pattern, high nuclear grade and cellularity and necrosis. These criteria were observed in our case also. PEComa showed hypercellularity, hyperchromasia, high mitotic activity, atypical mitotic figures and coagulative necrosis.

Small PEComa <5cms without any above said criteria are usually benign. Large PEComa >5cms without any features are uncertain malignant potential. While PEComa with 2 or more high risk features should be considered malignant. Fadare et al. in 2008 suggested that only feature that indicates definite potential for aggressive course is mitotic count >1/10 HPF and/or coagulative necrosis both have been observed in the present case.

In this case the patient underwent two laprotomies at intervals of 6 months and tumor excised were sent for

histopathology examination. They were showing predominantly smooth muscle cells with spindle shape and were positive for CD117 and CD34 and hence a diagnosis of GIST was made. However present tumor was found to be negative for both CD 117 and CD34 and predominantly showed perivascular cells with atypia and high mitotic figures. These histologic features helped in diagnosis of Malignant PEComa.

PEComas have documented CD34 positive staining in the capillary network surrounding tumor cells. Depending on the specific microenvironment locations PEComas can modulate their morphology and immunophenotype. In some conditions PEComas can pronounce muscle features and in some others can exhibit more epithelioid morphology with strong positivity for HMB45. This led to the diagnostic confusion in our case with early sections being diagnosed as GIST and now being diagnosed as a case of PEComa.

Natural history of malignant PEComa is very aggressive with patients having mean survival time of 28months in ileum and caecum and 27-35months in colon and mesentery. However literature also shows malignant PEComa with worst histologic criteria having indolent and benign course. Due to rarity of pathologic reporting histologic criteria cannot be taken to determine prognosis in a case of malignant PEComa however increasing age at presentation, metastatic disease and receipt of additional chemo/radio therapy indicate worse prognosis.

Surgery remains the mainstay of therapy when possible in PEComa of nearly every anatomic site. Adequate surgical resection allows longer symptom free and disease free survival even in metastatic disease. Even in relapse case surgery is the initial and best considered treatment option. Radiation therapy has been utilized in a number of cases in both neoadjuvant and adjuvant settings without convincing results. Cytotoxic chemotherapy has similarly been integrated into multimodality therapy. A newer approach utilized primarily in the setting of recurrent or metastatic disease has been targeted therapy namely mTOR inhibition.

To conclude PEComas are rare and malignant PEComas are even rarer. We present a rare case malignant PEComa arising at previous bowel anastomotic site. They are ubiquitous and have varied clinical presentation. To diagnose a PEComa a strong degree of suspicion is needed based on histologic appearance and IHC markers are an important part. They have an aggressive course and treatment options are under study due to rarity of cases and reporting. Surgery forms an important part of treatment plan as it helps in debulking tumor and gives a histologic diagnosis. The study of mTOR inhibition and use of drugs like everolimus have helped to understand the pathogenesis and formulate treatment plans. Chemo and radio therapy have little role. However the 5yr survival rate is very low even with aggressive treatment. Present case is on regular follow up. At second and fourth month of follow up patient is symptom and disease free.

5. Conflict of Interest - Nil

6. Financial Support - Nil

7. Informed Consent - Obtained

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