Case Report

Perivascular Epithelioid Cell Tumor (PEComa) in the Ascending Colon: A Case Report

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Key Words
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Perivascular epithelioid cell tumor (PEComa) is a mesenchymal tumor composed of perivascular epithelioid cell (PEC).[1] The PEC is characterized by epithelioid appearance, clear to eosinophilic granular cytoplasm, perivascular location, and coexpression of smooth muscle and melanocytic markers.[1-5] The PEC-related tumors include angiomyolipoma (AML), clear cell sugar tumor of the lung (CCST), lymphangioleiomyomatosis (LAM), and very rare tumors in other locations. Many PEComas have been associated with the tuberous sclerosis complex, an autosomal dominant disorder characterized by seizures, mental retardation, and the development of tumors in multiple organs including the brain and skin.[1,6,7] We report a case of colonic PEComa with personal and family history of tuberous sclerosis complex (TSC).
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PEComa is a very rare mesenchymal neoplasm. Bonetti and colleagues proposed the concept of perivascular epithelioid cell (PEC) in 1992 and the term PEComa was suggested by Zamboni and colleagues in 1996.[8,9] Immunohistochemically, PEComas express myogenic and melanocytic markers, such as HMB45, HMSA-1, MelanA/Mart1, microophthalmia transcription factor (Mitf), actin and less common, desmin.[10]

The World Health Organization defines PEComa as a mesenchymal tumor composed of histologically and immuno-histochemically distinctive perivascular epithelioid cells.[8] PEComas have a wide range of morphologic appearances, but a consistent finding is the presence of nests of sheets of epitheloid cells and, less commonly, spindle cells, with a prominent delicate capillary network surrounding tumor cells. Tumor cells have variably eosinophilic granular or clear cytoplasm and prominent nucleoli and show variable degrees of pleomorphism. The precursor cell of PEComas is currently unknown. There is no known normal tissue counterpart to perivascular epitheloid cell. The name refers to the characteristics of the tumor when examined under the microscope. The etiology of PEComas remains uncertain. They more commonly affect young female patients.

PEComas have been associated with the tuberous sclerosis complex, an autosomal dominant disorder

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characterized by seizures, mental retardation, and the development of tumors in multiple organs including the brain and skin.

PEComa in the colon is very rare, with only a few reported cases so far. Because of its rarity, the clinical features and biological behavior of PEComa in the colon have yet to be established. Here we report the case of a female patient with PEComa in the ascending colon.

Case Report

A 57-year-old woman presented with intermittent cramping pain in her right side abdomen and rectal bleeding for a few months. Surgical history included abdominal total hysterectomy. The abdominal and rectal examination were unremarkable. Colonoscopy revealed a smooth-surfaced, round mass with focal ulceration in the ascending colon (Fig. 1). Multiple biopsies were taken and displayed benign mucosa with mild chronic inflammation. Abdominal computed tomography showed a large soft tissue mass in the ascending colon near hepatic flexure with proximal focal colonic-colonic intussusception (Fig. 2). All laboratory tests including liver, renal function tests, complete blood count, and carcinoembryonic antigen (CEA) were within normal limits. She underwent right hemicolectomy. There was a 4.0 × 3.0 × 5.0 cm smooth-surfaced, round tumor at anti-mesenteric side of the proximal ascending colon (Fig. 3). The surgery and postoperative course were uneventful. The histopathological examination report and the subsequently performed immunohistochemistry (strongly positive for HMB-45, Melan-A and Smooth Muscle Actin) were suggestive of a malignant PEComa (Fig. 4). The mitotic index is more than 2/10 high power fields (HPF).

Multiple similar sessile and firm nodular growths were noted over bilateral toes, and fingers (Fig. 5). She underwent tumor excision. The histologic find-

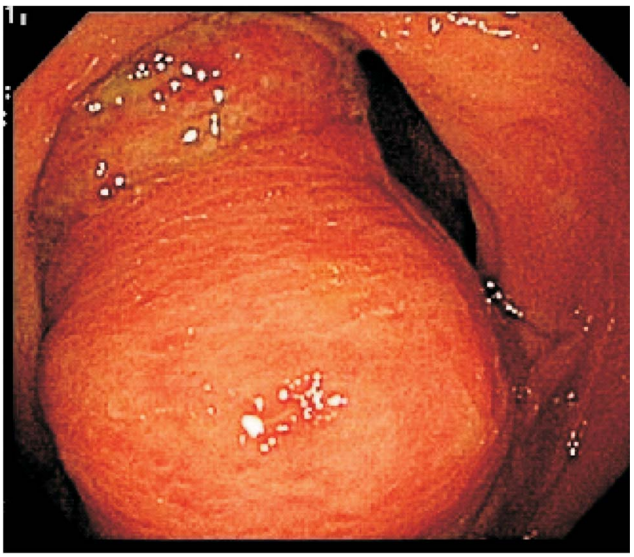

Fig. 1. Colonoscopic findings showing a smooth-surfaced, round mass with focal ulceration in the ascending colon.

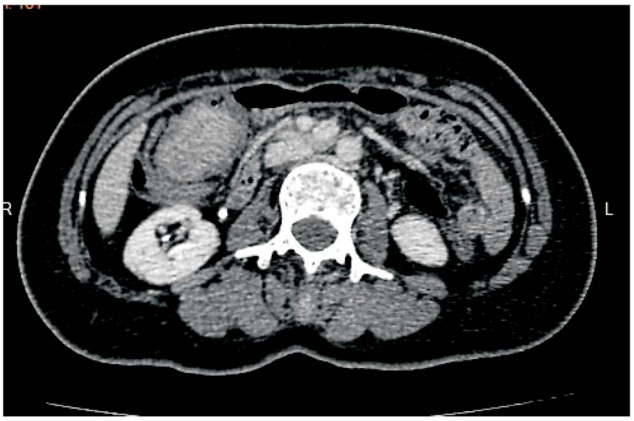

Fig. 2. Abdominal CT scan showing a large soft tissue mass in the ascending colon near hepatic flexure with proximal focal colonic-colonic intussusception.

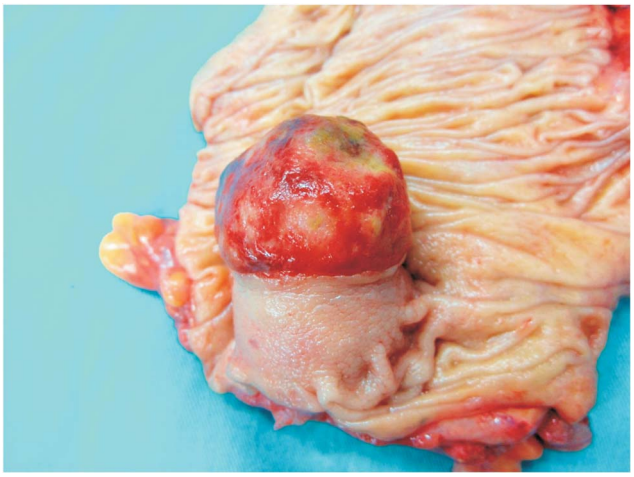

Fig. 3. The resected specimen was a round, submucosal mass with focal ulceration in the cecum.

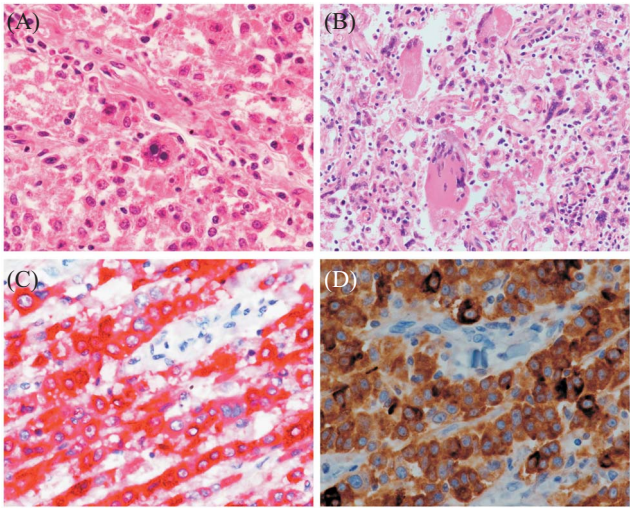

Fig. 4. (A) Pleomorphic cells with macronucleoli. This cell is remarkably larger than the adjacent cells. (B) Multinucleated tumor giant cells with eosinoiphilic cytoplasm. Many inflammatory cells in the background, including lymphocytes and plasma cells. (H&E, magnification ×400). (C) Positive for HMB-45. (D) Positive for Melan-A.

ings showed fibrokeratoma. Brain CT scans revealed several calcified nodular lesions involving bilateral ventricular walls and right frontal lobe. Tuberous sclerosis complex was diagnosed.

The patient's mother and a sister had epilepsy and nodules over the fingers/toes. Her three brothers have no symptoms. Her son and daughter presented with epilepsy and nodules over the toes/fingers and neck.

The patient did not receive any adjuvant therapy and was discharged on postoperative day 8 without complications. No sign of recurrence or metastasis was found 5 months after surgery. Then, she was loss to follow-up.

Discussion

The perivascular epithelioid cell (PEC) is a cell type constantly present in a group of tumors including angiomyolipoma (AML), clear cell sugar tumor (CCST), lymphangioleiomyomatosis (LAM), clear-cell myolelanocytic tumor of the falciform ligament/ligamentumteres and rare clear cell tumors arising at a variety of visceral (gastrointestinal, gynecologic, and genitourinary) and soft tissue (retroperitoneal, abdominopelvic, and cutaneous). The term perivascular epithelioid cell tumors-not otherwise specified (PEComas-NOS) was proposed to describe the latter subgroup.[11]

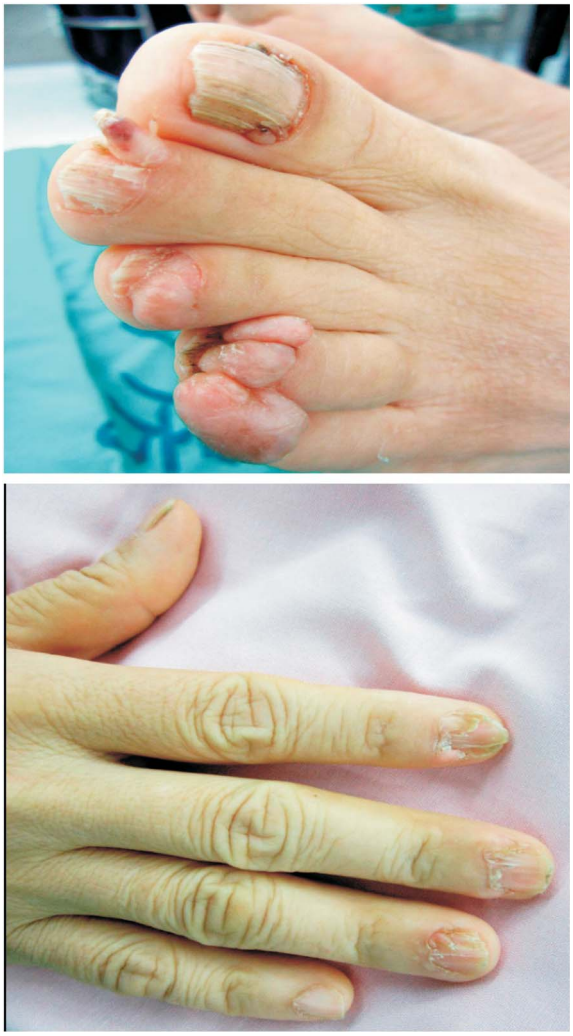

Fig. 5. Multiple similar sessile and firm nodular growths were noted over bilateral toes and fingers.

PEComas-NOS arises at diverse visceral and soft tissue sites. Perivascular epithelioid cell tumors of gastrointestinal tract (GI PEComas-NOS) takes a proportion of about 20% to 25% of PEComas-NOS.[12] It usually occurs in the middle age and more prevalent in women. The exact cause of GI PEComas-NOS is not clear. It is believed to originate from PEC but the natural histological counterpart and how it can be a potential neoplastic originator are out of clarity.

Pathologists generally face up challenges dealing

with the differential diagnosis of PEComa-NOS in the gastrointestinal tract, especially for GIST and malignant melanoma. Microscopically, both GI PEComa-NOS and GIST present great resemblance of a spindle or epithelial cell appearance. Moreover, the GIST-specific marker CD117 commonly displays immunoreactivity in histopathological examination of PEComa-NOS as well. Given the morphological and immunophenotype similarity between both types of neoplasm, it is mandatory to detect the expression of melanocytic markers including HMB45 and Melan A, whose positive appearance could beneficially distinguish PEComa-NOS from GIST in intractable cases. Featuring immunochemical expressions of S-100 and c-kit, the malignant melanoma explored in gastrointestinal tract is generally subsequent to a primary skin lesion as well, which are of great assistance for the differential diagnosis since melanoma and PEComa-NOS simultaneously express melanocytic markers of HMB45 and Melan A.[13]

PEComa is a tumor of uncertain malignant potential. Firm histologic criteria for malignancy have not been completely defined, but Folpeand colleagues[14] have previously shown that tumor size > 8 cm, mitotic index > 1/50 HPF, and necrosis were associated with local recurrence and/or metastasis; however, the study group included tumors from various sites, such as uterus and somatic soft tissues, and these findings have not been validated in larger series. Clinical feature is nonspecific, so preoperative diagnosis is difficult to accomplish.

PEComas are related to the TSC or to the genetic alterations of TSC, an autosomal dominant genetic disease due to losses of TSC1 (9q34) or TSC2 (16p13.3) genes.[15,16] TSC, a tumor suppressor gene syndrome, characterized by mental retardation, seizures and cellular proliferations (AMLs, subependymal giant cell tumors, cutaneous angiofibromas, cardiac rabdomyomas, lymphangioleiomyomatosis, pulmonary multifocal micronodular hyperplasia). Similar alterations of the TSC genes have been demonstrated in a significant number of PEComas, both occurring within the TSC and in sporadic cases. TSC genes seem to have an important role in the regulation of the Rheb/mTOR/p70S6K pathway.[17] Kenerson and colleagues[18] have recently demonstrated increased levels of phospho-p70S6K, a marker of mTOR activity, in sporadic AMLs. The associated reduced phospho-AKT expression is consistent with the disruption of TSC1/2 function. Similar findings were obtained analyzing extrarenal PEComas. Activation of the mTOR signaling pathway is common in PEComas, mTOR inhibitors such as rapamycin have been successfully applied as medical treatment.[16] Although no large series of patients treated with mTOR inhibitors exist, preliminary data suggest that complete response is possible.

The consistently effective treatment of GI PEComas is yet to be established. Complete resection is served as mainstay of treatment. Chemotherapy had been implemented in some potential or distinct malignant cases but its role remained out of clearity. Immunotherapy such as IFN-α 2b had also been tried in some patients with unproven effect.[19]

Although there is no definitive treatment and no conclusive evidence about the efficacy of adjuvant therapy, the recommended treatment is radical resection of the tumor.

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病例報告

升結腸血管旁類上皮細胞瘤：病例報告

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血管旁類上皮細胞瘤 (perivascular epithelioid cell tumor) 是一群由類上皮細胞所形成的罕見腫瘤。這些類上皮細胞的特徵是會圍繞著血管分布，並可以同時表現出具黑色素細胞分泌功能的標記，以及肌肉組織的標記。此類腫瘤多發生於軟組織，有一些病例被報告發生於腎臟、肝臟、子宮等臟器中，但發生於結腸的病例很少。由於病例稀少，目前尚無標準治療方針與準確地預測病人臨床表現。我們報告一位升結腸血管旁類上皮細胞瘤的病例，表現症狀是右側腹痛及便血。經大腸鏡和電腦斷層掃描發現升結腸腫瘤併腸套疊。病患接受右側結腸切除手術，經過病理切片及免疫染色多種抗體檢查後確診是血管旁類上皮細胞瘤。

部分血管旁類上皮細胞瘤和結節硬化症 (Tuberous Sclerosis Complex; TSC) 有關，部分血管旁類上皮細胞瘤和結節硬化症的基因改變相似。

關鍵詞 血管旁類上皮細胞瘤、結節硬化症、升結腸。