Peripheral Primitive Neuroectodermal Tumor of Bowel Mesentery in Adults

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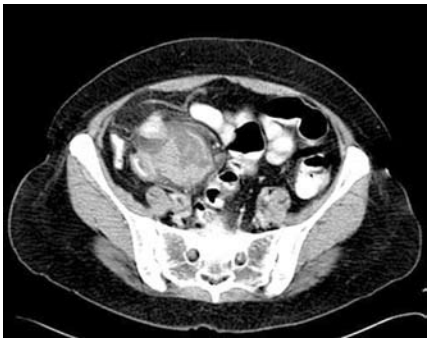
Peripheral primitive neuroectodermal tumor arises in soft tissue and is thought to be of neural crest origin. PNET has been found in several sites: chest (44%), retroperitoneum and pelvis (26%), extremities (20%), head and neck (6%), and others (4%) [1]. There are only three cases of PNET of the mesentery in the English-language medical literature: the origin of the tumor was the mesentery of the small bowel in two cases and the mesentery of the transverse colon in the third case [2-4]. We report an additional case of PNET involving the mesentery of the small bowel. We review the literature and describe presenting symptoms, imaging findings, operative procedures and adjuvant chemotherapy.

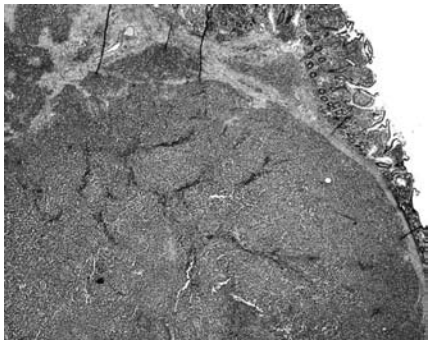
Patient Description

A previously healthy 57 year old woman presented to our department after 4 days of right lower quadrant pain and fever. There was no history of weight loss. Physical examination revealed a painful right lower quadrant mass. Computed tomography scan showed suspected abscess in the right lower quadrant and a thickened terminal ileum [Figure A]. The patient was treated with broad-spectrum antibiotics for 8 days and the fever resolved. During the next 2 months the patient was afebrile but continued to complain of non-specific abdominal pain. A non-tender abdominal mass was palpated in the right lower quadrant. Tumor markers, such as carcinoembryonic antigen and carbohydrate antigen 19-9, were normal.

PNET = peripheral primitive neuroectodermal tumor



[A] Computed tomography showing non-homogeneous right lower quadrant mass, measuring 7.5 x 5 x 6.5 cm, and thickened wall of terminal ileum.



[B] Section of the mesenteric mass and adjacent small bowel showing tumor infiltration into the bowel wall (hematoxylin and eosin x25).

Explorative laparotomy revealed a 12 cm mass in the mesentery of the terminal ileum 5 cm proximal to the ileocecal valve, which involved two adjacent loops of ileum. Enlarged lymph nodes were palpated in the root of the mesentery. Resection of the tumor *en bloc* with 90 cm of ileum and cecum was performed with ileocolic anastomosis. A frozen section of the specimen was consistent with malignant lymphoproliferative disease. The postoperative course was uneventful.

Macroscopic examination revealed a grey 12 cm, round, soft tissue mass with "fish flesh" consistency, partial necrosis and hemorrhagic foci. The mass penetrated through the small bowel wall and ulcerated the mucosa [Figure B]. The tumor was composed of small round cells with a finely distributed chromatin pattern and rosette formation. On immunohistochemistry the cells stained positive for vimentin, neuron-specific enolase, O-13, C-Kit, FLI-1, and negative for CK-7, CK-20, desmin, chromographin, CD-30, lambda, kappa, LCA, synaptophysin, CD-20, CD-3, and S-100. Electron microscopy demonstrated tumor cells with round nuclei, glycogen aggregates, and 100–120 nm high density cytoplasmic secretory granules. Based on the above findings we made the diagnosis of ulcerated PNET of the mesentery of small bowel with perforation. There was no tumor involvement of lymph nodes.

Postoperatively the patient received three 2 day courses of systemic chemotherapy consisting of cyclophosphamide 1200 mg/m^2/day for 1 day, doxorubicin 50 mg/m^2/day for 2 days, vincristine 2 mg/m^2 for 1 day, alternating with three 5 day courses of etoposide 100 mg/m^2, ifosfamide 1800 mg/m^2 and mesna 360 mg/m^2. CT scan performed after completion of adjuvant chemotherapy revealed no evidence of recurrence. The patient is currently without evidence of disease 8 months postoperatively.

Comment

PNET is a soft tissue sarcoma of neural crest origin that was first recognized by

A.P Stout in 1918. It belongs to the Ewing family of tumors, which include Ewing's tumor of bone, extra-osseous Ewing's, and Askin's tumor (PNET of the chest wall). Over 90% of cases occur within the first and second decades of life.

Patients with PNET usually present with pain and often have a palpable mass. Back pain may indicate a paraspinal, retroperitoneal, or deep pelvic tumor. Systemic symptoms of fever and weight loss can also occur and often indicate metastatic disease. There are no suggestive blood studies that can be used to diagnose PNET. The differential diagnosis of mesenteric PNET includes gastrointestinal carcinoid, desmoid, lymphoma, and metastases from colon, ovarian, breast and lung cancer and melanoma. Mimicking of symptoms of peri-appendicular abscess may cause a delay in surgery. Imaging studies such as CT scan can provide important information regarding the size, involvement of adjacent structures and the presence of metastasis. However, there are no radiologic features suggestive of PNET and none of the reported cases of mesenteric PNET was diagnosed preoperatively.

The histologic appearance of these tumors typically comprises round-to-ovoid hyperchromatic cells with minimal cytoplasm. The tumor cells are typically arranged in nests and trabeculae with variable rosette formation. The rosettes may have a central lumen, but are often ill-defined, and are composed of tumor cells arranged around an empty space. Histopathologic diagnosis is made by exclusion: neuroblastoma, rhabdomyosarcoma, lymphoma, and small cell osteosarcoma should be excluded by immunocytochemistry and electron microscopy.

Marina et al. [5] proposed criteria for the diagnosis of PNET, defined by the presence of three of seven diagnostic features. Rosette formation, positive staining for neuron-specific enolase, and neurosecretory granules were found in both our patients and the diagnosis of PNET was established based on the presence of these three diagnostic features.

Because up to 80% of patients with apparently localized disease have occult metastatic disease, multidrug systemic chemotherapy is indicated in the treatment of patients with PNET. Combination chemotherapy for Ewing sarcoma and PNET has traditionally included vincristine, doxorubicin, cyclophosphamide, and dactinomycin. The combination of ifosfamide and etoposide has shown activity in Ewing sarcoma and PNET, and a large randomized clinical trial demonstrated that outcome was improved when the ifosfamide-etoposide combination was given in alternating courses with vincristine, doxorubicin, dactinomycin and cyclophosphamide [5]. Based on the literature for peripheral PNET and Ewing sarcoma, the invasive features of tumor growth (involvement of bowel wall) and the poor prognosis associated with PNET, we decided to administer adjuvant chemotherapy to our patients.

The 5 year disease-free survival of patients without metastatic disease is more than 60% compared to 35% for patients who present with metastatic disease. The prognosis of mesenteric PNET is better compared to other sites and it is not related to the size of the tumor. Poor prognostic factors include: size > 5 cm, pelvic site, older age, elevated lactate dehydrogenase, poor response to initial chemotherapy, and metastatic disease at presentation. The presence of lymph node metastases leads to poor outcome.

In conclusion, we reviewed the five known cases of PNET arising from the bowel mesentery. Mesenteric PNET is a rare adult neoplasm. Good long-term prognosis can be achieved with wide *en bloc* resection of the tumor and involved structures. Adjuvant chemotherapy seems indicated for mesenteric PNET with invasive features such as involvement of adjacent loops of bowel and enlarged lymph nodes. Tumor size does not affect prognosis.

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