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Ileal Malignant Melanoma Causing Intussusception: Report of a Case

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Abstract
Cutaneous malignant melanoma (MM) often metastasizes to the gastrointestinal (GI) tract; however, primary MM of the small intestine is a controversial diagnosis. We report the case of a 76-year-old woman found to have a primary MM in the ileum. After clinical evaluation, the radiological workup, which included magnetic resonance enteroclysis (MRE), revealed a large polypoid intraluminal tumor. She underwent laparotomy and the lesion was excised. Histological examination of the resected specimen revealed morphological and immunohistochemical characteristics of MM and a detailed postoperative examination failed to identify a primary lesion on the skin, anus, oculus, or any other site. The patient died of brain metastasis 6 months after surgery. According to our review of the literature, this is the first case of primary MM of the small intestine diagnosed with the help of MRE.

Key words Primary malignant melanoma · Small bowel · Gastrointestinal tract · Magnetic resonance enteroclysis

Introduction

Malignant melanoma (MM) is an uncommon form of neoplasia, originating from anatomical sites where melanocytes are histologically present. These sites are the skin (cutaneous form) and, less frequently, the choroid layer of the eyes, leptomeninges, oral cavity, pharynx, esophagus, bronchus, and the vulvovaginal or anorectal mucosa (mucosal form).[1] Malignant melanoma represents only 4%–5% of all cancers diagnosed annually in the United States.[2] Distant metastasis of MM to the gastrointestinal (GI) tract accounts for one third of all metastatic disease in the GI tract, with the small intestine being the most common site.[3] Although rare, primary MM of the small intestine has been reported; however, its true existence remains controversial.[4] We report a case of MM of the ileum in a woman with no confirmed primary lesion. We discuss whether this ileal lesion should be characterized as primary or metastatic, focusing on experimental data and the origin of the lesion. We also review the literature on primary MM of the small intestine.

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Case Report

A 76-year-old woman was admitted to our department for investigation of diffuse, colicky abdominal pain, fatigue, vomiting, nausea, anorexia, and rectal bleeding. Her medical history included arterial hypertension, coronary heart disease, parathyroidectomy for adenoma with synchronous thyroidectomy for nodular hyperplasia, and cholecystectomy for cholelithiasis. According to her family history, one brother had had stomach cancer and another brother had had lung cancer. Her vital signs were stable and she was afebrile. On physical examination, she had only diffuse moderate tenderness over her abdomen, but no rebound tenderness. Her bowel sounds were normal. Routine laboratory data revealed severe anemia (Hgb = 7 g/dl, Hct = 21%, MCV = 83.7 fl). A plain chest radiograph was normal, but a plain abdominal radiograph showed air-fluid levels in the small bowel with moderate distension of the proximal bowel.

Upper abdominal and an intravaginal ultrasound showed no abnormalities and an upper GI endoscopy was normal. Barium enema and colonoscopy revealed two adenomatous polyps: one at the rectosigmoid flexure (d ~ 1.5 cm) and one near the hepatic flexure (d ~

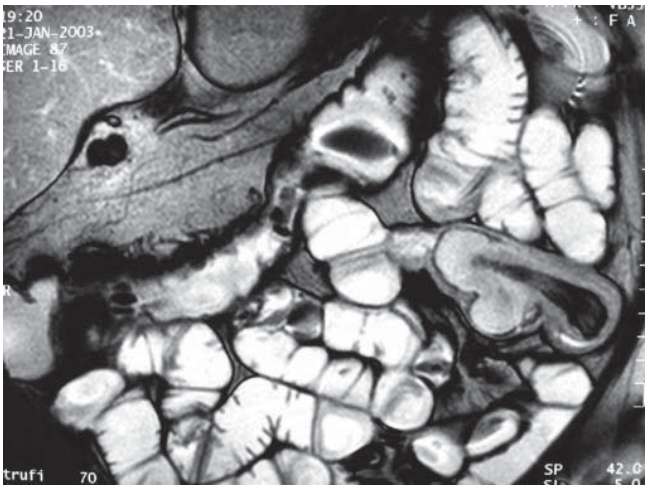

Fig. 1. Magnetic resonance enteroclysis showed an extensive sausage-shaped and bilobular intraluminal mass occupying a segment of the ileum on a coronal true FISP (fast imaging with steady-state progression) sequence

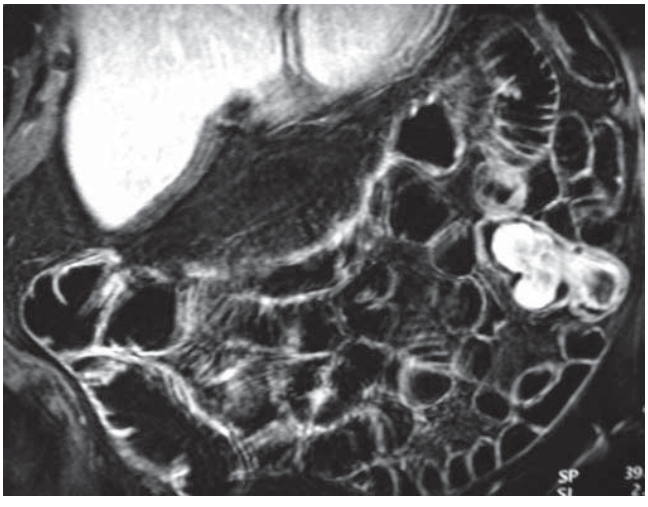

Fig. 2. Coronal post-gadolinium 3D FLASH with a fat saturation image, showing high signal intensity of the mass with contrast uptake. The central low signal intensity area in the mass corresponds to necrosis

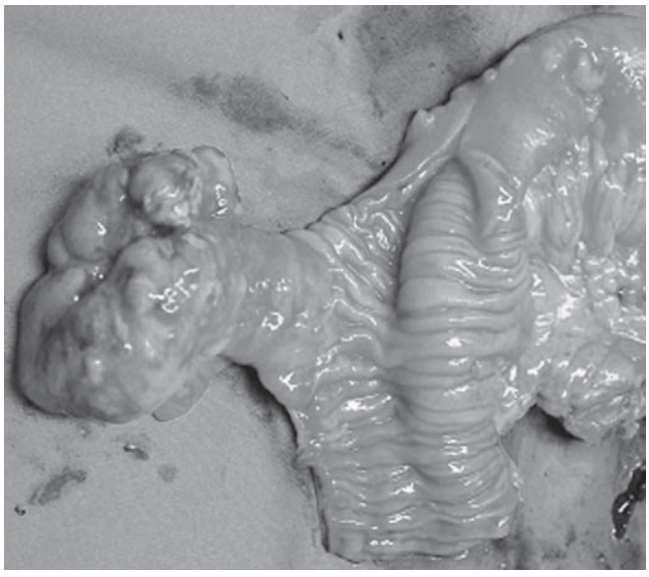

Fig. 3. Photograph of the large polypoid tumor arising from the antimesenteric margin of the ileum

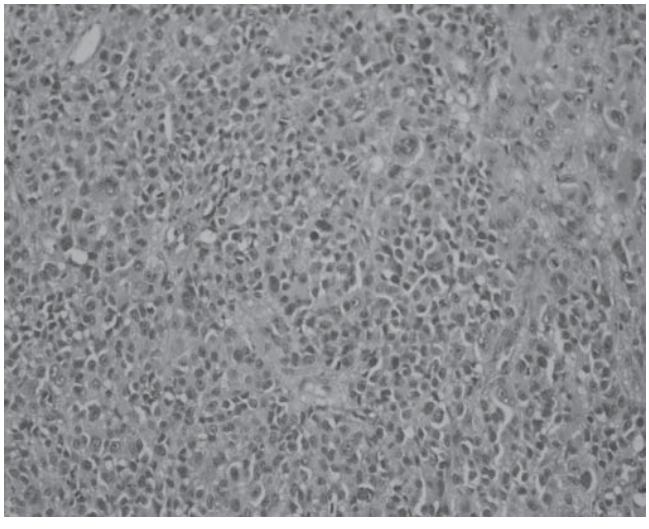

Fig. 4. Microscopic appearance of the resected lesion (×480)

1 cm), which were removed endoscopically. Histological examination of these polyps revealed severe dysplasia. An intravenous contrast-enhanced conventional computed tomography (CT) scan of the abdomen, with small bowel opacification, demonstrated a large polypoid intraluminal tumor (d ~ 15 cm) about 40 cm proximal to the ileocecal valve, with soft tissue density. A magnetic resonance enteroclysis (MRE) was performed to evaluate these findings further. This confirmed the CT findings and also showed intense enhancement of the lesion after the injection of paramagnetic contrast. No regional enlarged lymph nodes were detected (Figs. 1 and 2). These findings suggested a lymphoma or a gastrointestinal stromal tumor (GIST) of the small intestine.

After receiving repeated transfusions for the anemia, the patient underwent a laparotomy, which revealed a large tumor arising from the antimesenteric margin of the ileum, approximately 40 cm from the ileocecal valve, causing intussusception (Fig. 3). No macroscopic signs of metastases were detected in any other organ in the abdominal cavity, or in any regional or distant lymph node. Thus, we performed partial enterectomy, ensuring wide excision of the tumor, with an end-to-end anas-

tomosis. The patient suffered no major complications postoperatively.

Histological examination revealed a 22-cm longitudinally opened resected specimen containing a tumor, 7 × 5 × 4 cm in size, approximately 6 cm from the proximal margin of resection. Microscopically, the tumor was composed of epithelioid cells arranged diffusely or in uniform nests (Fig. 4). Immunohistochemically, the neoplastic cells revealed expression of S100, melanin A, HMB45, and vimentin, but they were negative for cytokeratin MNF116, LCA, L26, desmin, actin, CD34, and c-kit. Two of the ten lymph nodes examined showed malignant invasion. In view of these findings we made a diagnosis of MM with metastasis to the regional lymph nodes.

After the diagnosis was established, the patient underwent thorough clinical and laboratory examinations to identify the primary or metastatic nature of the lesion, but no primary MM was found. Therefore, the lesion was considered to be a primary MM of the small intestine. After surgery the patient was scheduled for follow-up at regular intervals every 3 months for the first year. A brain CT scan at the end of the first trimester revealed metastatic infiltration. Despite chemotherapy, multiple epileptic crises, severe anemia, and thrombopenia developed and she died about 3 months after the initiation of chemotherapy.

Discussion

Primary MM arising from mucosal epithelia is rare and described either in case reports or in small series of patients.[1,4] We found only 33 reports describing primary MM in the small bowel.[4–10] According to Bender et al. there are four types of primary MM in the small bowel, which are not always distinct: cavitary, infiltrating, exoenteric, and polypoid.[11] Our patient had a polypoid lesion with central necrosis.

When MM is found in the GI tract without any evidence of pre- or coexisting primary cutaneous melanoma, the uncertainty about primary GI origin versus GI metastasis from an "occult primary" exists, but the answer is rarely found. In a surgical series of patients admitted for GI symptoms with MM, an incidence of 20%–27% of "occult primary" was reported,[12] providing evidence that primary MM of the small bowel may exist.

Several diagnostic criteria for primary intestinal MM have been proposed. Most recently, Blecker et al. reported that a primary intestinal MM should be diagnosed when there is lack of concurrent or previous removal of a melanoma or atypical melanocytic lesion from the skin, lack of other organ involvement, and in situ change in the overlying or adjacent GI epithelium.[13] As our patient's condition fulfilled these criteria, we felt confident in confirming the diagnosis of primary intestinal MM.

Primary intestinal MM is thought to originate from either melanoblastic cells of the neural crest, which migrate to the ileum through the omphalomesenteric canal,[5] or APUD (amine-precursor uptake and decarboxylation) cells.[6] Although the human small bowel does not normally contain pigmented cells, migration studies have demonstrated the ability of melanocytes to migrate as far as the gut along ventral neural crest pathways.[14] Opposing the argument for a primary GI tumor is that of spontaneous regression of a pre- or coexisting cutaneous MM or a history of depigmentation of a lesion.[15]

Contrast-enhanced CT scan and small bowel follow-through or conventional enteroclysis have been used to establish the diagnosis in most reports in the literature. Unfortunately, the sensitivity of these imaging techniques does not exceed 60%–70%, suggesting that they provide inadequate preoperative information, apart from the detection of large lesions.[11] Their low sensitivity also helps to explain the discrepancy between autopsy results and pre-mortem GI findings.[16] Our patient underwent MRE as well as CT scans. The advantages of MRE include its multiplanar imaging capacity, superior tissue characterization, control over maximal luminal distension, ability to detect trans- and extramural lesions, and evaluation of disease activity, all without the use of ionizing radiation.[17] However, to our knowledge, imaging of a primary intestinal MM with MRE has not been reported before.

Extensive surgery, including wide resection of the tumor with a wedge of mesentery to remove the regional lymph nodes, especially if the disease is not disseminated, remains the gold standard.[4,7] Adjuvant options including chemotherapy, immunotherapy, and biochemotherapy have all been tried, but their effectiveness has not been established.[18] The prognosis of primary intestinal MM depends on the existence of metastases at the time of diagnosis and the age of the patient. Two groups of primary MM have been described and this division seems to affect prognosis: in one group, consisting mainly of younger patients, the disease is more aggressive with rapid metastasis and early death, whereas in the other group, consisting mainly of older patients, the disease is more indolent, with delayed metastasis, and surgical treatment seems feasible.[4]

In conclusion, primary small bowel MM appears to be a real, but extremely rare entity. To our knowledge, this case report describes the oldest woman with primary small bowel MM, and the first patient investigated with MRE. Magnetic resonance enteroclysis seems to be a more sensitive method of detecting MM of the

small intestine than CT scan or conventional enteroclysis. Future studies comparing these methods are needed to establish the true reliability of MRE as a diagnostic tool in this regard.

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