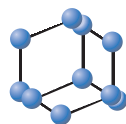
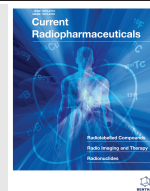


CASE REPORT

BENTHAM
SCIENCE

Ileal Melanoma, A Rare Cause of Small Bowel Obstruction: Report of a Case, and Short Literature Review

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Abstract: Background: Malignant melanoma frequently spreads to the gastrointestinal tract, with 60% of patients with advanced metastatic disease showing digestive involvement; however, primary MM of the small intestine is a controversial diagnosis. In fact, whether these lesions arise as true small bowel primary neoplasms or represent metastases from unidentified cutaneous melanomas remains debatable. The most common complications are intestinal obstruction, massive gastrointestinal bleeding, and perforation.

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Objective & Methods: We report a case of a 64-year-old patient, with an unremarkable medical history, in which a late diagnosis of primary ileal malignant melanoma in the setting of an emergency laparotomy due to small bowel obstruction, and where PET-scan showed costal metastasis. Therefore, we provide a narrative review of the scientific literature about this topic.

Results: 36 cases of primary small bowel melanoma, included that in the present study, were found through our search in the scientific literature

Conclusion: Primary small bowel MM appears to be an extremely rare entity which clinicians should be more aware of, in order to plan better a correct strategy of early diagnosis and appropriate treatment.

Keywords: Ileal Melanoma, PET, CT scan, Small Bowel Obstruction, metastatic disease, hypercaptation.

1. INTRODUCTION

Malignant melanoma (MM) is the cause of 1–3% of the global neoplastic diseases [1].

MM frequently spreads to the gastrointestinal tract, with up to 60% of patients with advanced metastatic disease showing digestive involvement [2-6]; however, primary MM of the small intestine is a controversial diagnosis [7]. In fact, whether these lesions arise as true small bowel primary neoplasms or represent metastases from unidentified cutaneous melanomas remains debatable [8]. The clinical presentation is usually aspecific, thus leading the affected patients to a late diagnosis, often with complication or when metastatic disease is also present. The most common complications are intestinal obstruction, massive gastrointestinal bleeding, and perforation [6, 9].

We report a case of a 64-year-old patient, with an unremarkable medical history, in which a late diagnosis of primary ileal malignant melanoma in the setting of an

emergency laparotomy due to small bowel obstruction, and where PET-scan showed costal metastasis. Therefore, we provide a narrative review of the literature about this topic.

2. CASE REPORT

A 64-year-old patient was admitted, in November 2018, to our surgical department with a history of acute abdominal pain for two days, in which was furthermore suffering from fever, persisting vomiting, and no stool passage. The abdominal ultrasound performed at the emergency unit showed “flatus and intestinal enlargement”; plain abdominal X-ray revealed “central air-fluid level in the small intestine”. Routine laboratory tests showed WC: $16,7 \times 10^3$ (neutrophils 76 %); HB 8.1 g/dL; Hct 30, 7%, LDH 301. A nasogastric tube was positioned, which drained 600 cc of alimentary content. The past medical history was unremarkable. On physical examination, abdominal swelling air mainly in low hypogastrium and severe pain were reported, and peristalsis was markedly reduced. Tumor markers CEA, CA 19.9, AFP were normal. Due to the rapid worsening, during the hospital stay, of the clinical conditions (with vomiting, drop off Hb, acid-base imbalance), a computed tomography (CT) scan was performed. CT scan without contrast showed, in the pelvis, an ileal loop (with a diameter of 8 x 9 cm) with thickened walls, due to the presence of solid

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tissue that caused obstruction of the lumen, in association with multiple centimetric perivisceral lymph nodes in the mesentery, which appeared soaked (Fig. 1). The patient underwent emergency laparotomy, where a bulky tumor was found involving ileum and causing the obstruction. Resection of 20 cm of the ileum including the large tumor and the mesentery with lymph nodes was performed (Fig. 2). Pathology showed the presence of a bulky neoplasm (7 x 7 cm) extended up to the ileal mucosa with focal areas of ulceration and stenosis of the bowel lumen. Three of seven lymph nodes were positive for metastasis; the margins of resection were healthy. The immunophenotype of the neoplastic population was: Melan-A and S100 intensely and diffusely positive; CD-117 and HMB45 focally positive; CD-34, ML-Actin, Desmin, and H-Caldesmin negative; Ki67 12%. The diagnosis was conclusive for primary epithelioid cell malignant melanoma. The post-operative period was uneventful and the patient was discharged on the 5th postoperative day. He was referred to a melanoma oncological center and, 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. Furthermore, in order to check typical melanoma localization, the patient underwent Positron Emission Tomography (PET) scan, showing at the Xth intercostal space on the left hypercaptation of the metabolic tracer in the context of the intercostal muscle (SUV max 8.7), compatible with a metastatic lesion (Figs. 3a-c). Therefore, he underwent adjuvant chemotherapy with dacarbazine, and he is actually under oncological follow-up.

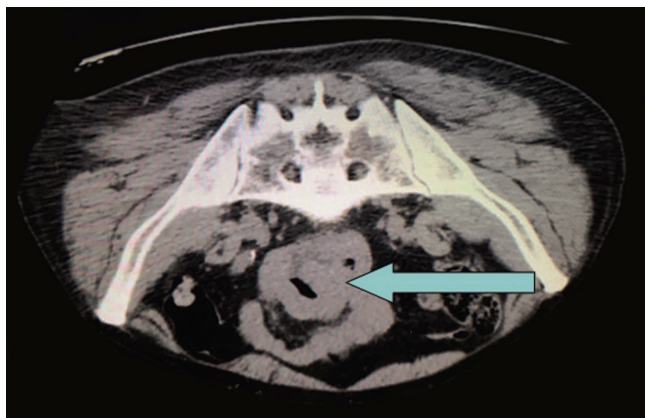


Fig. (1). CT scan without contrast showed, in the pelvis, an ileal loop (with a diameter of 8 x 9 cm) with thickened walls, due to the presence of solid tissue that caused obstruction of the lumen, in association with multiple centimetric perivisceral lymph nodes in the mesentery, which appeared soaked.

3. DISCUSSION

Primary mucosal melanoma can arise at any site within the GI mucosa, but it is most common in anorectal (anal canal, 31.4%; rectum, 22.2%) and oropharyngeal (32.8%) regions, whereas esophagus (5.9%), stomach (2.7%), small intestine (2.3%), gallbladder (1.4%), and large intestine (0.9%) are extremely rare sites of origin [10, 11].



Fig. (2). Emergent laparotomy showing a bulky tumor involving ileum and causing the obstruction.

There are different theories for the origin of malignant melanomas in the small bowel [12]. Although small bowel does not contain melanocytes, these cells have been found in the alimentary tract occasionally, thus supporting the theory of primary lesion in these sites [12]. Furthermore, a second theory suggests that malignant melanoma develops from intestinal Schwann cells, even if this theory is not confirmed [12]. Finally, a third theory suggests that malignant melanomas originate from the neural crest, and these potential cells migrate via the umbilical-mesenteric canal and later differentiate into specialized cells, i.e. amine precursors uptake and decarboxylation (APUD) cells, which undergo neoplastic transformation [12]. According to this theory (APUD theory), ileum, representing the distal end of the umbilical mesenteric canal, should be the commonest site of primary malignant melanoma of the small intestine [12-14].

In order to obtain the best therapeutic path for the affected patients, a clear distinction between primary intestinal melanoma and intestinal metastatic deposits should be made; however, often it can be difficult when the diagnosis is considered based on histopathological features alone. The clinical importance of this distinction lies within the differential in prognosis. Prognosis is worse for primary intestinal melanomas which tend to grow faster and more aggressively [8, 15]. A primary GI mucosal melanoma is considered in patients with no obvious primary cutaneous melanoma or those with an isolated GI lesion in the absence of other extraintestinal metastases.

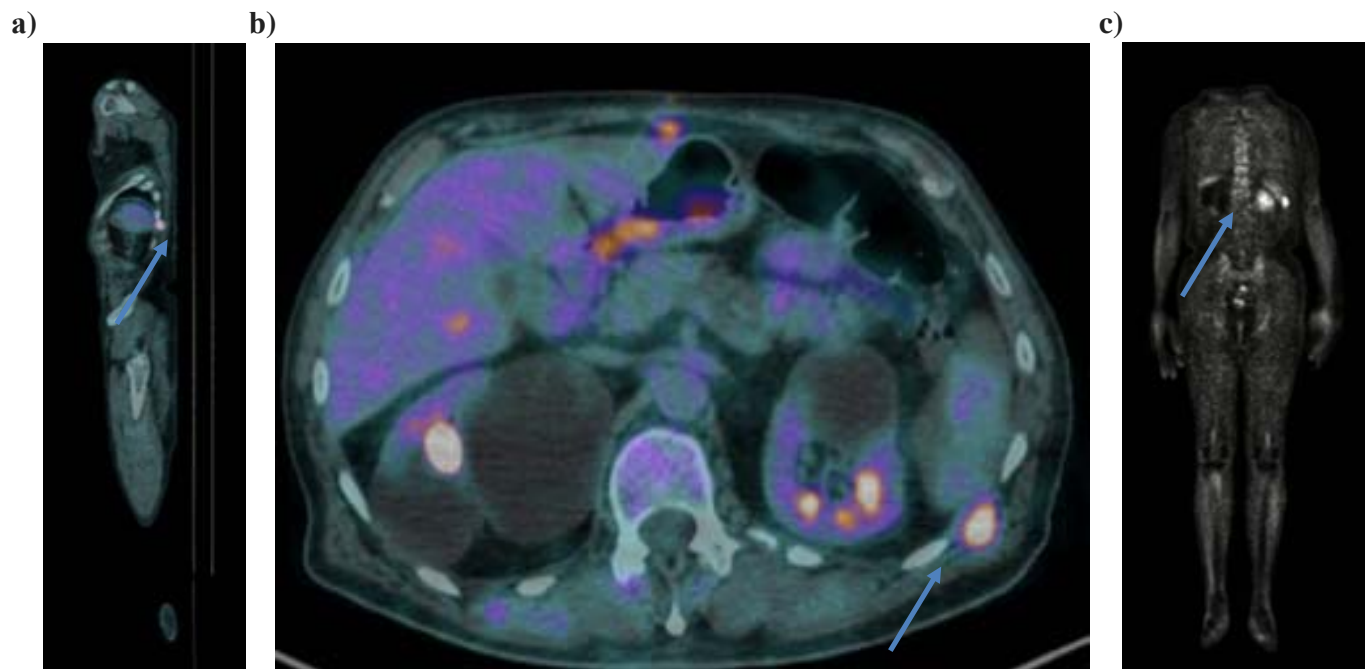


Fig. (3a-c). showing at the Xth intercostal space on the left hypercaptation of the metabolic tracer in the context of the intercostal muscle (SUV max 8.7), compatible with a metastatic lesion.

Table 1. In this table are reported all the previous cases of primary small bowel melanoma.

Case	Author	Sex	Age	Clinical Presentation	Location	Diagnostic Method	Nodal Involvement	Treatment	Outcome	Reference
1	Amar A.	F	46	NA	Distal ileum	NA	NA	Surgery	Follow-up absent	[18]
2	Krausz M.M.	F	70	Gastrointestinal bleeding	Distal ileum	Barium enema	No	Surgery	Follow-up absent	[13]
3	Manouras A.	M	72	Abdominal pain	Proximal jejunum	Computed tomography Scan	No	Surgery	Death at 1 year	[19]
4	Manouras A.	F	45	Gastrointestinal bleeding	NA	Abdominal Plain X-ray	No	Surgery	Disease-free at 2 years	[19]
5	Manouras A.	F	56	Strangulated umbilical hernia	Ileum	Abdominal laparotomy	Yes	Surgery	Death at 6 months	[19]
6	Atmatzidis K.S.	M	72	Gastrointestinal bleeding	Ileum	Computed tomography scan	Yes	Surgery	Disease-free at 1 year	[20]
7	Kadivar T.F.	M	73	NA	NA	NA	NA	Surgery	Follow-up absent	[21]
8	Timmers T.K.	M	25	Abdominal pain and diarrhea	Proximal ileum	Computed Tomography Scan	No	Surgery	Disease-free at 1 year	[22]
9	Christova S.	M	46	NA	NA	NA	Yes	Surgery	Follow-up absent	[23]

Table (1) contd....

Case	Author	Sex	Age	Clinical Presentation	Location	Diagnostic Method	Nodal Involvement	Treatment	Outcome	Reference
10	Christova S.	M	43	NA	Ileum	NA	No	Surgery	Follow-up absent	[23]
11	Khosrowshahi E.	M	37	NA	Ileum	NA	No	Surgery	Disease-free at 2 years	[24]
12	Kogire M.	M	57	Ileal intussusception	Ileum	Computed tomography Scan	Yes	Surgery	Metastatic recurrence at 1 year	[25]
13	Krueger S.	M	81	Gastrointestinal bleeding	Ileum	Computed Tomography Scan and Endoscopic Videocapsule	Yes	Surgery	Disease-free at 5 months	[26]
14	Lizasoain Urcola J.	M	73	Diarrhea	Ileum	Computed Tomography Scan and Small Bowel Transit	NA	Surgery	Follow-up absent	[27]
15	Mittal V.K.	NA	NA	Abdominal pain	Ileum	NA	NA	Surgery	Follow-up absent	[28]
16	Ramadan E.	F	75	NA	NA	NA	NA	Surgery	Follow-up absent	[29]
17	Raymond A.R.	F	42	Abdominal pain and diarrhea	Duodenum- Jejunum- Ileum	Endoscopy	Yes	No treatment	Death	[30]
18	Soerensen Y.A.	F	42	NA	Jejunum	NA	Yes	Surgery	Follow-up absent	[31]
19	Tabaie H.A.	F	26	NA	Ileum	NA	Yes	Surgery	Follow-up absent	[32]
20	Wade T.P.	M	38	Abdominal pain and constipation	Ileum	Abdominal laparotomy	Yes	Surgery	Disease-free at 21 months	[33]
21	Yanar H.	M	78	Gastrointestinal bleeding	NA	NA	NA	Surgery	Disease-free at 3 months	[34]
22	Yashige H.	M	30	Gastrointestinal bleeding	Duodenum	Endoscopy and Small Bowel Transit	NA	Surgery	Recurrence at 4 months, Deaths at 8 months	[35]
23	Kim W.	F	36	Abdominal pain	Distal Ileum	Computed Tomography Scan	No	Surgery	Recurrence at 1 year	[36]
24	Crippa S	M	58	Intestinal obstruction	NA	Computed Tomography Scan	No	Surgery	Death at 7 months	[37]
25	Guarda S.Y.	M	76	Gastrointestinal bleeding	Jejunum	Computed Tomography Scan	No	Surgery	Follow-up absent	[38]
26	Iijima S.	M	71	Gastrointestinal bleeding	Jejunum	Small bowel transit	Yes	Surgery	Death at 7 months	[39]

Table (1) contd....

Case	Author	Sex	Age	Clinical Presentation	Location	Diagnostic Method	Nodal Involvement	Treatment	Outcome	Reference
27	Katsourakis A.	M	71	Abdominal pain	Jejunum	Computed Tomography Scan	NA	Surgery	Follow-up absent	[40]
28	Resta G	F	48	Gastrointestinal bleeding and small bowel intussusception	Jejunum	Computed tomography Scan	Yes	Surgery	Disease-free at 1 year	[41]
29	Kumari N.S.	M	60	Intestinal obstruction	Jejunum	Abdominal laparotomy	Yes	Surgery	Follow-up absent	[42]
30	Sachs D.L.	F	41	Abdominal pain and diarrhea	Jejunum	Abdominal laparotomy	No	Surgery	Disease-free at 53 months	[43]
31	Schoneveld M.	M	77	Gastrointestinal bleeding	Jejunum	Computed Tomography Scan	No	Surgery	Follow-up absent	[44]
32	Hadjinicolaou A.V.	M	60	Gastrointestinal bleeding	Jejunum	Endoscopic videocapsule	Yes	Surgery	Death at 1 month	[8]
33	Karmiris K.	F	76	Small bowel intussusception	Ileum	Magnetic resonance imaging	No	Surgery	Death at 6 months	[7]
34	Spiridakis K.G.	M	68	Gastrointestinal bleeding	Jejunum	Endoscopy	No	Surgery	Disease-free at 11 months	[12]
35	Kouladouros K.	F	42	Intestinal intussusception	Distal Ileum	Computed tomography scan and Enteroscopy	No	Surgery	Death at 7 months	[45]
36	Sinagra E.	M	58	Intestinal obstruction	Distal Ileum	Computed Tomography Scan	Yes	Surgery	Still alive at 2 months	Present Study

The diagnostic criteria, proposed by Blecker and coworkers [8, 16], necessary to support the diagnosis of true primary melanomas of the small intestine consist of:

1. The existence of a single solitary tumor in the intestinal mucosa;
2. The presence of other intramucosal melanocytic lesions in the surrounding intestinal epithelium;
3. The absence of cutaneous or mucosal malignant melanoma or other atypical melanocytic skin lesions such as dysplastic nevi.

The clinical diagnosis of SBM is really challenging, due to the aspecific origin of its symptoms and signs. Non-specific GI features include rectal bleeding, which is the commonest symptom, along with chronic persistent abdominal pain, vomiting, diarrhea, weight loss, and microcytic anemia. Acute presentations with small bowel obstruction (like in the case presented), intussusception, and perforation are really rare; nevertheless, an awareness of these possibilities is important [8]. Upper endoscopy and colonoscopy almost universally fail to identify small intestine pathology as reported in all the cases reviewed in the literature (Table 1). Alternative diagnostic modalities must be considered, such

as abdominal ultrasound, CT scan, barium/ technetium studies, PET and capsule endoscopy, the latter of which permitted a diagnosis in the case reported by Hadjinicolaou and coworkers [8] (Table 1).

Also when curative surgery is impossible because of the extent of the disease, gastrointestinal metastatic tumor resection is recommended, to relieve acute symptoms or avoid future complications [6, 17]. They can also be useful as a palliative treatment in metastatic intestinal melanoma but their role is still unclear [6]. Adjuvant options including chemotherapy, immunotherapy, and biochemotherapy have all been tried, but their efficacy has not been established [7]. In Table 1, the literature about the primary small bowel MM is extensively reviewed. In conclusion, primary small bowel MM appears to be an extremely rare entity which clinicians should be more aware of, in order to plan better a correct strategy of early diagnosis and appropriate treatment.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

Not applicable.

CONSENT FOR PUBLICATION

Consent was obtained from the patient for publication of this report and any accompanying images.

STANDARD OF REPORTING

CARE guidelines and methodologies have been followed.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Declared none.

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