Case report

**Intestinal metastasis of malignant melanoma of unknown primary localization**

Cătălin Toma¹, Bogdan Filip¹,², Fawzy Akad¹, Karina Bilavschi³, Cristina Terinte³, Viorel Scripcariu¹,²

¹¹st Surgical Unit, Regional Institute of Oncology, Iasi, Romania, ²Department of Surgery, “Grigore T. Popa” University of Medicine and Pharmacy, Iasi, Romania, ³Pathology Department, Regional Institute of Oncology, Iasi, Romania

**Abstract**

Malignant melanoma (MM) has been shown to metastasize with relative affinity to the gastro-intestinal (GI) tract, especially through the small intestine, mostly within, but also later than the first 5 years after initial diagnosis. MM appears to less often originate in the GI tract. Surgical excision is reported to be safe and capable of improving oncological outcomes in the absence of other metastatic disease. We hereby report the case of a patient without a history of MM presenting in our clinic with severe anemia due to a tumor located in the small bowel diagnosed on abdominal tomography. Surgery consisted in a radical resection of the affected small bowel segment. Pathological examination revealed a MM metastasis to the jejunum. On further investigation of the patient, a cutaneous lesion suggestive of MM was identified on his right upper limb, which was excised, and the patient has been referred to the multidisciplinary team for initiation of adjuvant chemotherapy. Further follow-up is required due to MM’s propensity for multiple metastases. This case emphasizes the fact that in a patient diagnosed with an intestinal tumor a thorough clinical examination should be performed, as one of the possible differential diagnosis of intestinal tumors is the metastatic localization of a cutaneous MM.

**Keywords:** malignant melanoma; intestinal metastasis; enterectomy; gastro-intestinal bleeding; anemia

**Introduction**

The gastro-intestinal (GI) tract has long been reported as a preferred metastasis location by numerous studies for different primary tumors. Malignant melanoma (MM) metastases occur mostly within the first 5 years after initial diagnosis of the primary lesion, although later events have also been reported [1]. Though, it is still not fully clear why there is a tropism for the gastro-intestinal tract, advancements have been made in this area, identifying the chemokine receptor 9 (CCR9) as a predisposing factor, due to its motility enhancing effects of the cells, in conjunction with the presence of its ligand, CCL25, expressed predominately in the thymus and the epithelium of the small intestine [2]. Surgery has been successfully performed to mitigate GI symptoms (bleeding, obstruction due to stenosis or intussusception) and improve the patients’ quality of life [3, 4].

**Case report**

We hereby present the case of a 50 years old male patient without any significant medical history, who presented in another
hospital one month previously with diffuse abdominal pain and a severe anemic syndrome with hemoglobin levels of 5.6 g/dl requiring blood transfusion. Abdominal ultrasound investigation identified a digestive segment with walls of up to 23 mm thickness, with present vascularization, a circular lumen of 4 mm and gassy contents (a "bullseye"-like image), with the initial diagnosis being a tumor originating at the level of the sigmoid colon. Colonoscopy identified only a pale mucosa, without any lesions up to the level of the ileo-cecal valve; the gastroenterologist performed an upper GI endoscopy that showed the absence of blood or potentially hemorrhagic lesions up to the level of the duodenum. Abdominal CT (Figure 1) was performed, identifying an enlarged liver (diameter of right lobe 172 mm and of left lobe 79 mm) with a homogenous structure and the presence of an expansive mass at the level of a small bowel loop in the hypogastrium, with a circumferential development which appears to be solid, with a inhomogeneous structure, vegetating, causing digestive tract stenosis of up to 2 mm, without upstream dilation, hypervascular, with a maximum thickness of 38 mm, approximately 55 mm in length with an irregular contour, without infiltration to surrounding structures; it comes in contact with ileal loops, the sigmoid colon and the dome of the urinary bladder, compressing them, but with an apparent separation plane to them. At least 7 small, enlarged perilesional lymph nodes along the mesenteric vessels, of maximum 10/11 mm were identified. The tomography report concluded that the tumor formation could be a cT$_2$N$_2$M$_0$ intestinal neoplasia.

![Fig. 1. Abdominal CT - a transverse section through the midplane of the intestinal tumor](image)

At admission, the patient presented with mild abdominal pain at palpation in the hypo- and mesogastrum, pallor and fatigability, but otherwise stable. No immediately obvious skin lesions were identified and he reported no history, personal or familial, of MM, nor one of prolonged sun exposure or multiple skin nevi. Blood tests revealed moderate anemia with Hg=7.3 g/dl and Ht=24.6 %, thrombocytosis of 584000/µl, and a mildly elevated CA19-9 tumor marker (6.31 UI/ml) with a normal CEA tumor marker. Chest X-ray did not identify any secondary lesions. Surgery consisted in median laparotomy, which revealed a whitish
tumor at the level of a jejunal loop of 6 cm in length with apparent invasion of the visceral peritoneum on the dome of the urinary bladder (Figure 2a). A radical enterectomy was performed with an end-to-end manual anastomosis together with partial pelvic peritonectomy and the placement of one abdominal drain tube. The postoperative evolution was uneventful, resulting in the patient’s discharge on the 6th day after the surgery. The patient received one unit of matching blood type transfusion in the first postoperative day.

The histopathological report describes macroscopically a 30 cm long intestinal segment, which presents at about 8.5 cm from one end a quasi-circumferential tumor mass of 5 cm long and 3.5 cm thick, which is obstructive, ulcerated and vegetating, infiltrative, ashen-white and of an elastic consistency. The serosa of the tumor is opaque, whitish, with slight brown deposits. The radial edge is situated at 3.5 cm away from the tumor (Figure 2b). Microscopy (Figure 3a) reveals an intestinal wall with tumoral infiltration consisting of monomorphic cells with eosinophilic cytoplasm, vesicular nucleus with apparent nucleolus, creating a diffuse, solid architecture. Focally, the tumor cells are plasma-cell-like. The tumoral growth interests the entire wall with ulceration on the luminal side and the perforation of the visceral peritoneum. There is important tumoral necrosis and lympho-vascular invasion. Resection edges are tumor-free. There were 25 lymph nodes with no apparent metastases. The vesical peritoneum fragment contains a few smooth muscle fragments, most probably vesical muscle; it contains focal submesothelial tumor infiltration. Immunohistochemistry describes CKAE1/AE3, Synaptophysin and CD56 – negative; CD20, CD79alfa, CD3, CD5, CD30, ALK1 – negative; CD10, MUM1, CD45 – negative; S100 (Figure 3b), HMB45 (Figure 3c), and Melan A (MART1) (Figure 3d) – diffuse positive. The histopathological diagnosis is of metastatic lesions of the small bowel in the context of an epithelioid MM.

The patient was recalled for further investigation of a possible primary lesion. During a full physical examination a complex lesion was identified on the lateral aspect of the right upper arm: a discolored, roughly ovoidal skin patch of 2/1.2 cm in diameter; an elevated, vegetating light brown nevus anteriorly and inferiorly to the previous lesion, without apparent contact to it, with a wide base and clearly defined edges, a slightly discolored superficial layer, oblong and 2.3/1.5 cm in diameter, which the patient declared had been there since childhood and had not caused any problems; another, smaller lesion (0.8/0.5 cm) at a distance of about 1 cm from both of the two previous ones, deep brown with tonal...
variations, with undefined edges and a slightly elevated surface, which the patient declared was rather new, but which he had ignored thus far. The patient has been referred to the plastic surgery department for local excision of the skin lesion and the case was discussed in the multidisciplinary oncologic meeting.

![Image of skin lesion](image-url)

**Fig. 2.** Microscopical and immunohistochemical aspects of the malignant melanoma showing: a) mucosal and vascular invasion, (HE, x25); b) S100 positivity, (IHC, anti-S100 Ab, x100); c) HMB45 positivity (IHC, anti-HMB45 Ab, x200); d) Melan A positivity (IHC, anti-Melan A Ab, x100).

**Discussion**

Intestinal metastases of MM are usually multiple and the patients usually present symptoms of GI bleeding, abdominal pain and, less frequently, intussusception. The usual time form diagnosis of the primary tumor to that of the metastases usually falls within 2-5 years [1], although only about 1.5–4.4% of all patients with melanoma are diagnosed antemortem [5], while 50-60 % of patients known with MM present metastases at autopsy.

CT scans are reported to have 69% sensitivity in detecting small bowel metastases of MM. In contrast, PET-CT scans have a sensitivity approaching 100%, making them, when readily available, the investigation of choice. In our case the CT scan was enough to diagnose the source of the bleeding [6].

Current systemic therapies for metastatic MM according to the ESMO guidelines [7] and their most recent updates include anti-PD-1 antibodies (nivolumab, pembrolizumab) or anti-CTLA4 inhibitors (ipilimumab) if BRAF is wild-type, or BRAF+MEK inhibitors (veumafenib, encorafenib, dabrafenib with or without binimetinib, cobimetinib, trametinib) as an additional option for BRAF mutated variants. If BRAF testing reveals a wild-type variant, then additional NRAS, c-KIT, GNA (11 or Q, for uveal primaries) testing should be performed to help in targeting therapies, since traditional chemotherapy alone is not very...
effective. Nonetheless, there is no definitive standard regarding the exact systemic therapeutic approach in metastatic MM.

Surgery, on the other hand, has repeatedly been proven to alleviate symptoms and increase quality of life as well as endpoint survival, provided there was an R₀ resection [3, 6]. The five-year survival increased to 27%, as opposed to the 9.5% predicted by the AJCC staging system in 2002 [6]. A reported adverse effect of targeted therapy would be the higher risk of anastomosis leakage [8]. However, our patient had not begun therapy prior to surgery. Therefore, we can safely assume surgery was the right course of action given his immediate clinical problems (severe anemia) as well as the good palliative results and local symptom control reported by previous studies.

Conclusion

The reported case has several noteworthy particularities. One of them is the lack of a previous diagnosis of MM, which decreased the likelihood of a differential diagnosis of a primary intestinal tumor versus a metastatic lesion from MM. The cutaneous primary that was later identified on the upper right arm is currently under investigation. However, the patient refused further medical or surgical procedures, making his prognosis rather grim in the absence of chemotherapy or biological therapy. The clinical presentation, though nonspecific, was rather frequent for small bowel metastasis of MM, with GI bleeding leading to severe anemia and weight loss.

This all raises the question of how thoroughly we need to investigate patients to rule out even the more remote diagnostic possibilities. In this case, a more detailed physical would have identified the lesion and perhaps changed the treatment course, by making the necessity of a multimodal approach clearer for the patient as well as for the medical team. It serves as a warning for all doctors to always keep their guard up when approaching a patient.

Consent

Written informed consent was obtained from the patient for publication of this case report.

Competing interests

The authors declare that they have no competing interests.

References