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Case Report
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Small Bowel Metastasis in a Stage IV Melanoma Patient: A Report of Multimodal Approach

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Abstract

Among all skin cancers melanoma is the most aggressive and the first responsible of death because of its metastatic power. Small bowel melanoma metastases are a rare condition, probably underestimated if we consider the high incidence in autoptic findings. Usually, it comes as a single or multiple protruding lesions with polypoid aspects that is able to cause intussusception, blood loss anemia, and palpable mass and abdominal pain. We present a case of a 58-year-old male, diagnosed in July 2018 for melanoma that in 2021 showed sudden anemia. Video Capsule Endoscopy demonstrated an ulcerated lesion in the proximal ileum. Several approaches are available for the treatment of this lesion, but specific indications for surgery have not yet been defined. We adopted a watchful waiting approach to not let the patient undergo an excessive surgical stress, considering the risk of tumor progression. Surgery was performed after multidisciplinary revision of the case.

Keywords: Small Bowel; Melanoma; Surgery; Metastasis

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Introduction

While it accounts for less than 10% of skin cancers [1], melanoma represents the first cause of deaths among them due to its metastatic power. In Italy, the incidence of melanoma has increased significantly over the past 10 years. The estimated incidence for 2020 is 14,863 new cases, an increase of 15% compared to 2011 and of 12% compared to the estimate made in 2011 for 2020. Melanoma is the second most frequent cancer in men and the third in women under the age of 49 and over 50% of cases are diagnosed within the age of 59. About 15,000 new cases are recorded in 2020 [2]. The prognosis is related to the stage of the disease at the time of diagnosis [3]. A localized disease is found in 86% of cases, a loco-regional disease in 10% of cases and a metastatic disease in 4% of cases. So in the last five years in Italy deaths for skin melanoma have been 4,000 in males and over 3,000 in females [4]. In a study conducted between 2009 and 2015 on patient with diagnosis of metastatic melanoma it was observed that 5-year survival from diagnosis was about only 25% [5]. Updates about KEYNOTE-006 and Checkmate-067 clinical trials where metastatic patients were treated with first-line immunotherapy, have shown that 38% and 52% of patients were alive after 5 year from first diagnosis of metastatic disease, respectively [6-8]. These recent findings on the efficacy of systemic therapy in advanced melanoma have allowed a significant improvement in the prognosis of this subset of patients [9]. Until now surgery has found a prominent place in the therapeutic management of early-stage melanoma through wide local excision, sentinel lymph node biopsy for staging and radical lymph node dissection, when indicated [1]. As part of an increasingly multidisciplinary approach to cancer, surgery represents a mainstay also in the metastatic setting, both as a palliative approach and as an integral part of disease control after response to systemic therapy [9].

Case Presentation

In July 2018, a 58-year-old man underwent an excisional biopsy of atypical melanocytic lesion in lumbar region diagnosed as superficial spreading melanoma of 5.5 mm Breslow, ulcerated, and with an extensive regression (Figure 1). Total body CT scan was negative for distant metastases. Wide excision and sentinel lymph node biopsy in left inguinal basin were negative for malignancy, while sentinel lymph node biopsy in the right inguinal basin was positive for neoplastic

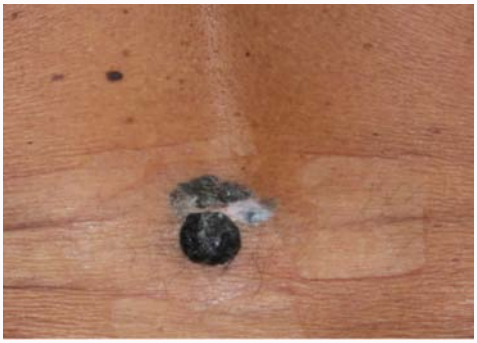

Figure 1: Thick superficial spreading melanoma located to the lower back of a 54-year-old patient. The nodular component, developed from the inferior part of this large lesion, was ulcerated and reached a Breslow thickness of 5.5 mm. The flat component is characterized by an abrupt border, multiple colors and a large area of regression.

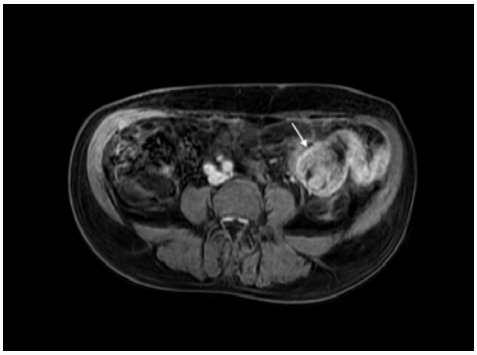

Figure 2: Bowel loop involvement Entero-MRI view (arrow).

Figure 3: Bowel loop melanoma metastasis surgical resection.

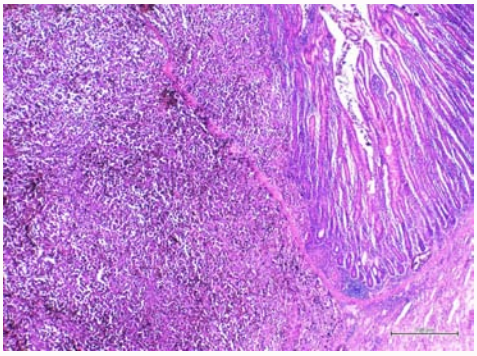

Figure 4: Ileal wall site of melanoma metastases. Melanoma (left) is localized in the submucosa and partly "attacks" the ileal mucosae (at the top left). Hematoxilin-eosin, original magnifications 4x.

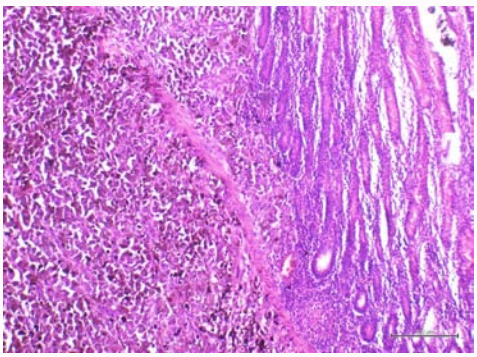

Figure 5: High magnification shows a melanocytic proliferation invading the overlying intestinal mucosa. Hematoxilin-eosin, original magnifications 10x.

infiltration. As standard of care in 2018, he underwent right inguinal lymphadenectomy; all nodes were free from neoplasm. TNM staging was pT4b N1a cM0 corresponding to IIIC stage (AJCC VIII Ed) [10]. Braf and Nras mutational analysis resulted wild type. In consideration of stage and molecular characteristics, from March 2019 to March 2020 the patient undertook adjuvant immunotherapy with Nivolumab 3 mg/kg every 14 days. At the instrumental re-evaluation with total body CT performed at the end of the treatment, hepatic, pulmonary and lymph node recurrent disease was detected. Research of the Braf mutation, carried out by liquid biopsy (Biocartis Idylla), was again negative, thus, from April 2020 to June 2020, he received first line immunotherapy with Ipilimumab 3 mg/kg every 21 days for 4 cycles. No relevant toxicities during both checkpoint inhibitor treatments occurred. Pulmonary, hepatic and lymph node disease stability were maintained until June 2021 with 15 months of progression free survival. In August 2021, due to severe asthenia, patient underwent a blood count exam with evidence of severe anemia. After blood transfusion and supportive cares, colon and upper gastrointestinal endoscopic exams were performed resulting negative for bleeding lesions. Exploration of the small intestine using video capsule endoscopy showed an endoluminal lesion with active downstream bleeding. Further investigation with entero-MRI was recommended to evaluate the extension of the small bowel wall involvement. MRI highlighted a formation of 40 mm × 35 mm starting from the wall of an ileal loop in the center-abdominal region (Figure 2). A total body CT-scan showed no progression disease in others known metastatic sites. Due to progressive and persistent anemia, after multidisciplinary discussion and surgical evaluation, the patient was candidate to bowel resection with ileo-ileal isoperistaltic anastomosis (Figure 3). Histological evaluation confirmed an ileal wall melanoma metastasis (Figure 4, 5). Gastrointestinal function and patient condition were restored. He was alive in March 2022, his disease is still metastatic but since gastrointestinal metastasis was radically removed, anemia condition or other gastrointestinal metastases no longer occurred.

Discussion

The most common metastasis of stage IV melanoma are lymph nodes followed by lungs, liver, brain, bone and adrenal gland. Small bowel melanoma metastases are a rare condition, probably underestimated if we consider the high incidence in autoptic findings [9,11]. High incidence of metastasis in the small bowel is probably due to the abundant blood supply of this organ [12]. The symptoms can be intestinal occlusion, blood loss anemia, palpable mass,

abdominal pain or weight loss. In our case diagnosis was obtained only after sudden anemia for bowel bleeding. However about 30% of these metastases remain asymptomatic [13]. Bowel metastases could present as single or multiple protruding lesions [14]. These underestimated values may also be a consequence of poor sensibility of CT and PET in detecting lesions when still asymptomatic [15]. Today, thanks to the improving of radiologic imaging and a greater accessibility to endoscopic techniques, management of these patients has improved markedly consenting a faster diagnosis even of asymptomatic metastasis compared to the past in which multiple CT exams were needed to obtain a certain diagnosis [16]. Surgical approach is effective and associated with survival benefits, especially in case of complete resection [9,17,18], but specific indications for surgery have not yet been defined. We prefer surgical approach only in case of intestinal occlusion or bleeding to avoid the effects of surgical stress on tumor progression [19]. Furthermore, multidisciplinary approach for bowel metastasis is mandatory and surgery should be considered only as palliative care in case of severe symptoms.

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