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Gastrointestinal bleeding as presentation of small bowel metastases of malignant melanoma: Is surgery a good choice?



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ABSTRACT

INTRODUCTION: Melanoma shows a particular predilection in involving small intestine both in a single site and in multiple localization and acute or chronic gastrointestinal bleedings are often the first sign of tumour.

PRESENTATION OF CASE: We report two cases of GI metastases of malignant melanoma, one presented with only a big mass that cause intestinal obstruction and the other with a tumour spread throughout the small intestine that produce enterorrhagia.

DISCUSSION: Diagnosis and follow-up are very difficult: CT scan, PET-CT scan and capsule endoscopy should be complementary for the assessment of patients with GI symptoms and melanoma history.

CONCLUSION: What is the role of surgery? Several studies suggest metastasectomy to achieve both R0 results and palliative resolutions of acute symptoms, such as obstruction, pain, and bleeding.

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1. Introduction

Enterorrhagia is a common sign in patients who come to a surgical department; after the exclusion of benign diseases (such as haemorrhoids, anal fissures or IBD), we focus on gastro-intestinal malignant tumours. However, even if colic or colorectal carcinomas are very common, the incidence of tumours of the small intestine, both primary and secondary, is very low; this is even more true if we consider the intestinal localization of melanoma, both in case of metastatic and primary tumours.

What should we do in such clinical circumstances? We report two cases of malignant melanoma metastasis; one was presented with only a big mass and the other was with a tumour spreading throughout the small intestine. Diagnosis was not easy especially without a previous clinical history of melanoma, or when it is omitted at the hospitalization, as what happened in our second case. Nevertheless some old and new devices could help surgeons, like PET/CT scan and capsule endoscopy.^{14,16} Controversial is their use in melanoma follow-up, considering their costs and the prolongation of waiting lists. Despite that gastrointestinal investigations (such as faecal occult blood or colonoscopy) should be promoted by clinicians for patients with melanoma in order to prevent bowel metastasis complications.

In both our cases, surgery was performed with the aim to assure the best local control of symptoms and guarantee better prognosis, even in cases of spread involvement, according to several studies that support surgical treatment not only to obtain a complete resection but also for palliative intent.^{18,21,23}

2. Case 1

A 49-year-old man with abdominal pain, anaemia and tarry stools came to our attention in October 2009. He reported that the symptoms started ten days before. Sixteen months before he underwent a malignant melanoma excision from the right leg and two months later a wide removal of skin around the first excision with a bilateral inguinal lymphadenectomy because of sentinel node positivity. Furthermore a secondary localization on the left cheekbone was removed in September 2008 and the patient started traditional chemotherapy with Dacarbazine in January 2009.

In order to determine the source of disease we arranged a CT scan which showed an huge jejunal mass (8 cm of diameter) that reduced intestinal lumen and determined dilatation of its upper part. A bowel resection with L-L manual anastomosis was performed and the histological diagnosis was "bowel localization of melanocytic melanoma that involved 5 out of 7 mesenteric lymph nodes".

During the postoperative period the patient underwent PET/CT scan which showed multiple brain recurrences. No postoperative

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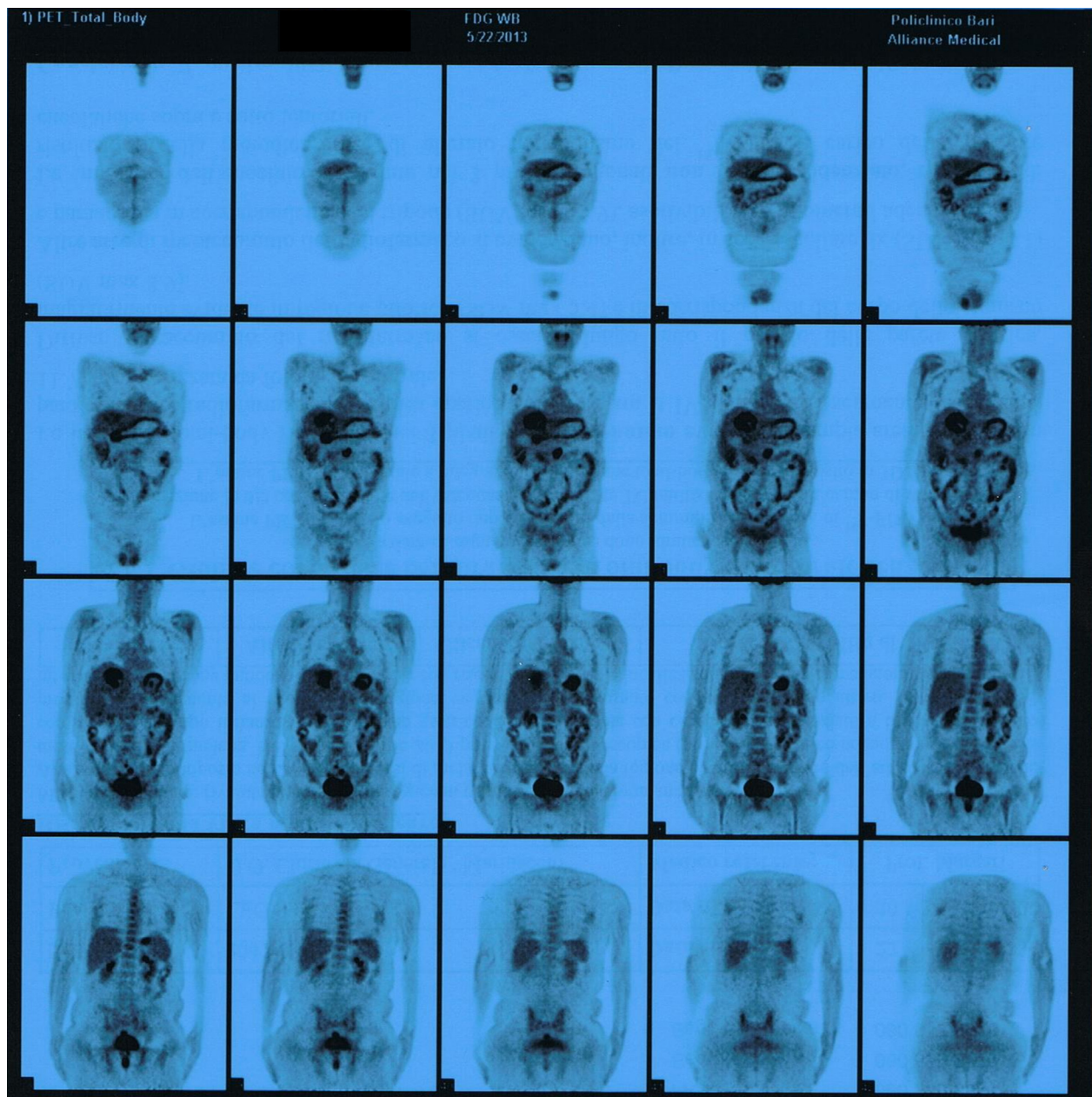


Fig. 1. 18-FDG PET-CT scan reveals the extension of the disease.

chemotherapy was carried out and he died because of intracranial bleeding three months after abdominal surgery.

3. Case 2

A 61-year-old man was admitted to our Department on May 2013 as emergency case because of gastrointestinal bleeding and anaemia. The patient's medical history was significant for hypertension, noninsulin-dependent diabetes mellitus and iron-deficiency anaemia.

Anamnesis is also characterized by a diagnosis of skin melanoma in the abdominal region on April 2011; however, the patient gave us such information only at the end of our surgical treatment. At that time a diagnostic excisional biopsy of the lesion was performed and the histological report confirmed: "III Clark level, Breslow thickness 0.55 mm malignant melanoma with the prevalence of superficial

diffusion and without regression or vascular infiltration". Consequently a wide skin removal was performed, because a melanoma was found on the skin near to the previous excision. However the patient did not have sentinel lymph node biopsy procedure or any follow-up control because he did not accept them.

At the beginning of 2013 the patient had several episodes of melena and, with the aim to discover the source of bleeding, we performed a colonoscopy with biopsy (the histological diagnosis was hyperplastic adenomatous polyp) and a gastroscopy which solely showed an antral gastritis and an inflammatory stomach polyp. Moreover the patient underwent abdominal US and MRI and a total body CT scan that showed right axillary lymphadenopathy, a nodular lesion in the medial lobe of the right lung and a big mass (7 cm of diameter) in the IV–VIII segment of the liver of which an US-guided biopsy was carried out. In addition we founded an increase in the tumour markers (TPA, NSE, S100B). For a more accurate diagnosis,

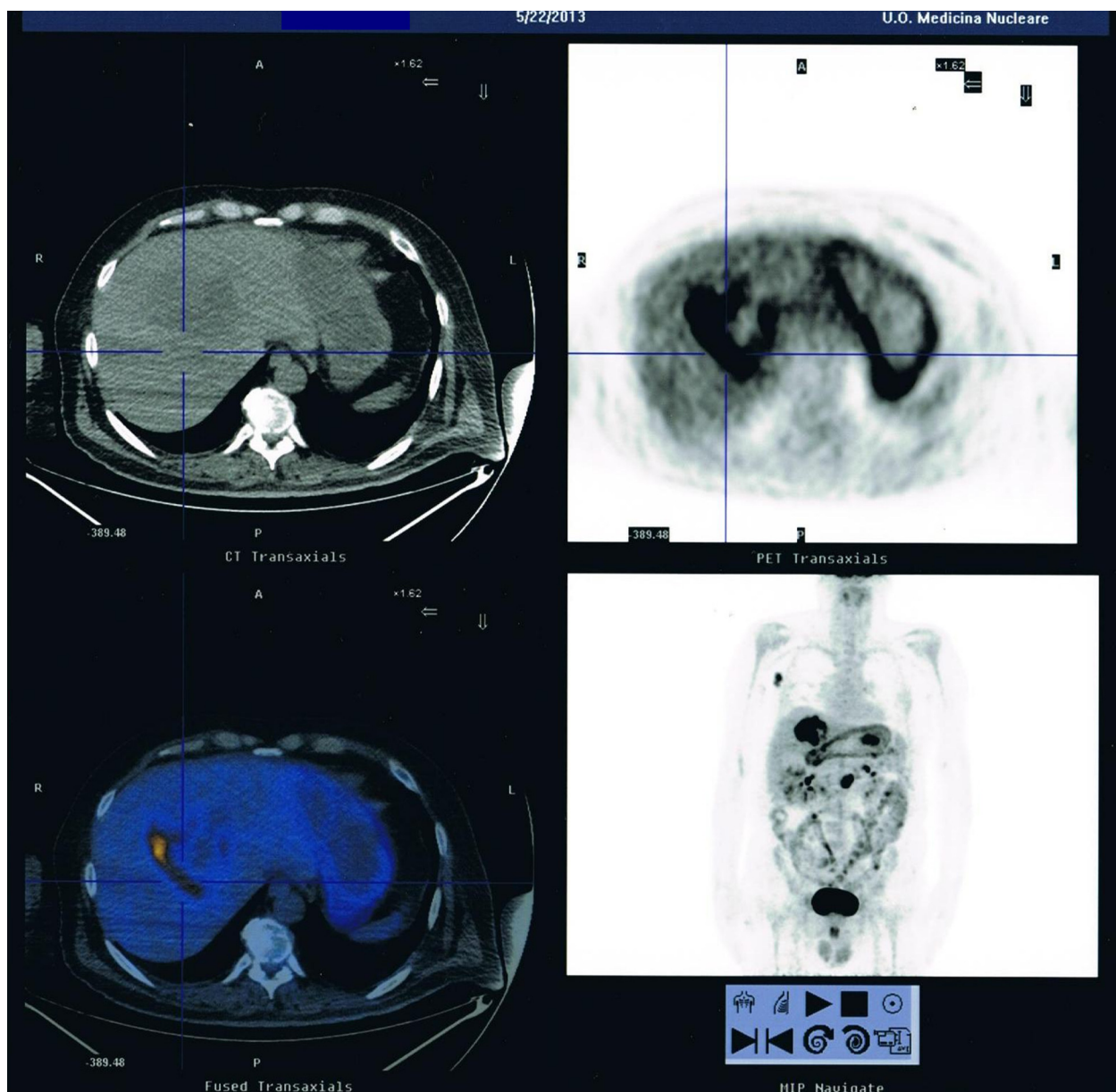


Fig. 2. 18-FDG PET-CT shows hepatic metastasis.

the patient underwent capsule endoscopy which showed a subtotal stenosing vegetating ulcerating neoplasm of the upper jejunum (just below the Treitz's ligament); because of this, it was impossible to end the examination.

While we were waiting for the histological response of the hepatic biopsy, the patient had a severe enterorrhagia and he went to ER, so we had to perform a laparotomy in order to remove the jejunal neoplasm. Surprisingly, we found a catastrophic situation: apart from the jejunal localization, there were several small bleeding nodes throughout the whole mucosal side of the small bowel, some of them appearing on the serosal surface as black spots, and some mesenteric lymph nodes increased in volume and also black. In order to reduce the risk of a rapid resumption of bleeding, we succeeded in removing the duodenum-jejunal tract (30 cm of length with 15 nodes from 1 to 5 cm of diameter) and the majority of the biggest nodes through both an ileal excision of a 17 cm segment which included 5 ulcerating neoplasm localizations from 0.5 to 2.5 cm of diameter and other three simple enucleations of lesions with a diameter of 2.5 cm.

The histological diagnosis about the bowel localizations was "melanotic melanoma" and the one about the liver was "metastatic localization of amelanotic melanoma".

Afterwards the patient underwent 18-FDG PET-CT scan which revealed the abnormal accumulation of radioactivity throughout the bowel and gastric wall, at the VIII hepatic segment and at the lymph nodes of the right axilla and the celiac tripod (Figs. 1 and 2).

In June 2013 the patient started traditional chemotherapy with Fotemustine because he was B-RAF wild type and N-RAS negative and he underwent the second cycle in July. During that period he had recurrent episodes of enterorrhagia and he needed blood transfusions. Unfortunately the disease did not stop its course and the patient died because of heart failure in September 2013, four month after diagnosis.

4. Discussion

Enterorrhagia is often the first sign of a gastrointestinal tumour and it is useful looking for bleeding localization. Intestinal lesions

are mostly primary tumours, however in rare cases they may be metastases. Secondary localizations of solid tumour rarely involve the small bowel; on the contrary melanoma shows an unusual predilection to metastasize to the GI tract, especially the small intestine, for reasons that remain unclear^{1,2}.

Only 1–5% cases of metastatic melanoma³ are diagnosed during life because they are generally clinically asymptomatic in the early stages. Diagnosis often takes place when an emergency complication occurs, such as intestinal perforation, obstruction, intussusception, and acute GI bleeding, as in our second case.^{4–9} In other circumstances, such as the first patient, symptoms are non-specific and a patient comes to our attention because of anaemia, fatigue, weight loss, abdominal pain, constipation, haematemesis, diarrhoea with tarry stools, faecal blood test positive, and the presence of a palpable abdominal mass.

In a study conducted by Sanki et al.,¹⁰ the median interval between treatment of the first melanoma and detection of GI metastasis was 48 months (range 0–489), for Gutman et al.,¹¹ 38.5 months (range 1–258). In our case reports this interval is 16 and 49 months respectively.

Which is the best approach to investigate an acute or chronic gastrointestinal bleeding in patients with positive history of melanoma? Unanimously the importance of routine investigations for patients with recently diagnosed melanoma is emphasized in order to discover occult stage IV disease and improve survival but there is not a common approach on the management of such patients. EGDS and colonoscopy are commonly used to identify bleedings from the upper or lower gastrointestinal tracts. We wonder if we have to perform them to all I–II stage melanoma patients.

Sometimes diagnosis could be obtained with computerized tomography (CT) even if its sensibility is only 68%.¹² PET-CT scan is more sensitive in detecting visceral and GI metastases than PET alone or CT alone.^{13–15} However this imaging technique does not help to localize lesions accurately. Therefore Prakoso et al.¹⁶ suggest capsule endoscopy as a complementary assessment for patients with GI symptoms and/or with melanoma history, even if FDG PET-CT scan results are negative.¹⁷ Nevertheless further randomized studies should be managed with the aim to detect the best sequence of diagnostic procedures and investigate if capsule endoscopy should be proposed even in emergency cases.

In our experience after sure diagnosis the best treatment of GI metastases should be an aggressive approach both in emergency cases and in the elective ones. According to several studies^{10,11,19–23} the first aim should be the complete resection with no tumour residual (R0). Indeed it was seen that surgical removal of all visible abdominal tumour was associated with a median survival of 17 months¹¹ and 1-year survival rate of 57%.¹⁰ Furthermore even palliative surgery guarantees better prognosis with a median survival of 11 months compared with 5 for those treated by systemic therapy and a 1-year survival rate of 34% instead of 41%.¹⁸

Thus surgery could improve local control of symptoms and give a great expectance of life, even though it was carried out with non-therapeutic intent. This was the goal in both of our cases. Nevertheless when disease is widespread with various gastrointestinal and/or extra intestinal localizations then metastasectomy is seen as a mere local therapy and a questionable solution of disseminate disease.^{24,25} Once again we would underline the importance of pre-operative assessment to achieve an accurate staging of melanoma with the aim to undergo surgery of only selected patients and to remove all metastases or solve a bowel obstruction, stop bleeding or relieve symptoms. According to ESMO guidelines adjuvant systemic therapy might be necessary. Unfortunately therapies for metastatic disease are not standardized and they only provide a palliative effect.

We are waiting for results from a new multicenter phase III, randomized trial that compares surgical resection versus medical

therapy as initial treatment for patients with resectable stage IV melanoma (NIH Clinical Trials Identifier, NCT010013623).

5. Conclusion

Melanoma shows a particular predilection in involving small intestine both in a single site and in multiple foci but diagnosis is made during life only in 1–5% of patients. Since signs and symptoms are unspecific routinely bowel examination is unadvisable. Nevertheless if enterorrhagia, anaemia or abdominal pain arise in patients with a history of melanoma, then investigation should be mandatory to understand if they could be possible manifestations of metastatic spread. Blood examination, especially rising serum S100 and LDH, PET-CT scan and capsule endoscopy may lead to an earlier diagnosis of systemic relapses. Surgery for patients with stage IV melanoma should be the first step of a combined therapy. To date, the role of surgery for disseminate melanoma is to obtain better survival incomes than systemic therapy even though it is carried out for palliative intent. In order to prevent advanced melanoma stage, we should emphasize the importance of regular follow-up.

Conflict of interest

None.

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Ethical approval

Written informed consent was obtained from the patient's wife (case 1) and the patient's daughter (case 2) for publication of these case reports.

Author contributions

Dario D'Abbicco – Consultant of the unit. Second surgeon for the first case report. Provided overall supervision, direction and suggestions.

Angelica Conversano – First author. Third surgeon for the second case report. Contributed in data collections, data analysis, writing and review.

Simona Macina – Second author. Assisted in writing and proof-read draft.

Rocco Indellicato – Third author. Contributed in literature search.

Domenico Lacavalla – Fourth author. Obtained consents and contributed in data collection.

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