

# Surgical treatment of metastases from cutaneous melanoma to the small intestine and the spleen.



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## Case reports and review of the literature

Lorenzo Di Libero\*, Valerio Sciascia, Daniela Esposito, Roberto Varriale, Ernesto Tartaglia, Luigi Santini

VII Divisione di Chirurgia Generale (Direttore: Prof. L. Santini), Seconda Università di Napoli, Italia

\*Divisione di Chirurgia Generale (Direttore: Prof. A. Tartaglia), Clinica Sanatrix in Napoli, Italia

### Surgical treatment of metastases from cutaneous melanoma to the small intestine and the spleen. Case report and review of the literature

*Cutaneous melanoma is found in the head and neck in 15% of patients, in the limbs in 22%, in the trunk in 40% and in occult sites in 16%. There is usually an interval of at least 3 years between the diagnosis of primary melanoma and the identification of metastases. Primary melanoma metastasizes most frequently to the lymph nodes (73.6% cases) and the lungs (71.3% cases). The small intestine and the spleen are the sites of 36.5% and 30.6% respectively of the gastrointestinal metastases from melanoma.*

*The cases reported provide evidence of the effect radical resection in patients with gastrointestinal metastases can have on survival.*

*The cases and a review of the literature suggest that a careful and multidisciplinary follow-up is of crucial importance since it is the only means of identifying metastases when they can be still cured with surgical treatment.*

KEY WORDS: Melanoma, Metastasis, Survival.

### Introduction

Primary cutaneous melanoma is found on the head and neck in 15% of patients, on the limbs in 22%, on the trunk in 40%, and in occult sites in 16%<sup>1</sup>.

Only 8% of patients are diagnosed so late that they already have distant metastases, since there is usually a long time interval between diagnosis of the primary tumor and discovery of secondary spread<sup>2</sup>. In a study conducted by Klaase and Kroon, this time interval was found to be 3 years<sup>3</sup>.

Splenic metastases are rare in most cases of cancer, and

are most commonly found in patients with breast or lung cancer, or malignant melanoma<sup>4,5</sup>.

A series of autopsies, performed on 216 cadavers demonstrated that melanoma most often metastasizes to the lymph nodes (73.6% cases) and the lungs (71.3% cases)<sup>6</sup>.

Less common sites of metastases described are the liver (58.3% cases), the brain (54.6% cases), the bones (48.6% cases), the adrenal glands (46.8% cases), and the gastrointestinal (GI) tract (43.5%)<sup>6</sup>. As regards GI metastases, the small intestine and the spleen are affected in 36.5% and 30.6% of cases respectively<sup>6</sup>.

Metastases to the biliary tree are comparatively rare<sup>6</sup>, and only one case of metastases to the ampulla of Vater, which caused icterus and melena, and was treated with a Whipple procedure, has been described in the literature<sup>7</sup>.

A rare case of metastases from melanoma to the small intestine and a synchronous primary gastrointestinal stromal tumor (GIST) has also been described<sup>8</sup>.

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Correspondence to: Lorenzo Di Libero, V. Elci 23, 82034 S. Lorenzo Maggiore (BN) (e-mail: diloren1974@libero.it)

According to some authors, the small intestine is the most common site of metastases from cutaneous melanoma since these metastases occur in 58-80% of cases<sup>9-11</sup>.

Patients with visceral metastases from melanoma have a poor prognosis and an average survival rate of less than one year, as shown by a multicentric study<sup>12</sup>. Nevertheless, survival rates of 20-40% at 5 years after complete resection of metastases in the lungs, GI tract, and adrenal glands<sup>13</sup>.

We present 2 case reports of patients with metastases from cutaneous melanoma, and discuss the relevant literature. The first patient underwent jejunal resection followed by splenectomy, and the second patient only underwent ileal resection.

## Case reports

### CASE N.1

In September 2006, a 56-year-old man presented to our department with severe pain in the left hypochondrium. There was guarding on abdominal examination, and blood tests revealed mild anemia. However the patient was hemodynamically stable.

The patient was a moderate smoker and on insulin therapy for diabetes mellitus. Over the years he had repeatedly undergone the removal of cutaneous nevi which were diagnosed as superficially spreading malignant melanoma.

In September 1989 a pigmented cutaneous periumbilical lesion was removed. On definitive histological examination the lesion was found to be a superficially spreading malignant melanoma, with a Clark III level of infiltration and a Breslow thickness of 0.75-1.5mm.

In October of the same year, after the removal of 2 lozenge-shaped pieces of skin containing pigmented lesions from the right inframammary and left thoracic regions, the lesions were diagnosed as superficially spreading melanoma with a Breslow thickness of 0.25mm.

In May 2000, the definitive histological exam of a cutaneous lesion in the right mammary region identified a superficially spreading melanoma with a Breslow thickness of 0.6mm.

In October 2003, a cutaneous neof ormation on the right hemiabdomen was found on histological examination, to be a nevus of Clark.

Since all the above lesions were less than 1mm in diameter there were no indications for systemic adjuvant therapy, radiotherapy, or immunotherapy.

In May 2006, the patient underwent resection of a jejunal loop, with its mesentery, circa 30 cm long, because of the presence of a stenosing and bleeding lesion circa 60 cm from the ligament of Treitz. (Hemoglobin 8.5g/dl, hematocrit 28.7%, red blood cells  $3,2 \times 10^6/\mu\text{L}$ ).

The histological exam of this lesion, which on immunos-

taining was positive for the proteins S-100, MART-1, HMB-45, tyrosinases, CD43, CD68, CD163, resulted in a diagnosis of metastases from melanoma involving the entire thickness of the bowel wall and causing ulceration of the mucosa. In this case as well treatment was purely surgical.

In September 2006, the magnetic resonance imaging (MRI) performed on admission revealed the presence, in the left hypochondrium, of a lesion that appeared to be a locoregional recurrence, and was characterized by a large, dishomogeneous area of increased tissue density, with a maximum diameter of circa 10 cm, inseparable from the inferior pole of the spleen and the neighboring loop of the jejunum (Figs 1,2). The mediastinal, retroperitoneal, and pelvic lymph nodes did not appear to be involved at all.

A computed tomography (CT) scan of the thorax, abdomen and pelvis without contrast agent, performed in conjunction with a positron emission tomography (PET) scan, confirmed the MRI findings.

The results of PET scintigraphy after administration of the radiotracer <sup>18</sup>fluorodeoxyglucose (<sup>18</sup>FDG) revealed a large, dishomogeneous area of hyperaccumulation of the tracer in the left hypochondrium, which corresponded to the formation found on the other imaging tests (Fig. 3).

As a result, the patient underwent open surgery. A left subcostal incision was used to provide the best possible access to the left hypochondrium. When the peritoneum was opened, circa 250 ml of serosangiuneous fluid was aspirated and sent for cytological examination.



Fig. 1: MRI: high tissue density, circa 10 cm in diameter (maximum), inseparable from the inferior pole of the spleen and the nearby jejunal loop.



Fig. 2: MRI: lesion of the inferior pole of the spleen which appears inseparable from the nearby jejunal loop.

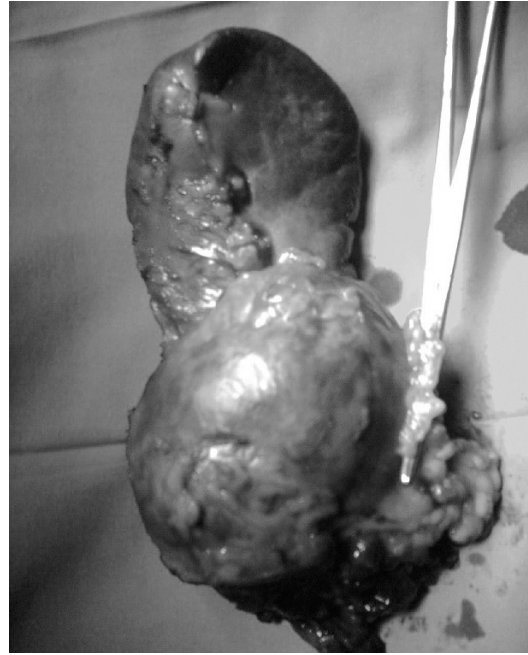


Fig. 4: Surgical specimen: the spleen with a lesion circa 10 cm in diameter (maximum) at its inferior pole.

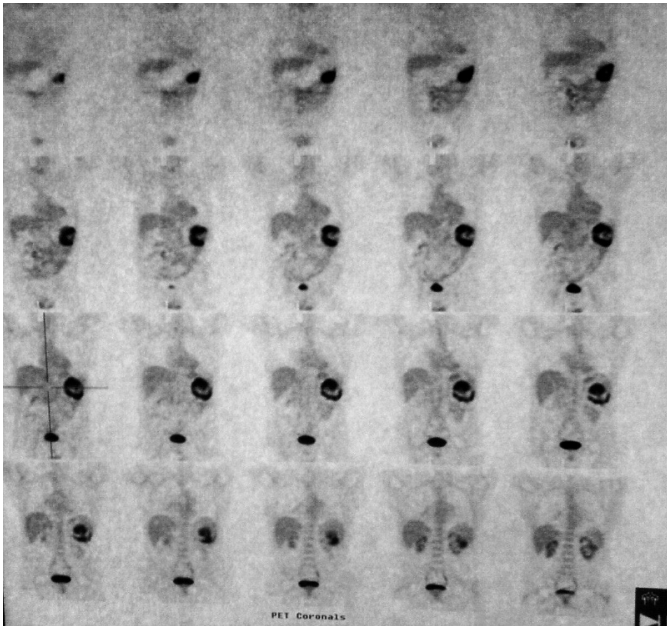


Fig. 3: <sup>18</sup>F FDG PET scan: large area of dishomogeneous hyperaccumulation of radiotracer at the level of the left hypochondrium spleen.

After the left colic flexure was lowered the spleen was exposed and prepared. There appeared to be a neof ormation circa 10 cm in diameter involving the inferior pole of the spleen (Fig. 4). However, contrary to what diagnostic imaging had revealed, the jejunum did not seem to be involved at all (Fig. 2).

There was a bleeding laceration at the inferior pole of the splenic capsule. After the hilar vessels and short vessels were prepared and ligated, the spleen and the neof ormation attached to it were removed en bloc.

The patient's postoperative course was uneventful. On postoperative day 2 the patient passed flatus and on postoperative day 3 a stool. He was discharged on postoperative day 5.

The definitive histological exam of the surgical specimen identified a malignant tumor with round/oval, uniform, nucleolated cells that were positive to immunohistochemical staining for vimentin, protein S-100 and protein HMB45. The final diagnosis was metastasis from malignant melanoma.

At 24-month follow-up the patient appeared to be in good health and without any macroscopic signs of disease, even though he had not been given any additional therapy.

#### CASE N. 2

In June 2008, a 48-year-old man presented with severe anemia, discovered at his most recent blood test. (Red blood cells  $3.14 \times 10^6/\text{mm}^3$ , hemoglobin 5.89 g/dl, hematocrit 19.91%).

The patient had a history of malignant melanoma. Two years before admission he had undergone inferior lobectomy of the left lung due to metastases from a melanoma previously removed from his back.

Abdominal examination on admission was negative, and digital rectal examination revealed 3<sup>rd</sup> degree hemorrhoids and normal stool in the rectal ampulla. Blood tests were then ordered. The patient underwent esophagogastroduodenoscopy (EGDS), colonoscopy, and contrast CT scan of the thorax, abdomen and pelvis.

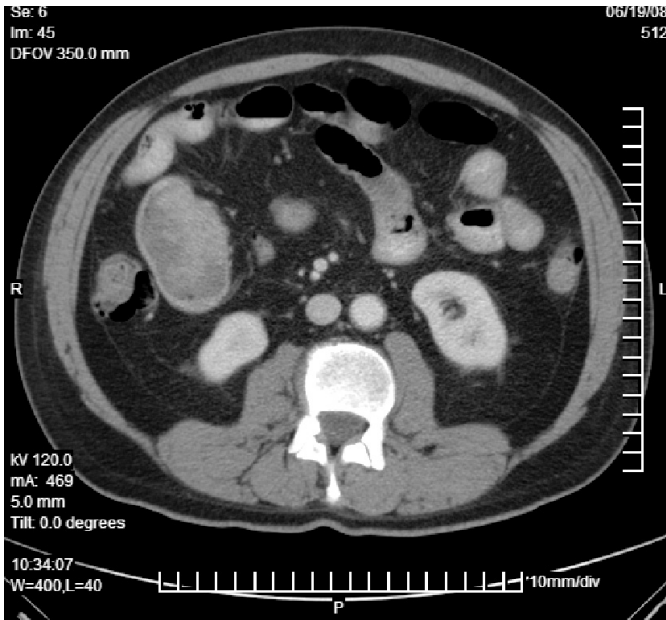


Fig. 5: CTscan: a large heteroplasic lesion occupy-Ing the lumen of a loop of the mid-proximal ileum.



Fig. 6: Surgical specimen: the involved ileal loop with its mesentery and lymph nodes.

There were no important findings on colonoscopy aside from a polypoid formation, in the right colon, which was removed and found, on definitive histological examination, to be an adenomatous polyp with mild glandular dysplasia.

Abdominal CT scan with contrast agent (Fig. 5) revealed a heteroplasic formation occupying a large part of the lumen of a loop of mid-proximal ileum in the right hemiabdomen. The walls of the colon at this level were irregularly thickened and hard to distinguish from the perivisceral fat. Enlarged mesenteric lymph nodes (on average 25mm in diameter), as well as enlarged iliac and intercaval and lomboaortic nodes completed the picture. After the infusion of 4 units of blood (A positive), the

patient underwent surgery, during the course of which a neof ormation circa 8 cm in diameter was found in the ileum at circa 1m from the ligament of Treitz. The ileal loops distal to the lesion were distended and edematous. Various mesenteric lymph nodes were considered suspect for metastatic spread.

A resection of circa 80-90 cm of the small intestine, which included the neoplastic lesion, was performed, and an accurate superior mesenteric lymphadenectomy was performed (Fig. 6). Intestinal continuity was reestablished with a T-T single-layer anastomosis was constructed using interrupted sutures.

The patient's postoperative course was uneventful. On postoperative day 3 he passed flatus and on postoperative day 4 a stool. He was discharged on postoperative day 5.

On definitive histological examination the pigmented, vegetating, ulcerated formation that infiltrated the intestinal wall reaching the perivisceral fat, was shown to be a metastasis from melanoma (Fig. 6).

The resection margins and the lymph nodes removed from the superior mesenteric vein appeared to be tumor-free, but there were metastases in 2 of the 29 lymph nodes isolated from the peri-ileal fat.

After the definitive histological diagnosis the patient was referred to an oncologist and currently has no residual disease or disease recurrence.

## Discussion and conclusions

Malignant melanoma that involves the GI tract can be either a primary tumor or metastatic disease<sup>14</sup>.

Primary lesions can involve any part of the digestive tract, from the mouth to the anus. The presence of the proteins HMB45 and S-100 in the cancerous tissue is immunohistochemical confirmation of both primary and secondary melanoma<sup>16</sup>.

Usually cutaneous melanoma more than 1mm thick, located on the head or neck of a male, and associated with malignant lentigo, is at increased risk of metastasizing. On the other hand, if a lesion is less than 0.75 mm thick, survival at 5 years is over 90%<sup>15,17</sup>

Superficial melanoma, besides being the form of the disease most often found on the skin (76.2% of cutaneous melanomas), as shown in a study of 2302 patients, is also the histotype that most frequently metastasizes to the GI tract<sup>14,17</sup>.

Caputy reports that patients with GI metastases from melanoma present with weakness (63%), abdominal pain (56%), anorexia (46%), and intestinal obstruction (44%), and that only 20% have positive fecal occult blood tests<sup>10</sup>. Therefore if patients with a history of melanoma begin to have GI symptoms, visceral metastases should be suspected<sup>18</sup>.

Splenic metastases, often asymptomatic, are more difficult to identify but may be discovered as an incidental finding during follow-up of a primary tumor, if com-

plicated by splenic rupture, or in more extreme cases, at autopsy<sup>13,19</sup>. In the literature there are various cases of spontaneous splenic rupture due to metastases from melanoma<sup>13,20-22</sup>.

According to Klein et al, the presence of splenic metastases from melanoma is an indication of diffuse disease and therefore associated with a poor prognosis<sup>4</sup>. Schön and colleagues, after reviewing the results of all autopsies performed at their hospital between 1980 and 1999, confirmed that patients with splenic metastases from melanoma had a worse prognosis than those with metastatic melanoma involving other organs. They also noted that such metastases, besides being most commonly found in younger patients, had a significant association with synchronous metastases in multiple organs<sup>23</sup>.

The spleen can be the site of numerous pathological processes, and the differential diagnosis of splenic disease should be kept in mind. If there is any sign of alterations in the parenchyma of the spleen, the following pathologies should be taken into consideration: diseases such as mononucleosis, malaria, and typhoid fever, splenic infarction, haematological cancers and cancers of the hematopoietic organs, primary and secondary melanoma, and cancers of the lung, breast, uterus, ovary, and colon<sup>13</sup>.

Ultrasound imaging and CT scan (which has a sensitivity of 60-70%) are currently the techniques most commonly used to study primary melanoma and its metastases. However some authors report using MRI<sup>24,25</sup>.

In recent years the use of <sup>18</sup>F-FDG-PET in the diagnosis of melanoma has increased because of the capacity of metastatic cells to take up the radiotracer<sup>26,27</sup>.

In the literature ultrasound-guided fine needle aspiration has been reported to be a diagnostic method that is safe and can identify suspect lesions with a great degree of accuracy<sup>28</sup>.

Immunoscintigraphy, however, appears to have a field of application limited to the study of lymph node metastases for which it has high diagnostic accuracy<sup>29</sup>.

Due to the frequent coexistence of metastases from melanoma in multiple sites in the viscera, as reported by Klein, and Schön, and again by Kamaya in 2006, there is some doubt as to the curative effect of surgical therapy<sup>4, 23,30</sup>.

It has been reported in the literature that average survival for patients who underwent complete resection of visceral metastases from melanoma is 48.9 months, compared to 5.4 months after palliative surgery and 5.4 months after non-surgical procedures<sup>18,25</sup>.

Ollila found that 5-year survival after complete resection of GI metastases was high<sup>25</sup>.

Ricaniades reports that a patient survived 27.6 years after complete removal of a single metastasis from melanoma to the GI tract.

It therefore seems clear that surgical intervention in patients with metastases from melanoma to one or more organs is always justified provided it is possible to perform a complete resection<sup>13</sup>.

In fact, in the literature, there is no dearth of cases of patients with multiorgan disease, treated with ample surgical demolition, who had good survival rates, and remained disease-free.

Mukaiya, in 1999, described a patient who was still disease-free 5 months after total pancreatectomy, right adrenalectomy, and retropancreatic lymphadenectomy performed to treat metastases from a primary melanoma of the distal esophagus which had been surgically treated 2 years previously<sup>32</sup>.

Belágyi, when he reports the case of a young woman who died 4 months after multiorgan resection (right ovary, jejunum, stomach, pancreas) for metastases from cutaneous melanoma, asserts that radiofrequency ablation of synchronous metastases in multiple organs is associated with survival rates similar to those after radical surgery for metastases involving only one organ. He notes that after incomplete resection of metastases from melanoma, survival rates are, on the contrary, the same as those of patients who did not undergo surgery<sup>33</sup>.

From what has been said so far it appears that non-curative surgery should only be considered if required to prevent dramatic situations such as intestinal occlusion or perforation, bleeding, hemoperitoneum due to rupture of the liver or the spleen, or if needed for palliative care<sup>13</sup>.

However Petit, in 1996, reported that incomplete resection of metastases from melanoma can notably improve survival if associated with adequate systemic therapy<sup>34</sup>.

In conclusion, since the prognosis of patients suffering from metastatic melanoma is closely linked to radical resection, only early diagnosis of metastases, by means of an accurate and multidisciplinary follow-up, can, in our opinion, increase the number patients who are good candidates for curative resection, instead of for palliative surgery or systemic therapy.

## Riassunto

Il melanoma cutaneo si localizza per il 15 % dei casi al capo ed al collo, per 22% agli arti, per il 40% al tronco, e per il 16% in siti sconosciuti.

In genere intercorre un periodo di almeno 3 anni dalla diagnosi di melanoma primitivo all'individuazione delle lesioni secondarie.

Il melanoma primitivo metastatizza più frequentemente ai linfonodi (73,6%) ed ai polmoni (71,3%).

Il piccolo intestino e la milza rappresentano rispettivamente il 36,5% ed il 30,6% delle localizzazioni gastroenteriche.

I casi clinici riportati mostrano l'incidenza di una resezione radicale sui tassi di sopravvivenza.

I risultati ottenuti suggeriscono l'importanza di un follow-up attento e multidisciplinare; solo quest'ultimo infatti può individuare le localizzazioni secondarie quando sono ancora candidabili alla chirurgia curativa.

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