

Unusual Metastatic Site - Peritoneal Metastasis in Malignant Melanoma: Case Report

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Sítio Metastático Incomum - Metástases Peritoneais em Melanoma Maligno: Relato de Caso Sitio Metastático Raro - Metástasis Peritoneales en Melanoma Maligno: Reporte de Caso

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ABSTRACT

Introduction: Cutaneous melanoma is a tumor with great capacity for metastasis. One of the possible but quite rare scenarios is when the metastasis is lodged in the peritoneum (peritoneal carcinomatosis). **Case report:** 61-year-old female patient, referred by a suspected left inguinal mass and 2 cm hyperchromic lesion, with regression area in the left lower limb. The patient underwent left inguinal lymphadenectomy and resection of the skin lesion, which revealed invasive extensive superficial cutaneous malignant melanoma, Breslow depth 1.2 mm and Clark II level, as well as lymph node metastasis. Adjuvant treatment included radiotherapy and chemotherapy. During follow-up, 8 months later, abdominal ultrasound and computed tomography showed hypoechoic, heterogeneous, and beveled solid nodular image, poorly defined and delimited in left para-aortic projection, with 12.7x6.7x4.8 cm. In exploratory laparotomy, a large retroperitoneal mass was found on the left flank, involving the Treitz angle, and revealed the presence of peritoneal carcinomatosis. The anatomopathological report showed a poorly differentiated malignant infiltrative epithelioid neoplasm, compatible with the clinical history of melanoma. The patient died after consultation with clinical oncology. **Conclusion:** There are few cases of peritoneal metastasis of melanoma reported in the literature. However, its possibility of occurrence and the therapeutic options available must be taken into account, in addition to understanding its impact on the patient's prognosis. Although rare, peritoneal carcinomatosis should be considered when patients with a personal history of melanoma have non-specific abdominal complaints, such as the patient in the case reported.

Key words: Melanoma; Peritoneum; Neoplasm Metastasis; Peritoneal Neoplasms.

RESUMO

Introdução: O melanoma cutâneo é um tumor com grande capacidade de metastização. Um dos quadros possíveis, mas bastante raro, é quando a metástase se aloja em peritônio (carcinomatose peritoneal). **Relato do caso:** Paciente feminina, 61 anos, encaminhada por massa inguinal esquerda suspeita e lesão hipercrômica de 2 cm, com área de regressão em membro inferior esquerdo. A paciente foi submetida à linfadenectomia inguinal esquerda e ressecção da lesão de pele, que evidenciou melanoma maligno cutâneo extensivo superficial invasor, de espessura de Breslow 1,2 mm, e nível de Clark II, bem como metástase linfonodal. O tratamento adjuvante incluiu radioterapia e quimioterapia. Durante *follow-up*, oito meses depois, ultrassonografia e tomografia computadorizada de abdome evidenciaram imagem nodular sólida hipocóica, heterogênea e bosselada, mal definida e mal delimitada em projeção para-aórtica à esquerda, com 12,7x6,7x4,8 cm. Em laparotomia exploradora, encontrou-se massa volumosa retroperitoneal em flanco esquerdo, com envolvimento do ângulo de Treitz e presença de carcinomatose peritoneal. O laudo anatomopatológico evidenciou neoplasia maligna pouco diferenciada epitelióide infiltrativa, compatível com história clínica de melanoma. A paciente evoluiu a óbito após consulta com oncologia clínica. **Conclusão:** Existem poucos casos de metástase peritoneal de melanoma relatados na literatura. Contudo, deve-se levar em consideração sua possibilidade de ocorrência e as opções terapêuticas disponíveis, além de também compreender seu impacto no prognóstico do paciente. Apesar de rara, a carcinomatose peritoneal deve ser considerada quando pacientes com histórico pessoal de melanoma apresentarem queixas abdominais inespecíficas, como a paciente do caso relatado.

Palavras-chave: Melanoma; Peritônio; Metástase Neoplásica; Neoplasias Peritoneais.

RESUMEN

Introducción: El melanoma cutáneo es un tumor con gran capacidad de metástasis. Una de las situaciones posibles, pero bastante rara, es cuando la metástasis se aloja en el peritoneo. **Relato del caso:** paciente femenina de 61 años, remitida por sospecha de masa inguinal izquierda y lesión hipercrômica de 2 cm, con área de regresión, en miembro inferior izquierdo. La paciente fue sometida a linfadenectomía inguinal izquierda y resección de la lesión cutánea, que demostró melanoma maligno cutáneo superficial extenso invasivo, Breslow 1,2 mm y nivel de Clark II, así como metástasis ganglionares. El tratamiento adyuvante incluyó radioterapia y quimioterapia. Durante el seguimiento, 8 meses después, la ecografía y la tomografía computarizada de abdomen mostraron una imagen nodular sólida hipocóica, heterogênea y biselada, mal definida y delimitada en proyección para-aórtica izquierda, con 12,7x6,7x4,8 cm. En la laparotomía exploradora se encontró una gran masa retroperitoneal en el flanco izquierdo, involucrando el ángulo de Treitz y presencia de carcinomatosis peritoneal. El informe anatomopatológico mostró una neoplasia epitelióide infiltrativa maligna mal diferenciada, compatible con la historia clínica de melanoma. El paciente falleció tras consulta con oncología clínica. **Conclusión:** Hay pocos casos de metástasis peritoneal de melanoma reportados en la literatura. Sin embargo, se debe tener en cuenta su posibilidad de ocurrencia y las opciones terapéuticas disponibles, además de comprender su impacto en el pronóstico del paciente. Aunque es poco común, la carcinomatosis peritoneal debe considerarse cuando los pacientes con antecedentes personales de melanoma tienen molestias abdominales inespecíficas, como la paciente del caso.

Palabras clave: Melanoma; Peritoneo; Metástasis de la Neoplasia; Neoplasias Peritoneales.

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INTRODUCTION

Cutaneous malignant melanoma is an aggressive cancer able to metastasize rapidly. The systemic spread of the disease can be direct, lymphatic or hematogenous¹. Peritoneal implants resulting from extra-abdominal primary neoplasms are uncommon and account for approximately 10% of the cases of peritoneal metastasis as breast cancer (41% of the cases), lung cancer (21%) and malignant melanoma (9%)².

In the population-based study of Flanagan et al.³, 9.4% (n=543) of the patients with peritoneal metastases had extra-abdominal primary neoplasm and the primary tumor was melanoma for 9.3% of them. Of the total population, only 0.5% had melanoma with diagnosis of peritoneal implants, 75% were males and more than 82% were diagnosed with peritoneal metastases after the diagnosis of primary cancer. The subtype nodular was the most common in this study (29%)³.

Few cases are reported in the literature. Lee et al.⁴ described a case of late recurrence of the tumor as peritoneal carcinomatosis⁴ in a patient after ten years of diagnosis and excision of the melanoma. McBride and Calhoun⁵ presented a case of anorectal melanoma which developed extensive peritoneal metastases.

A case of a patient with cutaneous melanoma who initially presented with inguinal lymphadenomegaly and later evolved with retroperitoneal metastases and peritoneal carcinomatosis is reported in this article.

CASE REPORT

Female, 61 years old patient, referred from a reference oncology service by suspected neoplasm due to upper left inguinal mass in evolution for three months. Inguinal ultrasound (US) of soft parts was performed in the origin and revealed heterogenous solid nodular lesion with associated cystic masses measuring nearly 6x4.5x4.4 cm. At palpation, the inguinal mass revealed lymphadenomegaly with approximately 7cm in the anteromedial portion of the left thigh and another smaller of 2 cm.

The patient had hyperchromic cutaneous lesion with regression area of approximately 2 cm, compatible with melanoma in posterolateral portion of the left lower limb, referring change of pattern in the last two months.

Denied alcohol, tobacco use and family history of neoplasm. Her personal background revealed systemic arterial hypertension. Resection of the skin lesion with local anesthetic and rotation of the local flap was performed without complications.

The anatomopathological analysis of the piece showed invasive superficial extensive malignant melanoma,

Breslow thickness 1.2 mm and Clark level II. No intra and peritumoral infiltrates or ulcerations and satellitosis were encountered and the surgical borders were neoplasm-free.

Computed tomography (CT) of head, abdomen and chest without particularities. No significant increase of the tumoral markers carcinoembryonic antigen (CEA) and lactate dehydrogenase (LDH). At that time, the staging was pT4N3MX (EC III). It was decided to perform left inguinal lymphadenectomy that showed extensive invasive necrotic metastatic melanoma in three lymph nodes of the six removed. The patient was referred for chemotherapy with 12 cycles of interferon and radiotherapy with 48Gy dose in left inguinal region.

During follow-up, the patient complained of strong intensity epigastric pain. Abdominal ultrasound revealed heterogeneous hypoechoic nodular image measuring nearly 3.9x2.2 cm in paraaortic retroperitoneal projection at left. Abdominal CT did not show abnormalities and follow-up proceeded.

Another abdominal ultrasound performed eight months after the first showed heterogeneous, hypoechoic, solid, nodular, bosselated poorly defined and delimited image measuring 12.7x6.7x4.8 cm in paraaortic projection at left without well-defined cleavage plane with the inferior border of pancreatic tail and with part of the enterocolic loops (Figure 1).

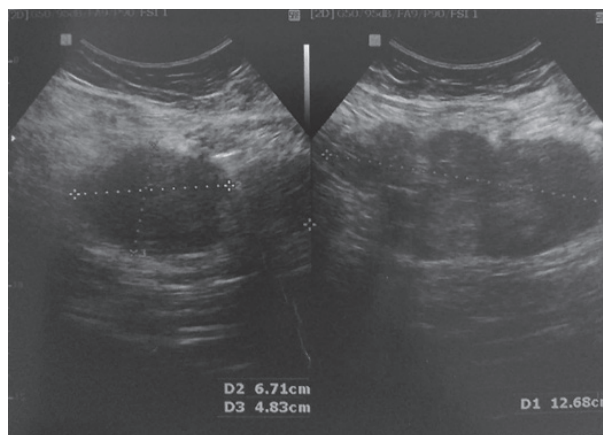
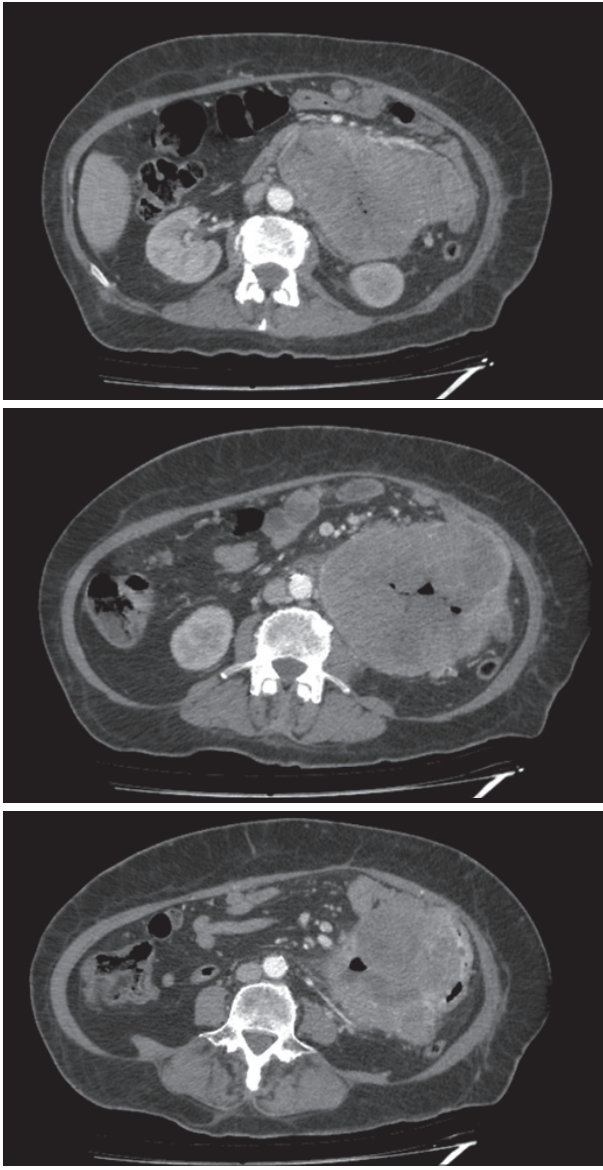


Figure 1. Ultrasound of abdomen showing lesion in paraaortic projection at left without well-defined cleavage plane with the inferior border of pancreatic tail and with part of the enterocolic loops

The investigation was complemented with CT of total abdomen with contrast showing heterogeneous invasive lesion with heterogeneous enhancement, measuring 9.7x6.7x6.4 cm, with ample communication with small intestine loops, not being possible to exclude primary lesion (Figures 2, 3 and 4). Head and chest CT within normality. Exploratory laparotomy was the therapeutic plan.



Figures 2, 3 e 4. Abdominal computed tomography with contrast showing extensive lesion in projection to the left paraaortic.

Intraoperative, a bulky retroperitoneal mass at the left flank, with involvement of the Treitz angle and presence of peritoneal carcinomatosis (Figure 5). Epiploon and peritoneum biopsies and gastroenteroanastomosis were conducted.

The anatomopathological report of the biopsies showed poorly differentiated infiltrative epithelioid malignant neoplasm compatible with melanoma clinical history. The patient received upstaging (T4N3M1, EC IV) and was referred to clinical oncology. The therapeutic plan was the novel palliative chemotherapy regimen with 12 cycles of DTIC (dacarbazine). The patient did not follow the proposed regimen and died 20 days after the consultation with clinical oncology.



Figure 5. Peritoneal implants evidenced during the surgery

The Institutional Review Board of “Hospital e Maternidade Angelina Caron” of Paraná approved the study, report number 4.304.361 dated September 28, 2020 (CAAE 38271120.0.0000.5226).

DISCUSSION

Malignant melanoma is an aggressive neoplasm with high metastatic potential that arises from melanocytes, may occur in several sites but is more typical in the skin⁶. Most common metastatic sites are lung, liver, lymph nodes, brain and meninges and gastrointestinal tract⁶.

The study of Flanagan et al.³ reported that the nodular melanoma was the subtype that most typically developed peritoneal implants³. The patient of this case had superficial extensive melanoma which, according to the authors³, would be a subtype with little propensity to develop peritoneal metastasis.

The term peritoneal carcinomatosis generally refers to metastatic involvement of the peritoneum and it often occurs in gastrointestinal or gynecological malignancies of advanced stages with locoregional involvement. Metastatic peritoneal involvement arising from extra-abdominal primary tumors is uncommon⁴. In despite of this, Lee et al.⁶ described a case of peritoneal carcinomatosis originated from a melanoma of a 22-years old patient.

Hematogenous spread is the most common in the case of peritoneal carcinomatosis by melanoma, lung and breast cancer².

In general, patients with peritoneal metastases are at advanced stages of the disease². Flanagan et al.³ reported that the mean global survival of patients with melanoma diagnosed with peritoneal implants was 1.8 months (0-99.3), while mean global survival in the group of patients with stage IV but without peritoneal compromise was 12.3 months³.

The two most important clinical findings of the presence of peritoneal implants are ascites and bowel obstruction,

however they are found in less than 50% of the patients. Another important sign is the presence of neoplastic cells in the ascitic fluid². The patient presented strong intensity epigastric pain, being a variant of the clinical findings that are commonly related to peritoneal disease.

Typically, this involvement is often an incidental finding detected during surgical exploration or in diagnostic imaging of as CT scan or magnetic resonance (MRI). Biopsy of suspected lesions is a confirmatory test to identify the type of cancer cells and to differentiate from possible conditions and primary peritoneal tumors as lymphomatosis, tuberculosis, peritoneal pseudomyxoma, sarcomatosis and mesothelioma^{2,5}.

It is important to conduct a proper investigation in case of peritoneal metastases which becomes one of the absolute contraindications for surgery with curative intent. In addition, it is essential to determine the extent, size and major organs involvement by metastatic cancer to evaluate the prognosis of the patient².

Sometimes, neoplastic lesions are visible in CT, MR and 18F-fluorodeoxyglucose (FDG) positron emission tomography PET/CT. The findings include focal or diffuse thickening of the peritoneal folds which could appear as sclerotic, nodular, reticular, reticulonodular, or large plaque-like structures. Occasionally a large, thick layer density would be visible between the abdominal wall and bowel loops, a structure called "omental cake"².

MR does not show any superiority over CT scan to detect peritoneal carcinomatosis. PET/CT detects the presence of cancer lesions based on the glucose uptake of the cells with great accuracy. Diagnosis laparoscopy is useful for peritoneal metastasis since it can avoid unnecessary laparotomy despite many surgeons fear port-site tumor recurrence in the trocar insertion site².

In this context, the non-appearance of peritoneal implants in abdominal CT in the follow up is justified by the limitation of the exam when this type of neoplasm is localized, that is, there is little sensitivity when the neoplastic site is small. Thus, the diagnosis of peritoneal carcinomatosis is complex and the golden standard is the direct visualization of the peritoneum through laparotomy or laparoscopy⁷.

Systemic chemotherapy is the golden-standard of therapy for patients with remote metastasis resulting from melanoma and dacarbazine is the chemotherapeutic most used even with mean response rate of barely 15%^{6,8}. Combined chemotherapies can increase the response rate when compared with monotherapy with dacarbazine, however, they do not increase the patients' survival and are associated with higher toxicity. High doses of interleukin-2 or interferon- α -2b can be used too in the treatment of metastatic melanoma⁶.

In a setting of advanced disease, immunotherapy with nivolumab (anti-PD1), ipilimumab (anti-CTLA4) and pembrolizumab (anti-PD1) can be used to treat patients and target-therapies as dabrafenib, trametinib and vemurafenib^{9,10} in the case of BRAF mutated. However, due to the high cost, its use is limited. Within a context of peritoneal carcinomatosis of malignant melanoma, the effects of nivolumab associated with surgical cytoreduction were investigated in animal model. In the nivolumab group, peritoneal carcinomatosis index (PCI) was significantly lower and higher lymphocytic response, lower tumor size and quantity of nodes and lower grading score of peritoneal regression (higher rate of complete response to the treatment). Therefore, the treatment with nivolumab in a scenario of metastatic malignant neoplasm becomes a promising option⁸. The guideline of the National Comprehensive Cancer Network (NCCN)¹⁰ updated in 2020 brings monotherapy with anti-PD1 agents and target-therapies for BRAF as first line therapy in cases of metastatic or irresectable disease¹⁰.

CONCLUSION

Peritoneal carcinomatosis is one of the most uncommon metastatic sites of malignant cutaneous melanoma with few cases reported in the literature. However, it should be considered its possibility of occurrence and the therapeutic options available in addition to understanding its impact in the prognosis of the patient. Although rare, peritoneal carcinomatosis should be pondered when patients with personal history of malignant melanoma claim they have unspecific abdominal complaints as the patient of the case reported.

CONTRIBUTIONS

Amanda da Silva Anjos and Diego Carvalho Duarte Mari contributed for the study conception and/or design, collection, analysis and interpretation of the data, wording and critical review with intellectual contribution. Bárbara Urnau Sfreddo contributed for the wording and critical review with intellectual contribution. Brenno Giovanni Hernando Vidotti, Maikele Ertel and John Carlos Claros Terraza contributed for the critical review with intellectual contribution. All the authors approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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