HOSPITAL DE CLÍNICAS DE PORTO ALEGRE
SERVIÇO DE GASTROENTEROLOGIA
TRABALHO DE CONCLUSÃO DE RESIDÊNCIA MÉDICA

METASTATIC MELANOMA WITH DISSEMINATED INVOLVEMENT OF THE GASTROINTESTINAL TRACT IN A IMMUNOCOMPROMISED PATIENT: A CASE REPORT

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FEVEREIRO, 2023

CIP - Catalogação na Publicação

DALLAGNOL, MARCELO KLOTZ
Metastatic Melanoma with disseminated involvement of the Gastro-intestinal Tract in a immunocompromised patient: a Case Report / MARCELO KLOTZ DALLAGNOL. -- 2023.
6 f.
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Trabalho de conclusão de curso (Especialização) -- Universidade Federal do Rio Grande do Sul, Hospital de Clínicas de Porto Alegre, RESIDÊNCIA MÉDICA - GASTROENTEROLOGIA, Porto Alegre, BR-RS, 2023.

1. Melanoma. 2. Metastatic Melanoma. 3. GI tract. 4. Gastrointestinal tract. 5. Immunocompromised. I. BREYER, HELENICE PANKOWSKI, orient. II. Título.

Elaborada pelo Sistema de Geração Automática de Ficha Catalográfica da UFRGS com os dados fornecidos pelo(a) autor(a).

ABSTRACT

Malignant Melanoma is an epithelial cancer that arises from melanocytes, which can be found in tissues like skin (91%), eye (5%), and mucous membranes - oral cavity, nasopharynx, anus, urinary tract and even the gastrointestinal tract (3-4%). It is the fifth most common cancer worldwide, with an increase of incidence in the past two decades, while the mortality rate remains stable.

Metastatic intestinal melanoma is seen in around 60% of patients who die from the disease. Although, only 1.5 - 4.4% are detected before death. The clinical presentation is extremely variable, with most patients being asymptomatic. Abdominal pain, GI bleeding, anemia and GI obstruction (including intussusception) are the most common symptoms. Altered bowel habits, fatigue, weight loss, dysphagia and abdominal mass can also occur.

One case of disseminated GI metastatic melanoma was reported after a patient developed colitis secondary to an immune checkpoint inhibitors (IPCIs) treatment. The patient was treated with high dose corticosteroids, along with Vedolizumab (an anti-integrin of T-lymphocytes on endothelial cells, reducing gut inflammation and, ultimately, suppressing only the gut immune-system). Although otherwise feasible in solid organ transplantation, no patient with that load of metastatic melanoma has been described so far.

KEYWORDS: Melanoma; Metastatic Melanoma; GI tract; Gastrointestinal tract; Immunocompromised

INTRODUCTION

Malignant Melanoma is an epithelial cancer that arises from melanocytes, which can be found in tissues like skin (91%), eye (5%), and mucous membranes - oral cavity, nasopharynx, anus, urinary tract and even the gastrointestinal tract (3-4%). It is the fifth most common cancer worldwide, with an increase of incidence in the past two decades, while the mortality rate remains stable. In autopsy series, the most common site of metastasis are the lymph nodes and lungs, followed by the GI tract (including the liver). We report a case of diffuse metastatic melanoma, particularly to the GI tract, in a immunocompromised patient.

CASE REPORT

A 37 year-old white male with a history of kidney transplant in 2009 (cryptogenic end-stage renal disease) in use of Tacrolimus, Azathioprine and Prednisone, along with a *in situ* cutaneous melanoma localized in the left subescapular region - completely removed in 2021 - presents in the emergency room with aqueous diarrhea, nausea, vomiting and fever. Physical examination shows hyperpigmentation in upper and lower gingiva, a conglomerate of 2-2,5cm wide right axillary lymph nodes and an innocent abdomen. Laboratory finds show pancytopenia, a stable kidney function - basal Creatinine ~4 - and negative results of stool culture, Clostridioides difficile toxins A and B and serum PCR for Cytomegalovirus. Chest CT shows a slight bilateral pleural effusion and right axillary lymph nodes, and abdomen CT shows a 6 centimeter hypodense lesion in the liver. Upper endoscopy and Colonoscopy showing innumerous slightly elevated 5mm black mucosal lesions in the esophagus, stomach, duodenum, rectum and all colonic segments consistent with haematogenic dissemination of melanocytic malignant cells. Lymph node, gingiva lesions, bone-marrow and GI tract biopsies confirm the diagnosis of Metastatic Melanoma.

DISCUSSION

The GI-tract is the second most common site of metastasis. The liver is the preferred site (58.3 - 68%), followed by the small bowel (35,6 - 58%), colon and rectum (22 - 33%), stomach (22.7 - 20%), esophagus (4 - 9.3%), biliary tract (1 - 8.8%) and anus (1%). In the GI-tract, the most common presentation is the metastatic disease, although the primary one can rarely occur - it is thought that primary intestinal melanomas derive from melanoblastic cells of the neural crest which migrate via the omphalomesenteric canal to the distal ileum. To diagnose a primary melanoma, it has to fulfill all the following criteria: (1) a solitary lesion, (2) an intraluminal mass with no other metastasis, (3) no evidence of disease in any other organs and no history of previous melanoma, and (4) disease-free survival period of 12 months after resection without any evidence of recurrence. The use of immunohistochemistry is cardinal in the diagnosis of primary and metastatic melanoma of the GI-tract. The expression of S-100, HMB-45, Melan A and MITF are the most used markers.

Metastatic intestinal melanoma is seen in around 60% of patients who die from the disease. Although, only 1.5 - 4.4% are detected before death. The most common type of cutaneous melanoma to metastasise to the small intestine are the Superficial Spreading (70-80%), while it is important to emphasize that any cutaneous type can do so. Around half of the patients presented with metastatic intestinal melanoma have another concomitant site with a metastatic lesion. The diagnosis of the intestinal metastasis can be presented and the time of diagnosis of melanoma or within a 6-month interval, although it typically develops 3-6 years after the excision of the primary cutaneous melanoma.

The risk of metastatic melanoma is directly associated with the tumor thickness (Breslow). Tumors with <1mm has been described at low risk - but still able to produce metastasis - with a longer interval of time between primary resection and diagnosis of the metastasis - 120.9 months; while tumors with 4mm are at high risk, with a shorter interval of 36.9 months.

The clinical presentation is extremely variable, with most patients being asymptomatic. Abdominal pain, GI bleeding, anemia and GI obstruction (including intussusception) are the most common symptoms. Altered bowel habits, fatigue,

weight loss, dysphagia and abdominal mass can also occur. Bowel perforation is rare and protein-losing enteropathy has been described.

The diagnostic tools evolved in the last few decades. Standard CT scan is probably the most available imaging method that can diagnose metastasis of melanoma, once US has its limitations, specially in the GI-tract. Nonetheless, CT scan has a sensitivity of only 60-70% to diagnose metastasis. The use of CT enteroclysis and whole-body PET-CT has increased the accuracy of this method. The definitive diagnosis of this neoplasia is histopathologic. Then, upper endoscopy and colonoscopy are the preferred methods to assess - at least initially - the GI-tract and to collect biopsies. If no lesions can be detected by these methods, the use of video capsule endoscopy (VCE) is probably the first step to evaluate the small bowel, being the single or double-balloon enteroscopy reserved to the patients who have a lesion detected in VCE.

Following the clinical presentation, the endoscopic presentation is also variable. In general, primary lesions are unifocal, while metastatic lesions - which spread are haematogenic - are multifocal. The type of the lesion can be submucosa-like or primary carcinoma-like tumors, being cavitary/ulcerated, infiltrating, exophytic/exoenteric and polypoid. Amelanotic lesions have been described, with some case series reporting these to be the majority of the lesions.

Resection of the primary or metastatic lesion or lesions, if feasible, is the treatment of choice. The excision must have sufficient free proximal and distal margins, aside with the removal of the mesentery and its respective lymph nodes. Surgery is responsible for symptomatic relief and a higher median survival - 28.5 to 48.9 months compared with 5.4 to 8.9 months in those undergoing palliative or nonsurgical interventions.

While conventional chemotherapy is not largely used for the treatment of Malignant Melanoma because of its low response, with the invention of the immune checkpoint inhibitors (IPCIs) and targeted BRAF/MEK inhibitors (BRAFi/MEKi), particularly after 2011, the prognostic of Malignant Melanoma has become better. The landmark clinical trial CheckMate-067 has proven that the combination of Ipilimumab and Nivolumab was superior to either one alone for advanced melanoma. Indeed, at this time, many drugs and their combinations have been studied.

The immunotherapy era revolutionized the treatment of advanced melanoma and significantly improved its survival. However, it is not well described which one is the best treatment for metastatic melanoma of the GI-tract.

There are several side effects of these therapies, being the most common adverse events were colitis, hepatitis, adrenocorticotropic hormone insufficiency, and hypothyroidism, followed by type 1 diabetes, acute kidney injury, and myocarditis. Skin, rheumatic toxicity and pneumonitis have also been reported.

One case of disseminated GI metastatic melanoma was reported after a patient developed colitis secondary to an IPCIs treatment. The patient was treated with high dose corticosteroids, along with Vedolizumab (an anti-integrin of T-lymphocytes on endothelial cells, reducing gut inflammation and, ultimately, suppressing only the gut immune-system). Although otherwise feasible in solid organ transplantation, no patient with that load of metastatic melanoma has been described so far.

CONCLUSION

This case report shows that in immunocompromised individuals with melanoma, a high-suspicious of metastatic dissemination need to be considered independently of the “low risk” status of the primary (often cutaneous) lesion. That said, the GI-tract must always be considered as a potential site, once it is one of the most common sites of metastatic disease.

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