



Malignant Melanoma Mestastatic to the Small Intestine, is it Possible? A Case Report



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Abstract

Malignant melanoma (MM) is a tumor that originates in melanocytes. Although its most frequent location is the skin, it can also compromise the gastrointestinal tract (GIT) [1]; this being the third most common site of distant metastases and the small intestine (SI) the most frequent location [2,3]. The clinical presentation of these cases is usually nonspecific and can range from abdominal pain to intussusception and intestinal obstruction [1,4]. For the detection of gastrointestinal (GI) metastases, whole-body PET with fluorodeoxyglucose (FDG PET) has higher sensitivity (74%) and specificity (86%) [5], with histological and immunohistochemical confirmation.

Next, we will describe the case of a 49-year-old male patient, with a history of cutaneous MM in the left paranasal region PT4N0M0 EC IIC, resected in December 2018, without subsequent controls; that he underwent surgery for intestinal obstruction, finding three tumors in the ileum; with histological and immunohistochemical confirmation of metastatic MM.

Keywords: Malignant melanoma; Small intestine; Intestinal obstruction

Abbreviations: MM: Malignant Melanoma; GIT: Gastrointestinal Tract; SI: Small Intestine; GI: Gastrointestinal; FDG PET: Fluorodeoxyglucose; CT: Contrast-Enhanced Tomography; PET-CT: Positron Emission Tomography; CT: Tomography

Introduction

Malignant melanoma (MM) is a tumor that originates in melanocytes, cells derived from the neural crest [4] and located in all body tissues, which explains why it can originate in any organ. Although its most frequent location is the skin, it can also compromise the gastrointestinal tract (GIT) [1]. Worldwide, it is estimated that 324,635 people were diagnosed with MM in 2020. The most frequent age of presentation is 65 years, however, in 2020, 2,400 cases of MM were diagnosed in patients between 15 and 29 years of age, therefore, this tumor can appear at any stage of life [6].

GIT melanoma can be primary or metastatic. In most cases, they are secondary lesions of a primary cancer, generally originating in the skin, anus, rectum, or eyes [7,8]. Only a small proportion

of patients (2-5%) can be diagnosed with GIT metastases during life, thus being a rare clinical entity. The definitive diagnosis is by histological and immunohistochemical study and the treatment of choice is surgical in cases of localized lesions [2,8].

Below, we present the case of a patient with metastatic malignant melanoma to the small intestine (SI) with histological and immunohistochemical confirmation.

Clinical Case

A 49-year-old male patient, from Trujillo, with a history of cutaneous MM in the left paranasal region PT4N0M0 EC IIC with free edges, resected in December 2018, without subsequent check-ups.

Patient with a disease time of 12 months of evolution, who presented changes in evacuation frequency, 1 time every 2 to 3 days. Two months before admission, she had intermittent colicky abdominal pain in the mesogastric region, which was partially relieved by taking analgesics and had no association with food intake; For this reason, she went to a private doctor, who requested an abdominal ultrasound in which an intestinal loop with a thickened wall of up to 6 mm was evident, in an extension of 57 mm at the level of the right iliac fossa.

Contrast-enhanced tomography (CT) of the abdomen and pelvis revealed a 30x30x40mm solid nodule in the gastrocolic ligament and at the level of the mid-ileum, presence of intussusception and a 31mm contrast-enhancing polyp.

In addition, an upper digestive endoscopy was performed, in which an ulcerated lesion with raised edges, with a friable glandular appearance on biopsy, was evidenced at 3cm from the duodenal papilla (Figure 1). Concluding as an ulcerated lesion in the duodenum: to rule out Crohn's disease versus Tuberculosis. The patient went to the emergency department of the "Virgen de la Puerta" High Complexity Hospital due to intensification of abdominal pain associated with asthenia and hyporexia and weight loss of 12kg in 2 months, being hospitalized for study.

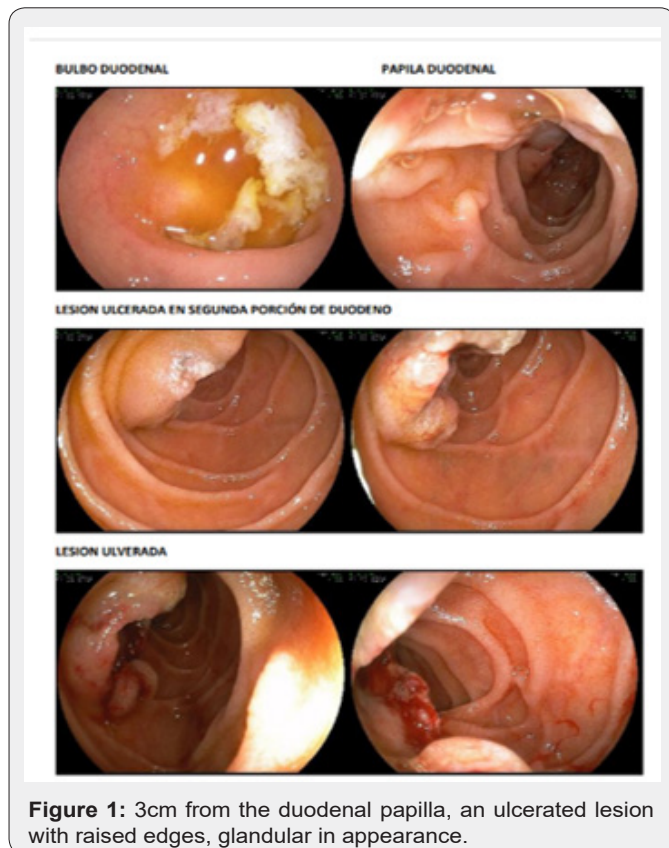


Figure 1: 3cm from the duodenal papilla, an ulcerated lesion with raised edges, glandular in appearance.

On physical examination, the patient presented marked pallor ++/+++ , moist oral mucosa. At the abdominal level, air-fluid noises present, soft, depressible, pain on deep palpation at the level of

the epigastrium and mesogastrium, increased tympanism. During the valsalva maneuver in the left inguinal region, a reducible mass was palpable.

The analysis showed Hemoglobin: 7.1g/dl (12.5 – 16), VCM: 54.2 fl (80-100), MCH: 15.2 pg (45), MCH: 28%, PQ: 755,000/mm³ (150,000-450,000), PT: 16.5sec (10-15), INR: 1.46 (0.8-1.10), Serum albumin: 4.19g/dl (3.4-4.8), PCR: 109.7, Creatinine: 1.10mg/dl (0.6-1.1), urea: 41mg/dl (10-50), glucose: 178mg/dl (70-110). Two days after hospitalization, the patient presented fecaloid vomit. On examination, a distended abdomen was found, decreased air-fluid noises, and pain on superficial palpation. Plain abdominal X-ray standing showed dilation of thin intestinal loops and the presence of air-fluid levels (Figure 2). Patient was evaluated for general surgery and scheduled for exploratory laparotomy; In the surgical findings, they reported three tumors: one in the distal ileum, 30cm from the ileocecal valve, causing obstruction and intussusception of the proximal loop, and two located at 70 and 250cm from the proximal end of approximately 30x20mm.



Figure 2: Signs of intestinal obstruction.

With the endoscopic and surgical findings, it was initially considered to rule out Crohn's disease versus tuberculosis; studies were complemented with BK in feces and sputum; with negative results. In addition, contrast-enhanced CT of the abdomen and pelvis was performed post-surgery and reported diffuse thickening of jejunal and ileal loops with fluid content and mesenteric adenopathies with contrast enhancement measuring up to 10mm. The histopathological study of the ulcerated lesion of the duodenum revealed a malignant neoplasm compatible with a poorly differentiated adenocarcinoma and the ileum tumor

compatible with a poorly differentiated malignant neoplasm that compromised the entire intestinal wall, even perforating its serosa (Figure 3). In addition, the presence of atypical melanocytic cells could be observed (Figure 4).

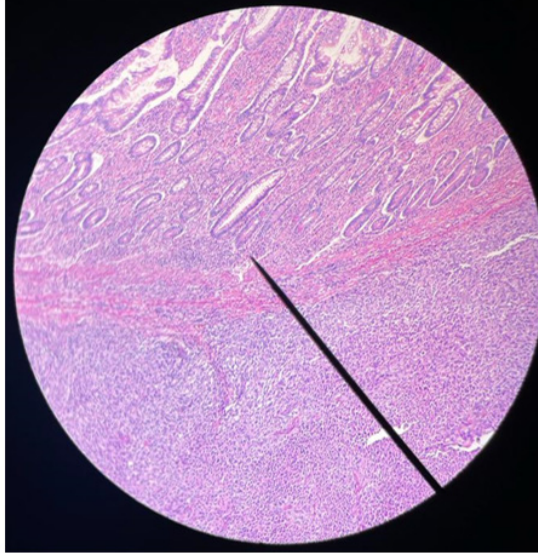


Figure 3: In a field of lower magnification (4x) analyzed in Hematoxylin-Eosin staining, a poorly differentiated malignant neoplasm infiltrated up to the muscular layer of the intestinal wall is observed.

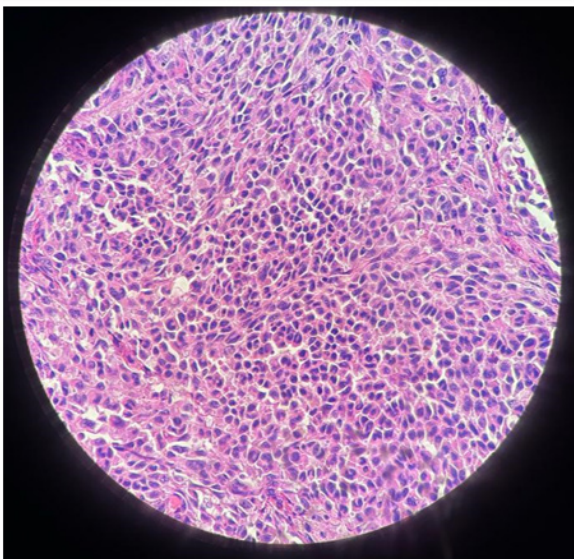


Figure 4: At higher magnification, a cell population of cells with an atypical melanocytic appearance is observed.

Immunohistochemistry of the duodenal lesion and those of the ileum were positive for S100 AND MELAN A, confirming the diagnosis of metastatic MM to the small intestine (Figure 5). The patient was evaluated by oncological surgery and medical oncology, indicating metastatic MM CD IV amenable to first-line immunotherapy with Nivolumab.

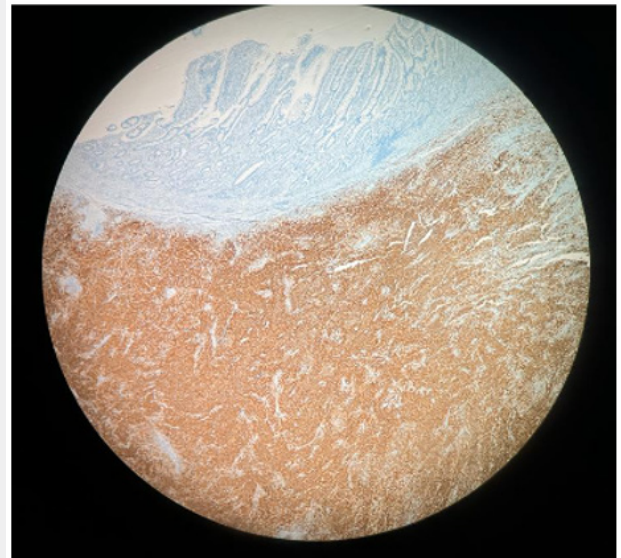


Figure 5: MELAN A positive in melanoma.

Discussion

The GIT is the third most common site of distant metastasis of MM. The stomach, small intestine, rectum, and colon may be affected; ID being the most frequent location of metastasis [2,3]. 60% of patients with gastrointestinal (GI) metastases are not diagnosed during their lives and only 5-6% of patients are diagnosed due to the different complications that occur [8-10].

The clinical presentation of these cases is usually non-specific, with abdominal pain, weight loss, anorexia, nausea and vomiting being the most common symptoms [10]. Melaena, anemia, intussusception, and clinically relevant intestinal obstruction are rarely seen in adults [1,4]. In our case report, the patient presented changes in bowel movement frequency, anemia due to occult intestinal bleeding, among other non-specific symptoms that gradually progressed to a picture of intestinal obstruction due to intussusception. Among the causes of intestinal obstruction in adults, intussusception represents only 1%, being more frequent in childhood. 90% of the cases of intussusception in adults are generally due to neoplasms [6]. Of these, 85% are benign tumors and the rest are malignant, mostly metastasis; malignant melanoma being one of the most frequent [7].

It is known that melanoma causes hematological metastasis to the small intestine and should be suspected in patients who develop gastrointestinal symptoms such as abdominal pain, weight loss, anemia due to chronic losses, among others, and an upper digestive endoscopy and a colonoscopy; however, they do not allow full exploration of the jejunum and ileum [5]. Anh JY et al. [7] described the endoscopic patterns of upper GIT melanoma; among which is the mass-forming pattern that includes elevated and ulcerated lesions and the single or multiple flat and nodular

hyperpigmented pattern. This last pattern of presentation is the most frequent at the duodenal level; however, the patient was found to form a pattern of ulcerated-type masses at the duodenal level.

Radiological studies have been used to diagnose ID melanoma; however, imagining this organ is difficult due to its length and complex loops. Among the radiographic studies to evaluate patients with a history of melanoma and symptoms, tomography (CT), positron emission tomography (PET-CT) and GI capsule endoscopy are recommended. Contrast-enhanced CT remains the most effective test to assess ID obstruction, with a sensitivity of 60-70%, but lacks specificity for diagnosing intestinal melanoma [11,12]. Whole-body fluorodeoxyglucose PET (FDG PET) has higher sensitivity (74%) and specificity (86%) than conventional CT for detecting gastrointestinal metastases in patients with melanoma [5]. In fact, some investigators believe that PET should be the primary staging test for disease recurrence [fifteen]. Capsule endoscopy can examine segments of the intestine that are inaccessible to conventional endoscopy; its limitation is taking a biopsy of lesions [11]. The patient had a contrast-enhanced CT of the abdomen and pelvis, showing a 30x30x40mm solid nodule in the gastrocolic ligament and at the level of the mid-ileum, presence of invagination and a 31mm contrast-enhancing polyp.

Emergency surgery remains the standard of care in cases where symptoms of intestinal obstruction due to ID intussusception from a malignant neoplasm become evident [11]. The patient was evaluated by general surgery and scheduled for exploratory laparotomy. In the surgical findings, three tumors were reported: one in the distal ileum 30 cm from the ileocecal valve, causing obstruction and intussusception of the proximal loop, and two tumors located 70 and 250cm from the proximal end. 30x20mm approximately. The anatomopathological study reported a poorly differentiated malignant neoplasm that compromised and perforated the intestinal serosa, and in the immunohistochemistry the S-100 and MELAN A were positive, concluding as an immunophenotype compatible with metastasis from malignant melanoma.

MM with distal metastases is considered a stage IV disease and most authors propose performing surgical resection associated with adjuvant systemic therapy with Nivolumab and Pembrolizumab. Regarding the surgical approach, there is no clear consensus; however, they recommend metastasectomy of the tumor, achieving a median survival of 64 months [2,12]. Taking into account that the three metastatic lesions of the small intestine were resected, the patient was eligible to receive therapy with Nivolumab. The time from excision of the primary skin tumor to diagnosis of GI metastasis is highly variable. They can range from 3 to 6 years and even more than 10 years [6,11,13]. In the patient, the diagnosis of primary melanoma was in 2018, and the

symptoms began 3 years later, placing it right at the expected time. The average lifespan for stage IV malignant melanoma is 2 months to 15 years after diagnosis [12,14,15].

Conclusion

Metastatic malignant melanoma is more frequent in the small intestine, therefore, in all patients with a history of cutaneous malignant melanoma, who presents persistent gastrointestinal symptoms, the possibility of metastasis should be considered in the differential diagnosis.

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