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Primary malignant melanoma of the bowel diagnosed following a bowel intussusception in an adult patient.
A case report and review of the literatureport

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Primary malignant melanoma of the bowel diagnosed following a bowel intussusception in an adult patient. A case report and review of the literatureport

AIM: *Primary small bowel melanoma is a very rare clinical entity with a paucity of publications in literature. Most cases of gastrointestinal melanomas are metastatic lesions arising generally from primary lesion of the skin, eyes, or anus. We present a case of a small bowel intussusception with primary malignant melanoma as lead point and a gluteal melanoma metastasis after four years free from disease.*
CASE REPORT: *A 77-year-old female has come to our attention with signs and symptoms of intestinal occlusion. She was subjected to a computerized tomography (CT) of the abdomen and pelvis that revealed small bowel intussusception caused by intestinal polypoid lesion. She was treated with a bowel resection. The histological exam has shown the presence of an amelanocytic malignant melanoma. The examination of skin, eyes, esophagus, colon and anus, a tot al body contrast-enhanced CT and a bone scintigraphy were negative for primary melanoma. So, the final diagnosis was primary melanoma of the ileum. After four-years disease-free survival, the patient came back to our attention for a gluteal melanoma metastasis, that was surgically removed. Afterwards she started immunotherapy, that is still ongoing.*
DISCUSSION AND CONCLUSION: *The diagnosis and the treatment of primary intestinal melanoma is a challenging due to the lack of scientific indications. Our case shows how an early diagnosis, although accidental, can offer a good survival free from disease. Moreover, a careful follow-up of our patients allows us to promptly identify neoplasm recurrence or distant metastasis that can be treated with surgery and systematic therapy.*

KEY WORDS: Intussusception, Primary bowel melanoma.

Introduction

Intussusception is one of the common causes of small bowel occlusion in children, but it is uncommon in adults. The overall incidence of intussusception in adults is around 2-3 cases per 1.000.000 person-years [1,2].

Malignant tumors, as lead point, cause about 60% of adult colonic intussusceptions and only 30% of small bowel intussusceptions [3]. It may be due to a tumor lesion such as a melanoma metastasis or, rarely, primary bowel melanoma [4]. Small bowel melanoma (SBM) represents for 1-3% of all intestinal tumours [5] and it is responsible for about 62% of malignant causes of small bowel intussusception [6]. We present a case of a small bowel obstruction caused by intussusception in a 77-years-old woman with primary malignant melanoma as lead point. After four years free from disease, the patient presented with a gluteal metastasis, that was surgically removed and also she underwent immunotherapy.

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Case Report

A 77-year-old female patient, with previous medical history of hypertension and hypercholesterolemia, who had never undergone surgery, presented to our Emergency Department complaining of peri-umbilical pain, postprandial bilious vomiting, and constipation for one day. Abdominal examination revealed abdominal distension, moderate tenderness in the peri-umbilical region, the auscultation revealed a minimal peristalsis. Rectal examination was normal. The haematological profiles showed leucocytosis and an increase of inflammatory indexes. The patient underwent abdominal X-Ray, that showed air intestinal levels. So she underwent contrast-enhanced Computed Tomography (CT) of the abdomen and pelvis, which revealed a short segment of small bowel intussusception at the left upper quadrant with a target sign appearance and endoluminal polypoid formation of about 25 x 20 mm at the level of the last ileal loops. No signs of distant metastasis were found. After improving patient's general condition, she underwent exploratory laparotomy that confirmed the presence of the intestinal occlusion due a small bowel intussusception with an ileal endoluminal palpable polyp. The exploration of the abdominal cavity did not detect further replicative lesions and confirmed the presence of a wide ileo-ileal intussusception. Resection of about 20 cm of ileum was performed and the whole underlying mesentery with its lymph nodes was removed. The intestinal continuity was restored through a latero-lateral anastomosis. The postoperative course was regular, and the patient was discharged on the sixth postoperative day. Histological examination of the specimen revealed the presence of a 25x20x16 mm ileal polypoid neoformation, proved to be an amelanocytic malignant melanoma. The tumor was composed by sheets of large pleomorphic epithelioid cells with pale cytoplasm and nuclei with vescicular chromatin and prominent nucleoli. Pigmentation was absent. The immunohistochemical examination showed positivity to S100, HMB-45, Melan-A, CD99, and negativity to AE1/AE3, EMA, CD 20 and chromogranin A. Based on the above findings, a diagnosis of amelanocytic malignant melanoma was provided. Resection margins were free from disease.

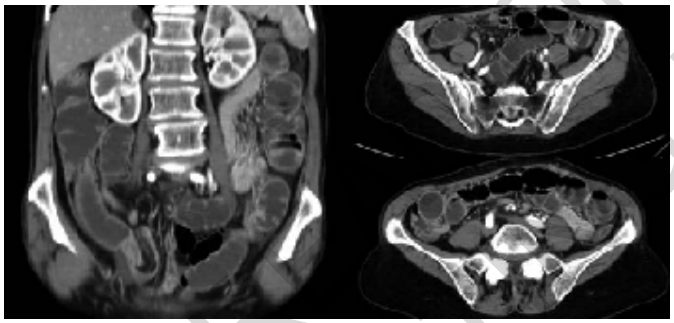

Fig. 1: CT imagine of the last ileal loop intussusception.

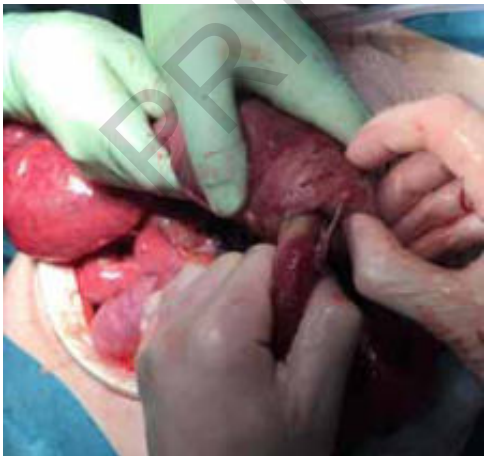

Fig. 2: Ileo-ileal intussusception during exploratory laparotomy.

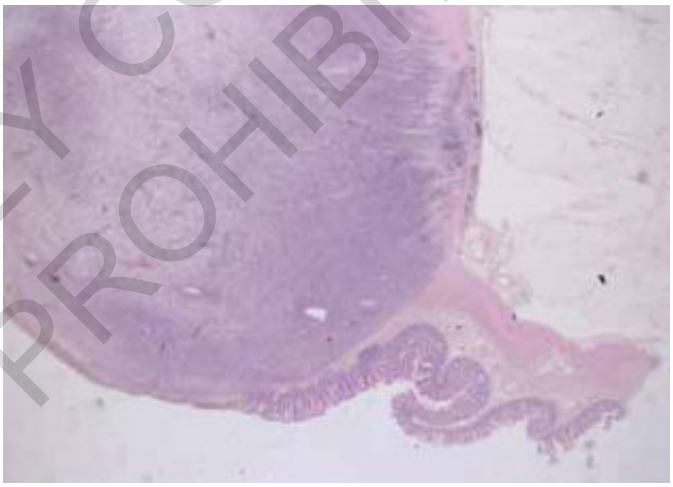

Fig. 3: Macroscopic aspect of the ileal polypoid neoformation. (Hematoxylin-Eosin 2X).

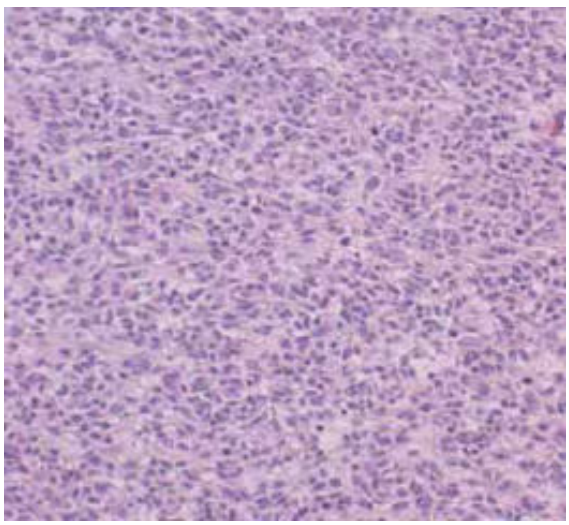

Fig. 4: Microscopic view showing ileal polypoid neoformation. Large Pleomorphic Epithelioid Cells. (Hematoxylin-Eosin 20x).

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The careful examination of skin, eyes, esophagus, colon and anus were negative for primary melanoma. A total body contrast-enhanced CT and a bone scintigraphy did not report other lesions. So, the final diagnosis was primary melanoma of the ileum. A four-years close follow-up has not revealed any metastasis or neoformations in other sites, until March 2020 when, during a surgical examination, we found a left gluteal tumefaction of hard-wooden consistency of about 5 cm. The patient underwent a pelvic RMN that showed a hyper vascularized rounded tumefaction with irregular margins attached to the fascia of the gluteus maximus muscle. The total body CT scan, performed to evaluate any distant metastatic localizations, did not reveal anything pathological. We immediately performed a wide exeresis of the neoformation which we sent to the pathologist for histological examination. The result was: melanoma metastasis positive for S100, melan A, HMB-45 and negative for AE1/AE3, EMA, CD 20, CD 56, CK 7 and chromogranin A, cell proliferation index ki 67 positive in 40% of cells, resection margins free from disease. Then the patient was sent to the oncology centre to be subjected to immunotherapy and to a close follow-up.

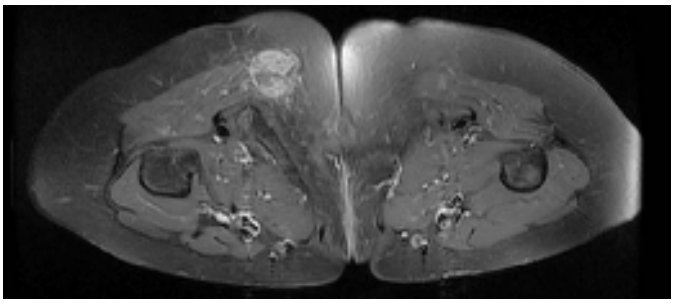

Fig. 6: Hyper vascularized gluteal swelling at the Pelvic RMN.

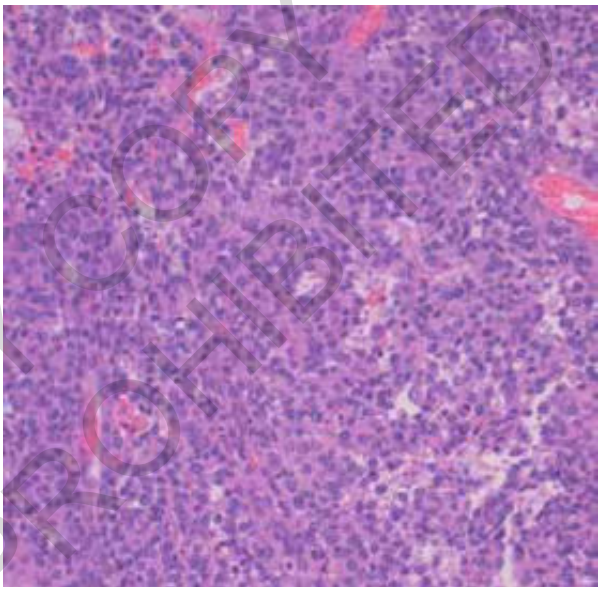

Fig. 7: Microscopic view showing gluteal neoformation. (Hema-toxylin-Eosin 20X).

Discussion and Review of Literature

About 5% of cases of intussusception occurs in adults and causes 1%-5% of intestinal obstructions in this population [7]. Adult intussusception is usually caused by a pathologic lead point in the bowel and over half of the cases were triggered by a malignant lesion [7]. In the small intestine, an intussusception can be secondary either to the presence of intra- or extra- luminal lesions (inflammatory lesions, Meckel's diverticulum, postoperative adhesions, lipoma, adenomatous polyps, lymphoma, and metastases) or iatrogenic [8].

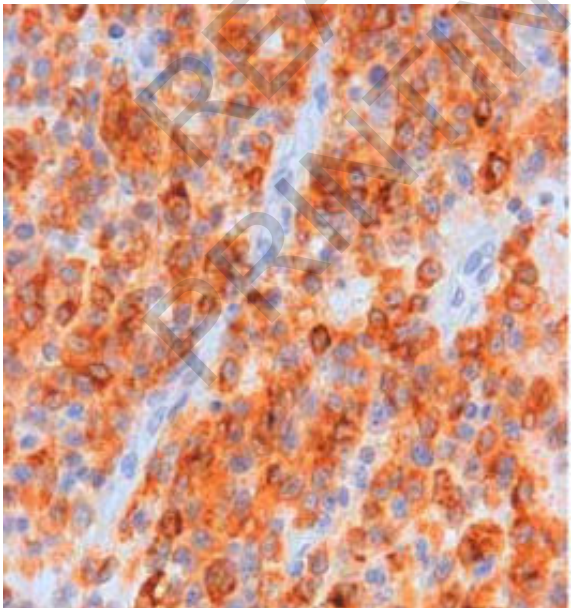

Fig. 5: Microscopic view showing ileal polypoid neoformation. Immunohistochemistry Staining For Melan-A. (40x).

Malignant melanoma accounts 1% to 3% of all malignant lesions of the gastrointestinal tract (GI) [9] and the third most frequent location, after cutaneous and ocular, is the anorectal area. Primary mucosal melanoma arises in any site of the gastrointestinal tract, but it is most common in anorectal area (31.4% in the anal canal and 22.2% in the rectum) and oropharyngeal region (32.8%), while esophagus (5.9%), stomach (2.7%), small intestine (2.3%), gallbladder (1.4%) and large intestine (0.9%) [10]. Most commonly small intestine is affected by metastatic tumors than primary lesions [11]. The average time required to a cutaneous melanoma to metastasize at the bowel level is 3-6 years [12]. In literature are not present data to identify the average time needed for a primary bowel melanoma to spread at skin or other side. In our case the free disease survival was 4 years. The diagnosis of primary intestinal melanoma remains a diagnostic challenge due to absence of early symptoms and the lack of universally accepted diagnostic criteria. Often

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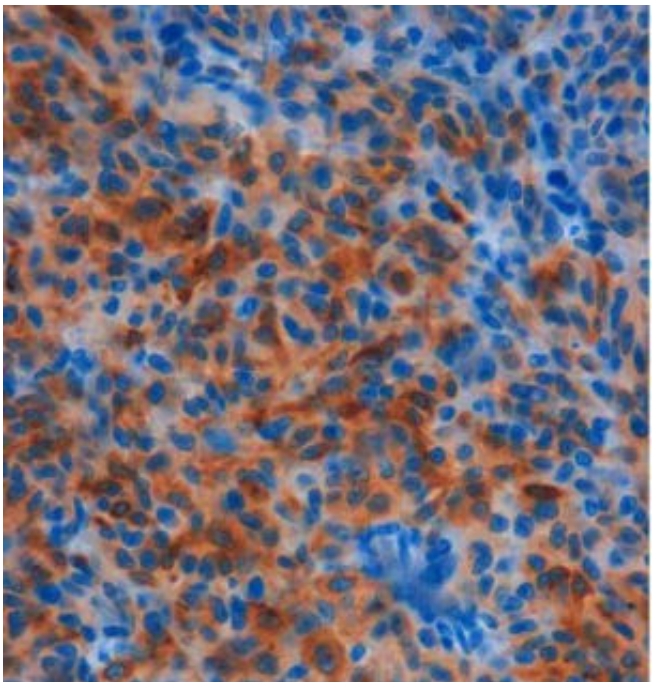

Fig. 8: Microscopic view showing Gluteal neoformation. Immunohistochemistry staining for Melan-A. (40x).

it remains asymptomatic in the early stage of the disease and it becomes symptomatic only belatedly with a specific symptoms like chronic abdominal pain [17-64%], weight loss [10-47%] bleeding (26-84%) [13] also occult causing an intramural hematoma [14]. There are several theories about the origin of primitive intestinal melanomas. According some authors primary intestinal melanomas derive from melanoblastic neural crest cells which migrate to the small bowel [15], according to others these tumors originate from enteric neuroendocrine non-cutaneous tissue in the form of amine precursor uptake decarboxylase (APUD) cells that have undergone neoplastic transformation [16]. Other authors suggest that the cancer cells arise from neuroblastic Schwann cells of the intestinal autonomic nervous system. Moreover, some researchers consider all GI tract melanoma to be metastatic lesions from cutaneous melanomas regressed spontaneously or undiagnosed [17].

Sachs et al. [18] identified, in 1999, three criteria that must be respected to be able to carry out a diagnosis of primary intestinal melanoma: 1) presence of a single lesion at the time of diagnosis; 2) absence of lesions in other organs and absence of lymph nodes increased in volume; 3) survival of more than a year after diagnosis. Blecker et al. [19] propose the following criteria for a diagnosis of primary melanoma of small bowel: 1) presence of a solitary mucosal lesion in the intestinal epithelium; 2) absence of melanoma or atypical melanocytic lesions of the skin; 3) presence of intramucosal melanocytic lesions in the overlying or adjacent intestinal epithelium. Primary intestinal melanoma seems to be associated with a worse prognosis and a more aggressive behaviour compared to cutaneous melanomas due to rapidly growth for a rich vascular and lymphatic supply of the gastrointestinal mucosa [20]. The poorer prognosis may be also associated with the delay in diagnosis.

The few cases of primary small bowel melanoma reported in literature do not allow us to identify a standardized treatment. A wide intestinal resection associated to the removal of the mesentery and the local lymph nodes seems to be the treatment of choice [20]. When elective surgery is possible it is mandatory a careful staging of the disease to exclude secondary locations. In case of obstruction, perforation or haemorrhage an emergency surgical treatment is mandatory [21]. Surgical resection allows to definite the diagnosis and can prolong survival. According to Ollila et al. the median survival in patients undergoing curative resection was 48.9 months, compared with only 5.4 months and 5.7 months in those undergoing palliative procedures and nonsurgical interventions, respectively [22]. The role of postoperative adjuvant chemotherapy and IFN treatment is limited, although may be beneficial for some patients[17-23]. No systemic therapy is known to effectively treat intestinal melanomas and significantly improve survival [24].

Chemotherapy, immunotherapy, and target therapy all have a role in medical treatment of small bowel melanoma, but they are almost invariably used palliatively [25]. Literature shows that a close follow-up is the main possibility to identify metastatic lesions that can be treated with surgery [26].

Conclusions

Primary malignant melanomas of the small intestine are rare neoplasm and it remains often misunderstood, with a poor prognosis. The diagnosis and the treatment are a challenging because we cannot relay up on a standardized surgical treatment. The surgery and a close follow-up, which allows an early detection of a relapse or distant metastasis, seem to be the best choice to improve the survival of this patients.

Riassunto

Il melanoma intestinale è una patologia estremamente rara e molto spesso difficile da diagnostica a causa della mancanza di manifestazioni sintomatologiche precoci e specifiche. La diagnosi tardiva e la rapidità con cui questa neoformazione diffonde attraverso i vasi sanguigni intestinali sono le due principali cause della sua peggiore prognosi rispetto al melanoma cutaneo. Raramente può presentarsi con sintomi intestinali aspecifici quali dolore addominale cronico, occlusione intestinale, rettorragia e calo ponderale il più delle volte nelle fasi avanzate della malattia. Una presentazione clinica acuta che

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richiede un intervento chirurgico urgente, come nel nostro caso, può permette una diagnosi precoce, seppure accidentale, e quindi assicurare un trattamento radicale con una buona sopravvivenza dei pazienti. L'esistenza dei melanomi primitivi intestinali è sicuramente oggetto di dibattito, ma l'assenza di lesioni melanocitiche cutanee, oculari e anali permette di escludere la presenza di un melanoma metastatizzato, rinforzando l'ipotesi di una lesione primitiva intestinale confermata dall'esame istologico definitivo. Data la sua bassa incidenza non esistono dei protocolli condivisi di trattamento. Sicuramente la resezione chirurgica ampia della neoformazione, con margini negativi, e l'asportazione dei linfonodi mesenteriali corrispondenti permette una buona sopravvivenza dei pazienti. Un attento follow-up a lungo termine con esame dermatologico, visita oculistica, visita chirurgica, gastroscopia e colonscopia periodiche permettono di individuare precocemente eventuali secondarismi trattabili chirurgicamente e con terapia sistemica, in particolar modo immunoterapia.

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