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Case report

Early diagnosis of primary melanoma of caecum. Case report and review of the literature

Beatrice D'Orazio[1,2], Sebastiano Bonventre[1], Bianca Cudia[1], Gaetano Di Vita[1], Girolamo Geraci[1].

[1] General Surgery Unit - Department of Surgical, Oncological and Stomatological Sciences, University of Palermo;
[2] Postgraduate Medical School in General Surgery, University of Palermo, Palermo, Italy

Summary. Malignant gastrointestinal melanoma is usually a metastatic lesion. We report the case of a 79-year-old female asymptomatic patient. Colonoscopy revealed one plane 15 mm pigmented lesion in the caecum. Neither CT scan of the abdomen nor right hemicolectomy revealed no metastatic disease. Histopathological examination of the surgical specimen was indicative of malignant melanoma. A set of additional enquires such as laboratory and imaging tests did not point out any suspicious lesions in the skin, eye, leptomeninges or other sites. Therefore, we made the diagnosis of primary colonic melanoma. The diagnosis of this disease is still a challenge and often demanding for a multidisciplinary approach, involving the surgeon, oncologist and even immunotherapy or radiotherapy. (www.actabiomedica.it)

Key words: colorectal melanoma, surgical oncology, non-cutaneous melanoma

Introduction

Melanoma is a quite rare finding in terms of gastrointestinal tract (GIT) location (1) and the metastasis related to it arising in the dig estive system are rare (4% in primary surveys to up to 60% in post-mortem assessments) (2).

The rare descriptions of primary melanoma at primary sites (oesophageal, stomach, small bowel, and anorectal) have been as polypoid, ulcerative, or submucosal lesions and on occasion causing intussusception or bleeding as a complication (3-5).

Even if the predominant origin of melanoma is cutaneous, it is still crucial to make a differential diagnosis between primary or metastatic gastrointestinal location.

The evidence for primary disease is strongest in the setting of solitary lesions by endoscopic and/or contrast radiographic findings without evidence of cutaneous disease. Furthermore, given the paucity of evidence of routine pre-melanocytic migration to colonic sites highlights the uniqueness of primary melanoma in the gastrointestinal tract (6).

Case presentation

CR, a 78-year-old female with a history of mild hypertension (medication with low dose aspirin and β-blockers), diabetes mellitus (medication with metformin). She referred an history of alvus alteration, reason why we performed a colonoscopy. No personal or family history of malignancy or melanoma was reported.

The initial physical exam was unrevealing in examination of all major organ systems

Colonoscopy has been performed that demonstrated left and right diverticulosis, internal haemorrhoids a single plane 15 mm pigmented lesions in the caecum, near ileo-caecal valve (Figure. 1).

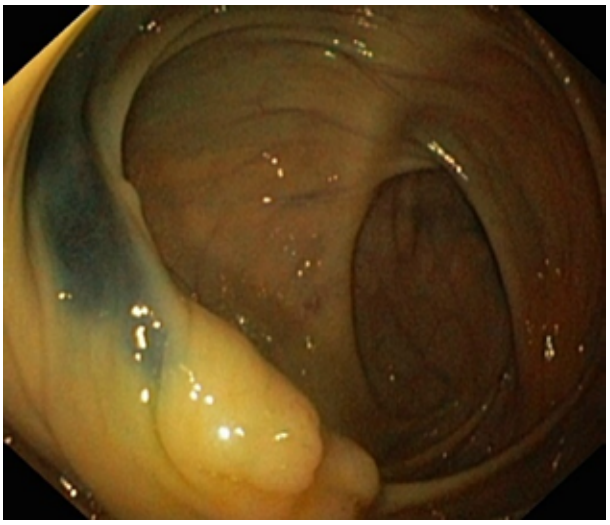

Figure 1. Colonoscopy: endoscopic view of caecum. At caecum level presence of a pigmented plane lesion of around 15mm.

The lesion was biopsied. Pathology revealed a poorly differentiated malignancy which was positive for Human Melanoma Black (HMB-45), Melanoma antigen (Melan-A), and c-kit immunostains and negative for cytokeratin AE/AE3, cytokeratin 7, cytokeratin 20, Cluster of Differentiation (CD34), and Epithelial Specific Antigen (MOC-31), suggesting melanoma (Figure 2).

A computed tomography (CT) scan of the abdomen and pelvis has been obtained and demonstrated no lymphadenopathy or metastatic sites.

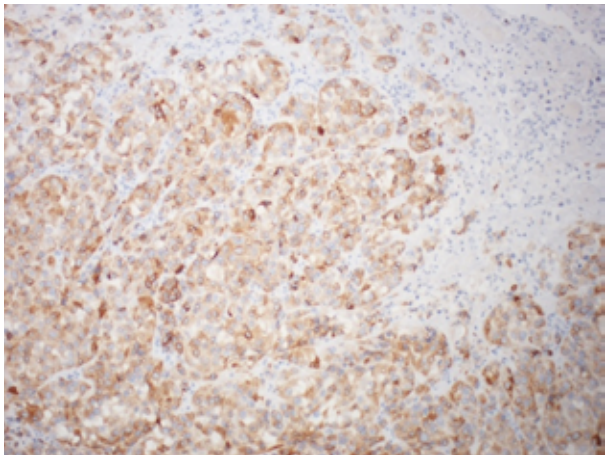

Figure 2. Histological picture, 45x: Melanoma antigen (Melan-A) positive

The patient then underwent a laparoscopic ascending right hemicolectomy with an ileocolic anastomosis. The histopathologic analysis of this lesion demonstrated two flat black mucosal lesion that invaded through the muscularis. The lesion consisted of a dense infiltrate of cells with large, pleomorphic nuclei with prominent nucleoli. The cells were positive for S100, HMB-45, Melan-A and C-kit by immunohistochemistry and had negative immunoreactions for cytokeratin AE1/AE3, cytokeratin 7, cytokeratin 20, TTF-1, MOC-31, CD34, p63, calretinin, actin and desmin. The sample was also proto-oncogene B-Raf (BRAF) V600K positive. This constellation of markers was deemed consistent with melanoma. None of 12 nodes obtained operatively were positive for melanoma, so pathological stage was T1 N0 M0.

The postoperative course was overall unremarkable and following discharge on postoperative day seven the patient underwent a whole-body positron emission tomography (PET)/CT scan that showed only postoperative changes. After discussion with the medical oncologic unit, it has been decided not to submit the patient to adjuvant chemotherapy.

Whole body dermatologic evaluation for an alternative primary were negative supporting a diagnosis of primary melanoma of the caecum. At 2 years follow up we did not record any recurrence.

Discussion

One review of over 84836 cases of melanoma showed that 91,2% were cutaneous, 5,2% ocular, 2,2% of unknown primary origin and 1,3% of gastrointestinal tract, predominantly in the small intestine and right colon (6).

In fact, primary colonic melanoma is a rare clinical entity: Khalid et al reported in 2011 only 12 cases of primary colonic melanoma (7) , while , a review of the literature from 2011 to 2020 shows 8 other cases in addition to ours (Table 1) (8-15).

Like any other colonic neoplasm, the clinical presentation of primary colonic melanoma is non-specific. Considering that colonic primary melanoma is an extremely uncommon entity, differentiating primary from secondary melanoma is a

Table 1. review of the literature (2011-2020)

Author	Region	Year	Sex	Age	Site	Clinic	CHT
Busuttil G [8]	Malta	2013	F	73	Right colon	Bleeding	No
Li WX [9]	China	2014	M	57	Ileo-caecal	Invagination	No
Gajda M [10]	Poland	2016	M	71	Right colon	Occlusion	Yes
Furudoï A [11]	France	2016		65	Right colon	Pain	NR
Raja J [12]	USA	2017	M	75	Transverse colon	Bleeding	No
Miliaras S [13]	Greek	2018	F	67	Right colon	Abscess	Yes
Alwani NH [14]	Arabia	2019	F	47	Caecum	Pain	No
Yi NH [15]	Korea	2019	F	50	Sigma	Hematochezia	No
Our case	Italy	2020	F	78	Caecum	Asymptomatic	No

NR = not reported; NV = not valuable; CHT = chemotherapy

challenge. Ozdemir et al (16) proposed a guideline to differentiate primary bronchial melanoma from secondary melanoma, these same criteria may be applied to colonic melanoma. These latter include: 1) the lesion must be solitary in the surgical specimen, 2) there must be no previously excised skin melanoma, 3) no previous or concurrent ocular tumour, 4) the morphology must be compatible with that of a primary tumour, 5) there must be no other demonstrable melanoma at the time of surgical exploration, and 6) the findings should be confirmed by careful autopsy for those patients who succumb to disease (16): except confirmation by autopsy, fortunately, all these criteria were met in our patient.

Histopathologic findings bring to light varying proportions of epithelioid areas and spindle cells. The tumour cells may be characterized either by abundant melanin pigment or be amelanotic. Immunohistochemical stains are highly sensitive for confirming the diagnosis of a melanoma. S-100 is very sensitive in detecting melanoma, HMB-45 and melan-A are highly specific in clinching the diagnosis of melanoma (9).

Differentiating metastatic from primary GIT melanomas remains a challenge. Primary lesions are much more common in the setting of solitary lesions by endoscopic and/or contrast radiographic findings without evidence of cutaneous disease. Anorectal melanoma is the most common primary gastrointestinal melanoma but accounts for less than 3% of melanomas. It can show up with important abdominal pain, tenesmus, and fatigue. Small intestine melanoma can be associated with intussusception causing small bowel obstruction possibly related to the submucosal location (5,12,17).

The proposed mechanism by which bowel mucosa is at risk for melanoma is via migration of neural crest cells from caudal branchial arches as amine precursor uptake decarboxylase (APUD) cells that can be melanocyte precursors, during embryogenesis, or a defect in ectodermal differentiation and migration causing the melanocytes to reside inappropriately in the GI tract (18-19). This is why it has been postulated that benign melanosis of the stomach can also occasionally be found (20). However, there is no established theory or evidence of migration of melanocytic precursor cells to the colon during embryogenesis (18).

The melanoma metastasis to the colon has been described to appear as polypoid, ulcerative, or submucosal lesions and on rare occurrence cause colonic intussusception (7).

The prognosis of primary gastrointestinal melanoma is poor, although the limited cases of colonic melanoma have had a marginally better outcome compared to other mucosal melanomas that carry a 47% risk of disease-specific mortality (20).

There is no general consensus on the treatment guideline proposed for primary colonic melanoma, by virtue of its rarity as a matter of fact the little number of cases reported in the literature underwent standard partial resection of the colonic affected site.

A review on primary melanoma of the colon did not reveal any specific criteria that authors have used

to assign specific surgical modalities to patients: each management approach was individualized according to the judgment and discernment of the surgeon. However, in general, it is easy to appreciate the general trend that patients with limited, controlled disease were managed with curative surgical therapy; moreover, patients with positive nodes had an average survival of 20.4 months while those with negative nodes lived an average of 34.7 months, with the average being 27.45 months (7).

Our patient underwent extended right hemicolectomy with ileocolic anastomosis. Final pathology showed 0 out of 12 harvested lymph nodes harbouring melanoma, with positivity to BRAF and, with the oncologist accordance we did not perform any other treatment.

Conclusions

Melanoma in the gastrointestinal tract is a rare occurrence in which primary lesions are exceedingly unique. It is still crucial to make a differential diagnosis between the primary or metastatic origin of a melanoma arising in the GIT to undertake the best treatment, nevertheless, this process still represent a challenge nowadays. This plan in modern oncology is almost certain to include immunotherapy but the decision regarding additional chemotherapy as well as the role of surgery is significantly impacted by whether the GIT lesion is a primary or metastatic melanoma. AS already pointed out, the chance to excise a primary melanoma of the GIT prior to metastasis is rare but it may hopefully determine a survival benefit as in our patient. However, the prognosis for these patients remains poor as many have disease progression at or around the time of diagnosis. As these cases are so uncommon, no standard of care exists but the use of immunotherapy adjuvancy following colorectal surgical resection of the primary mass is both feasible and safe.

Conflicts of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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Correspondence:
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Gaetano Di Vita
Tel/Fax 0039-091-655-2606 / 0039-091-655-2646
E-mail: divitagaetano@libero.it
General Surgery Unit - Department of Surgical, Oncological and Stomatological Sciences, University of Palermo. Via Liborio Giuffrè, 5 - 90127 Palermo, Italy.
ORCID ID https://orcid.org/0000-0003-2835-3273