

## Case Report

### METASTASIS FROM SKIN MELANOMA TO DUODENUM: CASE REPORT AND LITERATURE REVIEW

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#### ABSTRACT

Tumor mass was observed after PET-CT scan in the descending part of duodenum and pancreatic head by a 62-year-old Caucasian woman who had undergone skin melanoma resection from the anterior side of the right thigh (lower limb) associated with right inguinal lymphadenectomy 3 years earlier. Endoscopic examination with ultrasonography showed the tumor mass arising from the descending part of the duodenum, which had invaded the head of pancreas and caused loop obstruction. Endoscopic biopsy revealed neoplastic cells with melanin granules and positive cells for Melan-A/SOX10 staining, indicating the presence of a metastatic malignant melanoma. It showed no BRAF-Mutation. These additional stainings were evaluated after surgery. In the surgically resected Whipple specimen, the mass was 5 x 4 cm large, solid and ulcerated. Tumor infiltrated all duodenal layers and the tissue around them. Immunocytochemistry and electronic microscopy findings confirmed the diagnosis of metastatic malignant melanoma, and were similar to the skin specimen from the right thigh; therefore, the duodenal lesion was considered to be a metastasis from the right thigh.

**Keywords:** skin melanoma, duodenal metastasis, pancreas invasion.

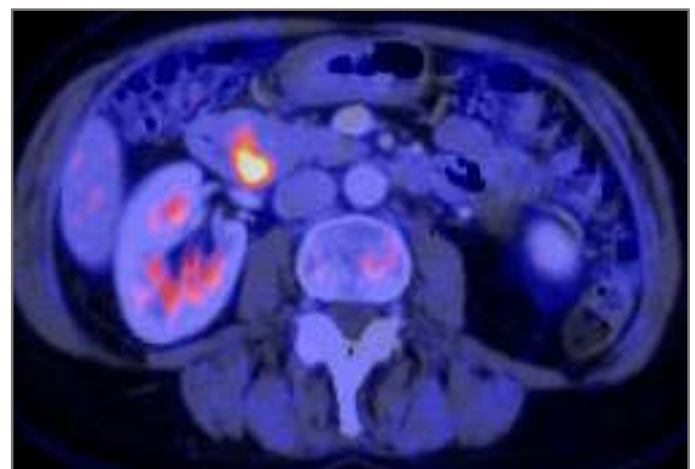
#### INTRODUCTION

Melanoma is a rare malignancy that originates from melanocytes and often metastasize to several organs. Malignant melanoma of gastrointestinal tract, either primary or metastatic, is an uncommon entity that usually remains undiagnosed in living patients, probably as a result of an asymptomatic course or nonspecific symptoms. However, duodenal metastasis from skin melanoma with pancreas invasion remain uncommon [1,2]. A study demonstrated that the secondary malignancies as for abdominal organ metastasis from stage IV melanoma, could occur in the liver (42.9%), gastrointestinal tract (20.7%), adrenal glands (8.5%), pancreas (2.3%), spleen (6.7%), or multiple sites (18.8%) [3]. We describe a case of duodenal metastasis with pancreas head invasion from skin melanoma (Clark level IV) which was resected 3 years ago from the right thigh (lower limb), associated with a right inguinal lymphadenectomy. We present our findings herein. Moreover, duodenal metastasis of melanoma is reviewed and discussed in reference to previous publications. A systematic search of literature data was undertaken using PubMed, Google Scholar, Research Gate, Publons, Academia.edu, Semantic Scholar, Sherpa/Romeo, Scopus from 1995 to 2017.

#### CASE REPORT

A 62-year-old Caucasian woman visited our hospital for investigation of a duodenal/pancreatic mass, which was identified on screening PET-CT after extended surgical removal of malignant skin melanoma from the right thigh (lower limb) associated with a right inguinal lymphadenectomy when she was 59 years old. At that time pathological skin specimen from the right thigh confirmed as malignant melanoma Clark level IV, TNM staging by pT2aN1bM0, positive cells for BRAF-Wild-type by Mutation Analysis. After a couple of months after the first surgery she also underwent removal of

malignant skin melanoma from the back area. Pathological results from the back area skin specimen confirmed as malignant melanoma Clark level II, TNM-Staging by pT1a. She received chemotherapy and heavy particle radiotherapy after surgery. No suspect mass was identified on regular follow-up. Two years later it showed a recurrence from melanoma in the scar on the right thigh (lower limb) and right inguinal site. No suspect mass was identified on follow-up CT-Scan's from head, lung and abdomen. She received immunotherapy and no additional chemotherapy or radiotherapy. Three years later after the first surgery she underwent investigations because of persistent high grade fever episodes. From PET-CT scan was observed a tumor mass arising descending part of duodenum and pancreatic head (Fig.1).



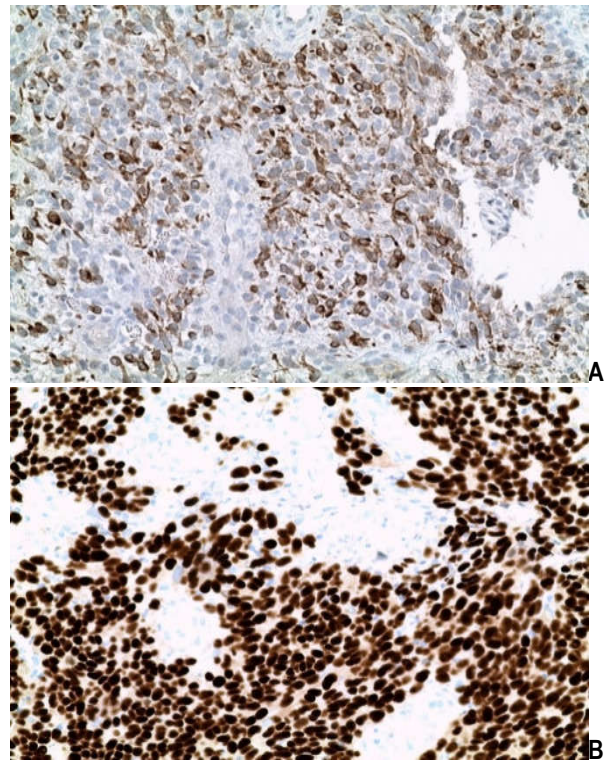
**Fig.1** View of the mass in the duodenum/pancreatic head by PET-CT scan

Endoscopic examination with ultrasonography showed a 30 mm tumor mass arising from the descending portions of the duodenum which had invaded the head of pancreas and caused loop obstruction

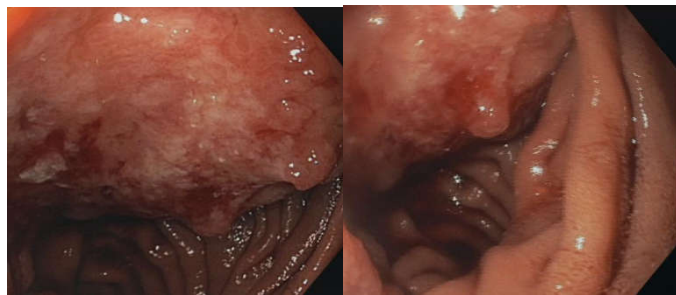
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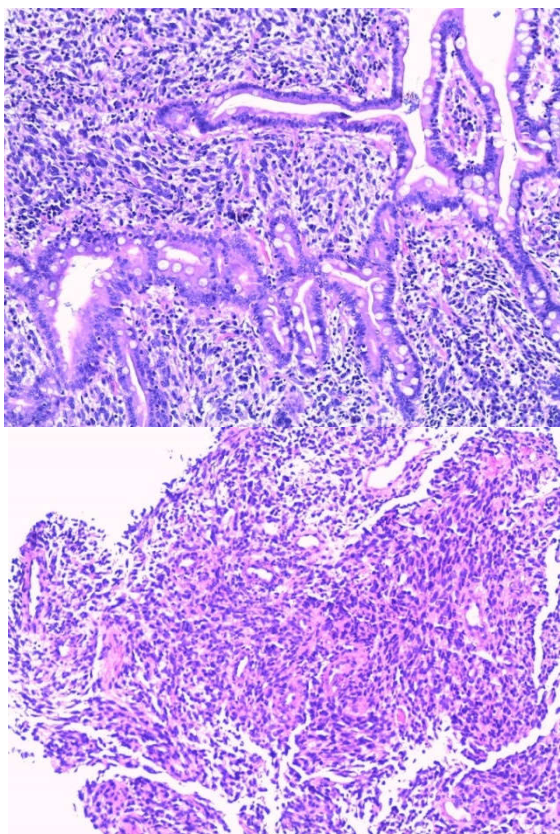
(Fig.2). Endoscopic biopsy revealed neoplastic cells with melanin granules and positive for Melan-A staining and SOX10 staining, indicating the presence of a metastatic malignant melanoma. It was discovered no BRAF-Mutation. The colonoscopy showed not tumor finding. We strongly recommended surgical resection, and the patient accepted surgery. She underwent pylorus preserving pancreaticoduodenectomy. From gross observation of the resected specimen, the mass was 4 x 5 cm large with invasion and alteration of all duodenal layers, also invasion of pancreatic parenchima. The tumor mass was solid and composed of multiple nodules, although most of the nodules were grayish and brownish. Microscopic observation revealed duodenal mucosa infiltrated by tumor cells after hematoxylin-eosin staining (Fig.3). Neoplastic cells were positive for expressing melanoma markers SOX10 and Melan-A stainings (Fig.A and B). Therefore, the diagnosis of a melanoma was pathologically confirmed, resulting in a diagnosis of duodenal metastasis with pancreatic invasion from the skin melanoma. Further adjuvant chemotherapy was considered less worthy and was not performed because of previous immunotherapies. She underwent immunotherapies with Ipilimumab and Nivolumab. The postoperative evolution was good. She was released from the hospital after 13 days. Melanoma did not recur during close follow-up for 5 months.



**Fig.A** Expressing melanoma markers Melan-A (20x10 Melan-A staining); **Fig.B** Expressing melanoma markers SOX10 (20x10 "SOX10" staining)



**Fig.2** View of the tumor invasion in the duodenum by endoscopy



**Fig.3** Duodenal mucosa infiltrated by tumor cells (10x10 hematoxylin-eosin staining)

**DISCUSSION**

The incidence of malignant skin melanoma is rapidly increasing in Europe and USA, the mortality still remains high[5]. The incidence rate of melanoma per 100,000 persons per year has been reported to be 1–2 in Japan [3,9]. Melanoma is a very aggressive malignant tumor arising from pigment-containing cells, which are mainly located in the cutaneous tissue. Primary tumors have a strong association with excessive sunlight exposure and commonly occur on the skin (over 90%). Melanoma can also develop from other tissues containing melanocytes such as meninges, gastrointestinal, mucosa and eyes[4,5]. On the other hand, the organs to which the melanomas metastasize are commonly skin, lymph nodes, and the digestive system. They rarely metastasize to the lung, the liver, the brain, and the bone[6]. Abdominal organ metastasis from stage IV melanoma, could occur in the liver (42.9%), gastrointestinal tract (20.7%), adrenal glands (8.5%), pancreas (2.3%), spleen (6.7%), or multiple sites (18.8%) [3]. According to post-mortem records, gastrointestinal metastasis from skin melanoma represent 50–60% of cadaveric studies, and usually represent the expression of an advanced and widespread disease; small bowel, colon and stomach are the most frequent localizations [4,5]. Gastrointestinal metastasis normally have an asymptomatic course or non-specific symptoms; clinical presentation is related when complications occur. So, only 1–9% of overall gastrointestinal metastasis from cutaneous melanoma are diagnosed ante-mortem [5,7,8]. At the time of diagnosis, in more than 50% of these patients, extraintestinal metastases are already detected[10]. In our patient, some lymph nodes from the right inguinal region were positive at the time of primary cutaneous excision on the right thigh (lower limb). Although intestinal metastases typically develop 3–6 years after excision of the primary cutaneous melanoma. This report described diagnoses of duodenal metastasis was done 3 years later after primary melanoma excision. Intestinal metastases are sometimes present at initial diagnosis or just 6 months after detection of primary cutaneous lesions(10,11,12). The



symptom-free period between surgical excision of primary cutaneous melanoma and the diagnosis of small-bowel metastases lasts between 6 months and 90 months (13,14). Our paper described 3 years symptom-free period. recurrent high fever episodes without digestive manifestation followed the symptom-free period. Because of persistent unexplained high fever episodes, our patient underwent a screening investigation using PET-CT-scan. It happened three years later after the first surgery. A mass was described in duodenum/pancreas head. In the early abdominal CT scan it was no tumor detected. Diagnosis of duodenal metastasis from skin melanoma was confirmed after endoscopy and biopsy. Whole-body PET-CT imaging with fluorodeoxyglucose has higher sensitivity and specificity than does conventional CT for detection of gastrointestinal metastases in patients with melanoma [15]. Many specialists suggest that PET-CT should be the main staging study, also for recurrent disease [16]. The sensitivity of CT imaging for detection of intestinal melanoma was only between 60% and 70% [12]. Complete endoscopic examination of the duodenum associated with endosonographie and biopsy is non-invasive, and is a mandatory procedure for diagnosis of duodenal tumours [17]. Colonoscopy is also mandatory to exclude other conditions. However, the jejunum and ileum are not easily examined by endoscopy, so the sensitivity to detect metastatic tumours to the small bowel is sometimes limited [18,19]. A combination of imaging techniques and endoscopy is recommended to improve the sensitivity and specificity of diagnosis, which is crucial for the early diagnosis of intestinal metastatic melanoma. Despite advances in diagnostic techniques, early detection of small-bowel melanoma remains a challenge for medicine. The final diagnosis is made by histological examination. Immunohistochemical stains, such as SOX10 and Melan-A, are particularly useful in confirming the diagnosis of metastatic melanoma. Accurate preoperative diagnosis and assessment of the extent of intestinal metastases, including pancreas invasion, is essential when selecting patients for surgery and planning the surgical procedure [12]. In Europe, several drugs, such as nivolumab, vemurafenib, ipilimumab, and trametinib have sequentially been approved for melanomas. Although the present case did not receive additional chemotherapy because she was encountered before such approval, these agents have improved prognosis for similar patient. Patients with a history of cutaneous malignant melanoma who present unspecific clinical picture should be investigated to rule out intestinal metastases. Symptoms of intestinal melanoma present late in the progression of the disease, resulting in a poor prognosis.

## CONCLUSION

Given the recent progress in radiology, endoscopy and molecular targeted agents for melanoma, preoperative assessment of duodenal metastases extent using superior endoscopy with biopsy associated with CT-scan and PET-CT are very important for determining clinical tactics. No standard therapy exists for the treatment of intestinal metastasis of cutaneous melanoma, although surgical removal is the treatment of choice in all patients with respectable melanoma.

## Author contributions

Dr. medic Ovidiu-Angel Matei: manuscript drafting, translate, review.  
Dr. Lorena Matei: manuscript design and drafting, translate

All authors have **no conflict of interest** to declare. All authors read and approved the final manuscript.

## Compliance with ethical standards

Informed consent was obtained from patient. Human rights All procedures have been performed in accordance with the ethical

standards laid down in the 1964 Declaration of Helsinki and its later amendments.

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