

PET-CT Incidental Finding of Duodenum Late Melanoma Metastasis: A Case Report

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Abstract

Case Report

Three years post-primary resection of a skin melanoma with right inguinal lymphadenectomy, a 62-year old Caucasian female patient presented with high grade fever episodes and was admitted to Helios Hospital Pforzheim for further medical evaluation. A suspicious mass was unexpectedly discovered in the descending duodenum and head of pancreas during PET-CT scan. Upper endoscopic examination with ultrasonography revealed a 30 mm tumor mass originating from the descending part of the duodenum, which had infiltrated the head of pancreas and caused/resulted in loop obstruction. Endoscopic biopsy confirmed the presence of neoplastic cells with melanin granules and positive for Melan-A/SOX10 staining, indicating the presence of a metastatic malignant melanoma. Importantly, the tumor showed no BRAF-Mutation. These additional staining was evaluated postoperatively, and colonoscopy did not reveal any tumors. After this procedure, the patient was strongly recommended to undergo surgical resection, to which the patient agreed. A pylorus preserving pancreaticoduodenectomy was performed at the Department of General Surgery at Helios Hospital Pforzheim. In the surgically resected Whipple specimen, the mass was 5 x 4 cm large, solid and ulcerated. Histologically the tumor infiltrated all duodenal layers and the tissue around them. Immunocytochemistry and electronic microscopy findings confirmed the diagnosis of malignant melanoma consistent with the skin specimen from the right thigh. Therefore, the duodenal lesion was a metastasizing skin melanoma originating from the skin melanoma in the right thigh. The postoperative course of the patient was favorable, therefore she was discharged from the hospital after 13 days. Subsequently, she underwent immunotherapy with Ipilimumab and Nivoluma, and no recurrence was identified during the close monitoring of the patient in the 5-month follow-up period. The patient's medical history began three years prior with resection of a skin melanoma located on anterior side of the right thigh (lower limb). Pathological evaluation at that time confirmed a malignant melanoma Clark level IV, pT2aN1bM0 as TNM-Staging, positive for BRAF-Wild-type by mutation analysis. A subsequent excision of skin melanoma from the back a region was carried out couple of months after the initial surgery, with the specimen classified/diagnosed as skin melanoma Clark level II, pT1a as TNM-Staging. After the surgery, the patient underwent chemotherapy and heavy particle radiotherapy. After a 12-month post-operative follow-up period, no recurrence was registered. After two years post-primary surgery recurrence was registered in the scar on the right thigh (lower limb) and right inguinal site. Follow-up CT scans of the head, lung, and abdomen did not reveal any additional suspect masses. The patient received immunotherapy without additional chemotherapy or radiotherapy for the recurrent lesions.

Keywords: Duodenal metastasis, pancreas invasion, skin melanoma, PET-CT Scan.

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1. INTRODUCTION

Melanomas are malignancy that arise from melanocytes and often metastasize to several organs. Metastatic melanoma to gastrointestinal tract unexpected identity which manifested asymptomatic course or nonspecific symptoms, that commonly remains undiagnosed in living patients. Duodenal metastasis from skin melanoma with pancreas invasion remain uncommon [1, 2]. Melanoma metastasis could befall in

the liver (42.9%), gastrointestinal region (20.7%), adrenal glands (8.5%), pancreas (2.3%), spleen (6.7%), or multiple spots (18.8%). Metastasis from stage IV melanoma was demonstrated to be the secondary malignancies for abdominal organ [3]. A case of duodenal metastasis with pancreas head invasion from the right thigh (lower limb) skin melanoma (Clark level IV) which was resected 3 years ago is analyzed and described as part of this paper. Melanoma excision was

associated with a right inguinal lymphadenectomy. The results are discussed and reviewed in reference to other publications.

2. CASE REPORT

A 62-year-old Caucasian female patient presented with high grade fever episodes and was admitted to Helios Hospital Pforzheim for further medical evaluation. A suspicious mass was unexpectedly discovered in the descending duodenum and head of pancreas during PET-CT scan, after extended surgical removal of skin melanoma located on the right thigh (lower limb). Removal of the melanoma was associated with a right inguinal lymphadenectomy, when the patient was 59 years old. Pathological evaluation at that time confirmed a malignant melanoma Clark level IV, pT2aN1bM0 as TNM-Staging, positive for BRAF-Wild-type by mutation analysis. A subsequent excision of skin melanoma from the back a region was carried out a couple of months after the initial surgery, with the

specimen classified/diagnosed as skin melanoma Clark level II, pT1a as TNM-Staging. After the surgery, the patient underwent chemotherapy and heavy particle radiotherapy. No suspect mass was identified on regular follow-up meeting. After Two years post-primary surgery, recurrence was registered in the scar on the right thigh (lower limb) and right inguinal site. Follow-up CT scans of the head, lung, and abdomen did not reveal any additional suspect masses. The patient received immunotherapy without additional chemotherapy or radiotherapy for the recurrent lesions.

Three years later, after the first melanoma removal, when the patient was 62-year-old, she underwent medical investigations after presenting to the hospital with high grade fever episodes.

A tumor mass was observed arising descending part of duodenum and pancreatic head from PET-CT scan (Figure 1).

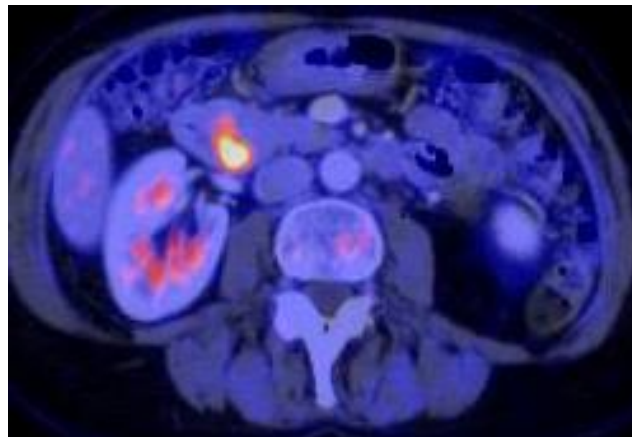


Figure 1: View of the mass in the duodenum/pancreatic head by PET-CT scan

Endoscopic examination with ultrasonography showed a 30 mm tumor mass originating from the descending portions of the duodenum which had invaded

the head of pancreas and caused loop obstruction (Figure 2).

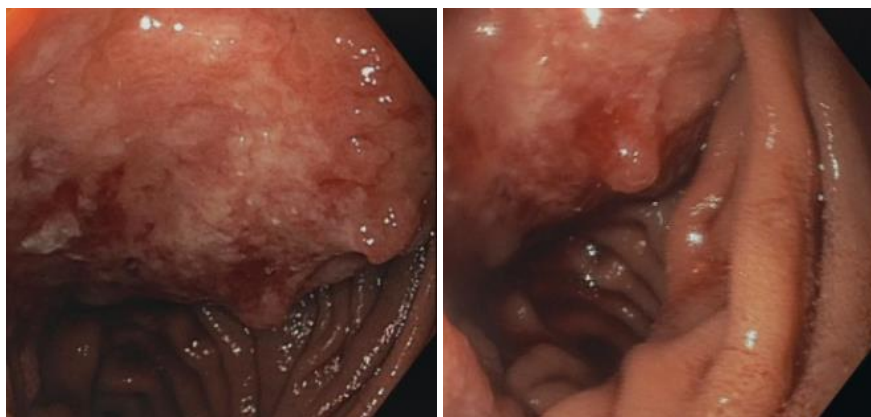


Figure 2: View of the tumor invasion in the duodenum by endoscopy

The biopsy revealed neoplastic cells with melanin granules and positive for Melan-A staining and SOX10 staining, suggesting existence of a metastatic

skin melanoma. No BRAF-Mutation was discovered, and colonoscopy did not reveal any tumors.

After tumor board procedure, the patient was recommended surgical resection, which she accepted. A pylorus preserving pancreaticoduodenectomy was conducted. In the surgically resected Whipple specimen, the tumor in duodenum and head of pancreas was approximate to 4 x 5 cm large, solid and ulcerated, with invasion and alteration of all duodenal layers and invasion of pancreatic parenchima. The mass was high solid and based of multiple nodules, although most of them were grayish and brownish. Hematoxylin-eosin staining revealed an infiltration by tumor cells inside duodenal mucosa (Figures 3 and 4). Histologically the tumor infiltrated all duodenal layers and the tissue around them.

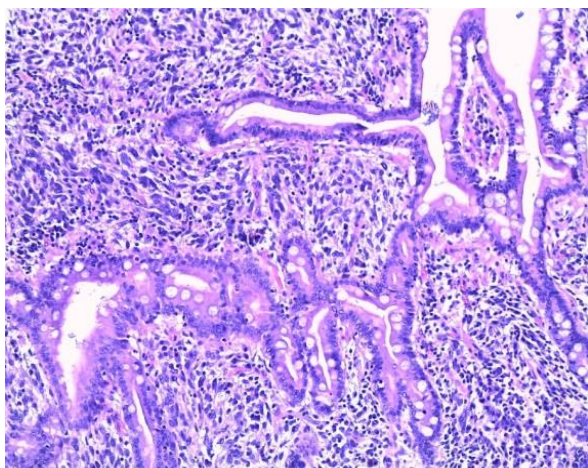


Figure 3: Tumor cells infiltration inside duodenal mucosa (10x10 hematoxylin-eosin staining)

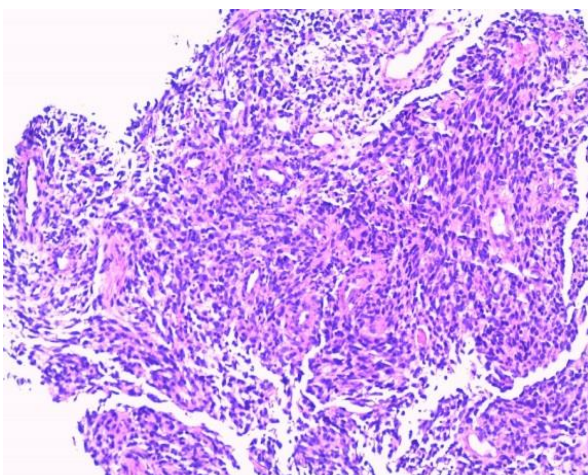


Figure 4: Tumor cells infiltration inside duodenal mucosa (10x10 hematoxylin-eosin staining)

A high-performance histological examination was performed to reach a valid and successful value of histology in the diagnosis of melanoma. Neoplastic cells were positive for expressing melanoma markers SOX10 and Melan-A stainings (Figures 5 and 6). Immunocytochemistry and electronic microscopy findings confirmed the diagnosis of malignant melanoma, similar to the skin specimen from the right

thigh. Therefore, the duodenal lesion was considered to be cutaneous melanoma metastasis from the right thigh.

In summary, the presence of melanoma was pathologically confirmed following intense medical evaluation, leading to the identification of a late-stage metastasizing skin melanoma which extended to the duodenum with involvement of the pancreas. Our patient was well informed about final histological results.

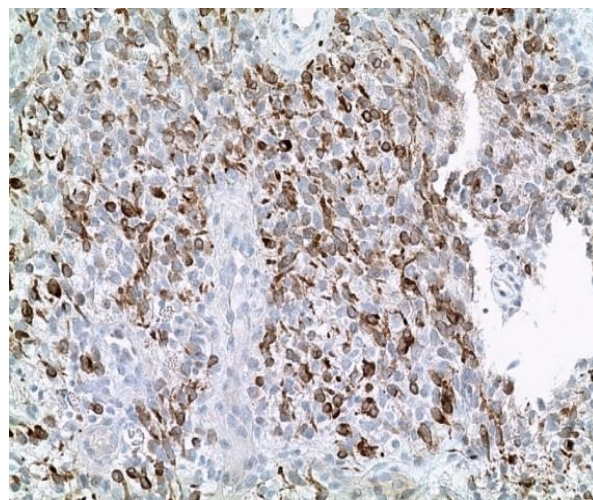


Figure 5: Expressing melanoma markers Melan-A (20x10 Melan-A staining)

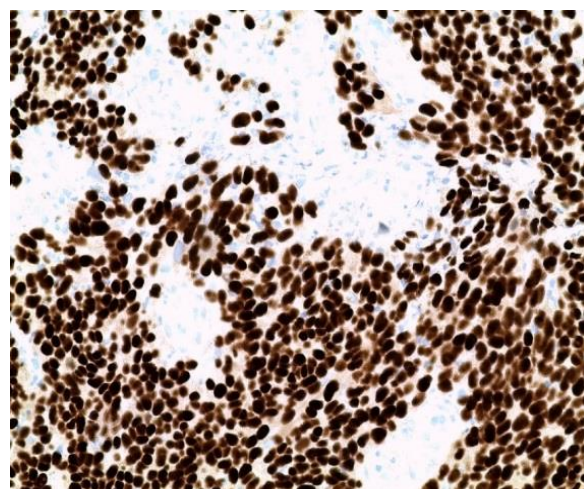


Figure 6: Expressing melanoma markers SOX10 (20x10 "SOX10" staining)

The postoperative course of the patient was favorable; therefore, she was discharged from the hospital after 13 days. An adjuvant chemotherapy was not performed because of previous immunotherapy. In this case we considered the therapy with adjuvant chemotherapy less worthy. Subsequently, she underwent immunotherapy with Ipilimumab and Nivoluma, and no recurrence was identified during the close monitoring of the patient in the 5-month follow-up period.

3. DISCUSSION

Due to increased patient access to health care in

Europe and the USA, the incidence and diagnosis of skin melanoma has rapidly increased in last decade; with mortality rates remaining alarmingly high [5]. The incidence rate in Asia, especially in Japan was reported to be 1-2 cases of melanoma per 100,000 persons per year [3, 9].

Pathological origin of melanoma arising from pigment-containing cells, mainly located in the cutaneous tissue. The highly aggressive nature of primary tumors is strongly correlated with excessive exposure to sunlight, with 90% of cases occurring on the skin. As the gastrointestinal tract, mucosa eyes and meninges containing melanocytes, melanoma can also develop in those tissues [4, 5]. Melanoma commonly metastasize to skin, lymph nodes, and the digestive system with rare occurrences to the lung, the liver, the brain, and [6].

Stage 4 is the most advanced phase of the tumor and means the cancer has spread to distant regions of the body, beyond the regional lymph nodes. The most commonly sites to abdominal organ metastasis from stage 4 melanoma were registered to the liver with 42.9%, gastrointestinal tract 20.7%, adrenal gland tissue 8.5%, pancreas 2.3%, spleen 6.7%, or multiple sites 18.8% [3].

The spread of cancer to the gastrointestinal system typically progresses without noticeable symptoms or mild manifestations; symptoms often become apparent only when complications arise.

Corresponding to post-mortem evidence, metastasizing melanoma to small bowel, colon or stomach are the most frequent localizations representing more than half in cadaveric studies, and usually suggesting the expression of an advanced and widespread disease [4, 5]. Alone 1–9% of overall metastasizing cutaneous melanoma to gastrointestinal organs are diagnosed during lifetime [5, 7, 8]. During diagnosis, in more than 50% of patients, extraintestinal metastases are already identified [10]. Assuming, intestinal metastases frequently arise 3–6 years after primary excision of skin melanoma.

Our patient presented with some lymph nodes from the right inguinal region at the time of primary cutaneous excision on the right thigh (lower limb). In our case report, a duodenal metastasis from melanoma was diagnosed, 3 years after primary skin melanoma surgical excision. Gastrointestinal metastases are from time to time present at primary skin examination or six months after detection [10-12]. Asymptomatic period between surgical skin excision of primary melanoma and the diagnosis of gastrointestinal metastases lasts between 6-90 months, as documented by previous research [13, 14]. This report described recurrent unclear episodes of fever, without digestive manifestation. Those episodes were described three years later after the primary melanoma

excision. Because of persistent high grade fever episodes, our patient underwent a screening investigation using PET-CT-scan. A very high suspicious mass of tumor was indirectly identified and described in the descending duodenum and head of pancreas after PET-CT scan. Diagnosis of duodenal metastasis from skin melanoma was confirmed after tissue sample during upper endoscopy. After colonoscopy, no tumor was identified.

Due to higher sensitivity and specificity, detection of metastasizing skin melanoma to gastrointestinal organs is better realized by performing whole-body PET-CT imaging with fluorodeoxyglucose compared to conventional CT scan [15]. Many specialists recommend that PET-CT should be the main staging study for recurrent disease [16]. The sensitivity rate of CT scan for detection of intestinal melanoma lay by 60-70% [12]. Complete endoscopic examination of the duodenum associated with endosonography and biopsy is non-invasive, and is a mandatory procedure for diagnosis of duodenal tumors [17]. Colonoscopy is also mandatory to exclude other conditions. Anyway, the small bowel tract is not easily examined by endoscopy. The sensitivity to detect metastatic tumors to the small bowel is very often limited [18, 19].

This study recommends utilizing a combination of imaging modalities and endoscopic procedures to enhance the accuracy of diagnostics, resulting in improved patient outcomes. The final diagnosis is made by histological examination. Immunohistochemistry is the most common application of immunostaining. Immunohistochemistry Staining, such as SOX10 and Melan-A, are used in histology to detect the presence of specific protein markers, which supports the classification of tumor with high accuracy, in this case study, certifying the diagnosis of metastatic melanoma. Precise preoperative diagnosis and evaluation of the extent to intestinal metastases, including neighboring organ invasion such pancreas, is essential when selecting patients for surgery, or planning the surgical procedure [12]. Surgical removal is the treatment of choice in all patients with resectable metastasizing melanoma to the gastrointestinal tract.

Immunotherapy is the first-line non-surgical therapeutic approach. It is recommended by eligible patients with histologically confirmed metastatic melanoma and positive BRAF-mutant. A durable clinical benefit was demonstrated with combination of immunotherapy and chemotherapy, radiotherapy, or targeted molecular therapy. Immunotherapy is better tolerated compared to common chemotherapy [20]. Immunotherapy with Nivolumab, vemurafenib, ipilimumab, and trametinib (mekinist), have been authorized in Europe for therapy of metastasizing melanoma.

Despite the fact that the patient did not receive

adjuvant chemotherapy due to later identification of the medical cause, similar patients who did receive these medical agents have shown improved outcomes.

Regular *medical* follow-up visits, which may include a physical exam, blood tests, and imaging tests are mandatory.

Despite modern diagnostic techniques, premature detection of melanoma metastasis to small bowel remains a laborious challenge for medicine.

Patients with a history of cutaneous melanoma who present unspecific clinical image should be investigated to prevent gastrointestinal metastases. Metastasizing intestinal skin melanoma to the small bowel exposes late set of symptoms in evolution of the disease, estimating a low chance of recovery and survival.

4. CONCLUSION

Given the latest development in radiology, imaging and endoscopy, preoperative assessment of duodenal metastases extent using superior endoscopy with biopsy, associating CT-scan and PET-CT are very important for determining clinical tactics.

However, to date, the treatment for advanced cutaneous melanoma is still unclear, although surgical removal is the treatment of choice in all patients with resectable metastasizing to the gastrointestinal tract.

A high degree of suspicion is required to make an advanced pre-operative diagnosis of metastasizing skin melanoma to the duodenum, even if another acute accompanying symptom was reported.

PET-CT scan should be done in patients with a history of metastasizing cutaneous melanoma and nonspecific symptoms.

Author Contributions

1. Dr. Ovidiu-Angel Matei: preparing manuscript, review.
2. Dr. Lorena Matei: preparing manuscript, design, translate.

Conflict of Interest: No conflict of interest was declared. All authors read and approved the final manuscript.

Ethical Standards Compliance

The patient was informed according with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Human rights All procedures have been performed and the patient gave her permission.

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