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Metastatic lesions in the gastroduodenum - an unusual manifestation of malignant melanoma and pulmonary adenocarcinoma

Case Report

Daniela Benedeto-Stojanov*[1,2], Goran Bjelaković[1,2], Maja Milentijević[2,3], Dragan Stojanov[2,4], Vesna Brzački[1,2], Gordana Petrović[1]

1 Clinic of gastroenterology and hepatology, Clinical Center Nis, 18000 Nis, Serbia

2 Medical faculty, University of Nis, 18000 Nis, Serbia

3 Institute of pathology, Clinical Center Nis, 18000 Nis, Serbia

4 Institute of radiology, Clinical Center Nis, 18000 Nis, Serbia

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Abstract: The gastrointestinal tract (GIT) is an unusual site for metastasis. The rate of GIT metastases detected clinically is very low because of unspecific symptoms and signs of GIT involvement, which include general weakness, tiredness, weight loss, unspecific abdominal pain, fatigue, and anemia. We report clinical, endoscopic, and pathological patterns of two patients (malignant melanoma and primary lung tumor) with metastatic lesions in the gastroduodenum. The first case is a 59-year-old man with unspecific symptoms as nausea, vomiting and abdominal pain. He underwent resection of skin melanoma on his back one year before. Upper gastrointestinal endoscopy revealed two melanotic polypoid masses with ulcerations at the tip, one in the stomach and one in the duodenal bulb. Endoscopic biopsy of these polypoid masses and immunohistochemical stains confirmed the diagnosis of metastatic malignant melanoma. The second case is a 73-year-old man with a two-day history of melena and unspecific abdominal pain. Three weeks before, the patient was operated on for the adenocarcinoma of the lung. Endoscopy of the upper gastrointestinal tract revealed irregular polypoid mass with ulcerations at the tip: three of the stomach mucosa, two in the duodenal bulb and more than ten hemorrhagic polypoid masses at the desendent duodenum. Biopsies of these lesions confirmed the diagnosis of metastatic lung adenocarcinoma. In patients with a history of malignant melanoma and lung cancer unspecific symptoms, like abdominal pain, anemia, and gastrointestinal bleeding gastroduodenal metastases should be suspected. The diagnosis requires careful endoscopic examinations of the mucosa for metastatic lesions and biopsy with special immunohistochemical stains.

Keywords: *Gastroduodenal metastases • Malignant melanoma • Pulmonary adenocarcinoma*

1. Introduction

Gastrointestinal tract (GIT) is an unusual site for metastasis [1-4]. Information on gastrointestinal metastases is generally limited to single case reports. The diagnosis is often delayed because most patients have nonspecific symptoms. GIT metastases can appear in various morphological forms and can mimic simple polyps endoscopically. The diagnosis requires the biopsy of lesions and special immunohistochemical stains.

We report clinical, endoscopic, and pathological patterns of two patients with malignant melanoma and primary lung tumor with metastatic lesions in the gastroduodenum.

* *E-mail: dbenedetostojanov@gmail.com*

2. Case report

A 59-year-old man was admitted to the Clinic of gastroenterology and hepatology with a five-day history of nausea, vomiting, and unspecific abdominal pain. His past medical history was significant for skin melanoma of the right side of the back. The tumor had been completely excised one year before, and microscopic examination confirmed a diagnosis of malignant melanoma, Clark IV, Breslow III. Physical examination revealed lymph nodes enlargement in the right axilla and epigastric tendereness on palpation. White blood cell count, hematocrit, serum electrolytes, urea, creatinine and liver enzymes were within normal limits. Abdominal ultrasonography showed liver steatosis with no evidence of liver or intraabdominal metastases. A chest x-ray and brain computer tomography was unremarkable for metastases. Upper gastrointestinal endoscopy revealed two melanotic polypoid masses with ulcerations at the tip, first in the corpus of the stomach (Figure 1) and the second in the duodenal bulb. The diagnosis of malignant melanoma metastases was confirmed by pathological examination of endoscopic biopsies, using immunohistochemistry. The presence of markers known to be important in the diagnosis of malignant melanoma, including HMB45, Melan-A, S-100 protein, CD63 and vimentin was detected. The melanoma cells exhibited marked nuclear and cytoplasmic pleomorphism and frequent mitoses; many cells contained severe amounts of melanin pigment (Figure 2).

The patient was sent to the medical oncology department for follow-up and treatment.

The second case is a 73-year-old man who was admitted to our hospital with a two-day history of melena and unspecific abdominal pain. Three weeks before, the patient was operated on for the adenocarcinoma of the lung with pleural metastases. He was a cigarette smoker for 50 years, smoking 20 cigarettes per day. He had an operation on nevus in the left axila eight years ago. His father died of lung cancer. On physical examination he was pale, with normal blood pressure and pulse

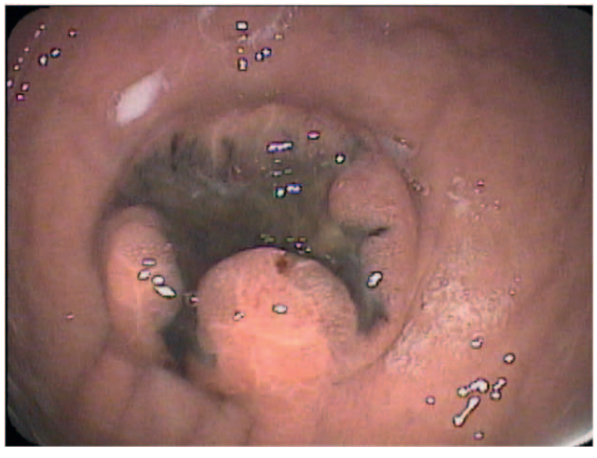

Figure 1. Polipoid melanotic mass with tip ulceration in the stomach

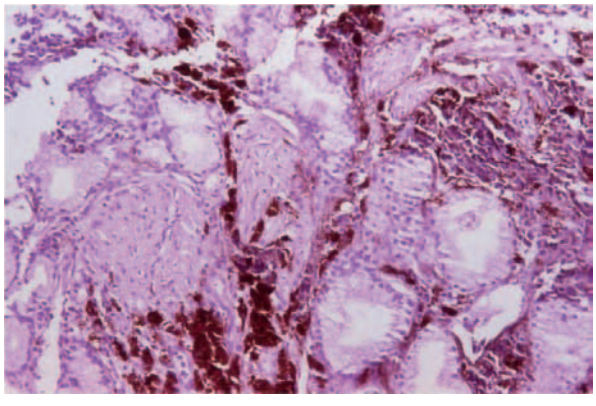

Figure 2. Malignant melanoma metastases in the stomach with abundant melanin pigment (H.E.)

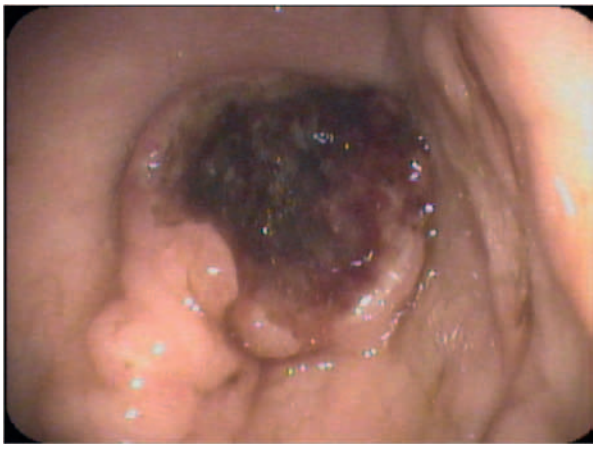

Figure 3. Metastatic lesion of the lungadenocarcinoma in the antrum with ulceration at the tip

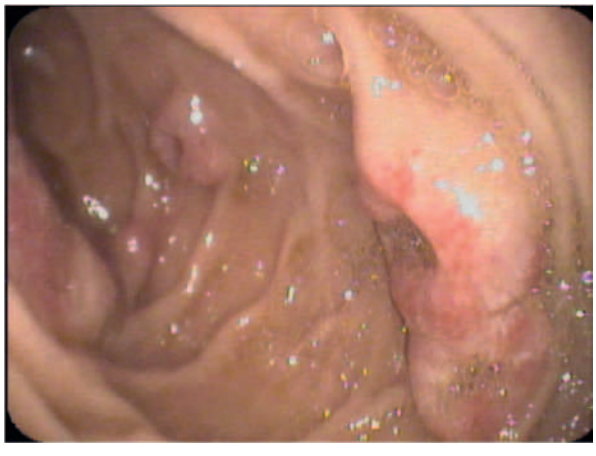

Figure 4. Metastatic lesions of the lung adenocarcinoma at the descendent duodenum

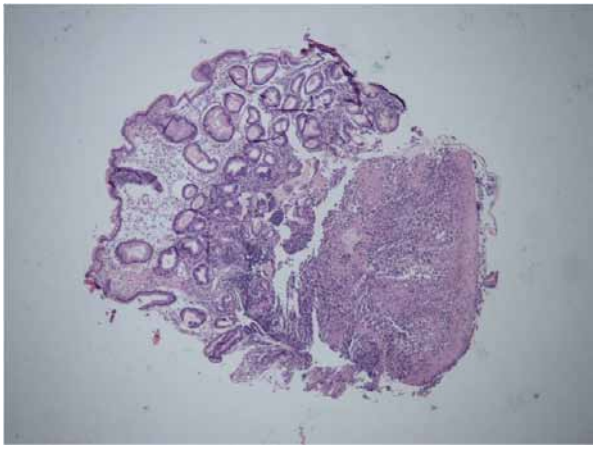

Figure 5. Metastatic deposit of the lung adenocarcinoma in the antrum (H.E.)

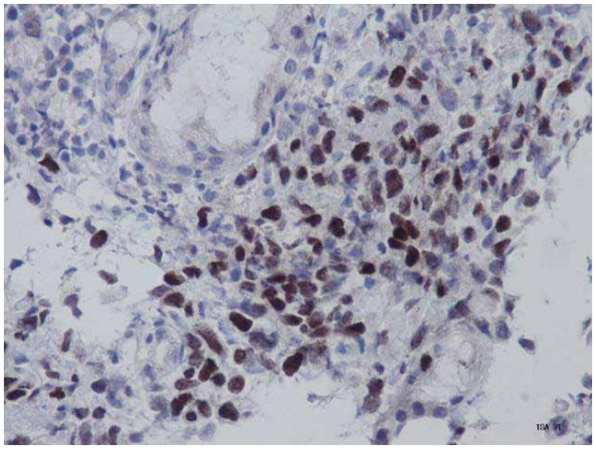

Figure 6. Metastatic cells (primary lung adenocarcinoma) stained with TTF-1 (immunohistochemistry)

rate. He had epigastric pain on palpation. Melena was proved by digital examination. Hematocrit was 26% and hemoglobin 8.2 g/dL. Endoscopy of the upper gastrointestinal tract revealed 3 irregular, nodular protrusions of the stomach mucosa with ulcerations at the tip 0.6 cm to 2.5 cm in diameter: one subcardial localized and two in the antrum (Figure 3). In the duodenal bulb two polypoid masses with ulcerations at the tip were found. At the desendent duodenum there were more than ten hemorrhagic polypoid masses about 1.5 cm in diameter (Figure 4). These findings were consistent with metastatic disease. The biopsies of antral lesions revealed poorly-differentiated neoplastic cells invading the mucosal bed and extending into the mucosal glands with sparing of the superficial epithelium (Figure 5). Infiltration of the lymph vessels was also noted. Immunohistochemical staining for CK 7 and thyroid transcription factor 1 (TTF-1) strongly supported the diagnosis of poorly-differentiated metastatic adenocarcinoma of the lung (Figure 6). All other keratins (CK 20, CK 5/6, CKHMW) were negative.

Staging of the disease followed by CT scan of the upper abdomen showed an ill defined hypodense tumor lesion in the pancreas head and duodenal flexure, as well as a tumor lesion in the antrum 2.8 cm in diameter. Retroperitoneal lymph nodes were enlarged up to 20 mm in diameter.

The patient was transfused with packed erythrocytes and fresh frozen plasma, and sent to the medical oncology department for follow-up and treatment.

3. Discussion

GIT is unusual site for metastases [1-4]. The common primary tumors that metastazises to the GIT are malignant melanoma, lung, breast, and esophagus [4]. Malignant melanoma is the most common tumor that metastazises to the GIT [4-6]. The small bowel is the most common site of GIT for melanoma metastases (35%-97%), followed by the colon, stomach and duodenum, oral cavity and esophagus [6-10]. One third of patients with metastases have two or more parts of the GIT involved.

Malignant melanoma metastases in the GIT are found in more than 60% of autopsies on patients who have died with disseminated melanoma; however, the rate of GIT metastases detected clinically averages only 2% [11]. This discrepancy seems to be attributed to the nonspecific symptoms and signs of GIT involvement, which include general weakness, tiredness, weight loss, unspecific abdominal pain, fatigue, and anemia [9,11-13].

Clinical presentation could be an acute abdominal emergency such as a bowel obstruction, intussusception, bleeding and perforation [9,14]. The patient described in case 1 had nausea, vomiting, and unspecific abdominal pain.

The primary melanoma usually occurs on the skin, retina, anal canal or occasionally at other organs such as the esophagus, penis or vagina [15]. Primary lesion is occult in 10%-26% of the cases [16].

The average time from the diagnosis of the primary tumor to the detection of GIT metastases

is 43.8 ± 11.3 months (range 21.6–54) [11]. It varies from 2 months up to 12 years. Metastases may present both at the time of primary diagnosis or decades later as the first sign of recurrence. Metastases to the GIT have been reported up to 26 years after the initial presentation of the melanoma [12]. Gastroduodenal metastases appeared in our patient one year after the operation from primary malignant melanoma.

Endoscopic appearances of metastases might take one of several forms: multiple small submucosal nodules, multiple ulcerated polypoid lesions, and large extrinsic tumor mass. These lesions could be melanotic and easily recognizable or amelanotic and therefore difficult to differentiate from other sources of metastases or tumors, e.g. mucosa-associated lymphoid tissue (MALT) lymphoma. Diagnosis requires careful endoscopic inspection of the mucosa for metastatic lesions and biopsy with special immunohistochemical stains. Immunohistochemistry is often useful in distinguishing between a malignant melanoma and other malignancies.

Because it is the most common subtype of melanoma, superficial spreading melanoma is the most common subtype to metastasize to the GIT, although all the histological subtypes of cutaneous melanoma may metastasize to the GIT [17].

Clinical characteristics associated with increased risk of disease progression in thin cutaneous melanomas included male patients and patients with lentigo maligna melanoma or acrolentiginous melanoma, which may be explained by their frequent location in the head and neck region [18]. Other authors have also found axial primary tumor site, Clark level III or IV, severe histological regression, ulceration, and high mitotic rate to be significant prognostic risk factors for disease progression in thin melanomas (variably defined as <0.76 mm, <0.5 mm, or <1.0 mm) [19,20]. The risk of melanoma spread to the GIT is higher among patients with a primary lesion classified as Clark III or above, occurring in 70%–100% of such patients, whereas it occurs in 5%–24% of the patients with Clark II and 0%–6% of the patients with Clark I. These characteristics are consistent with our patient, whose primary melanoma was located on the back and graded as Clark IV, Breslow III.

In most cases of malignant melanoma, recurrence and death occur within 10 years after treatment of the primary lesion [15,17,18]. The prognosis of patients with metastatic malignant melanoma is very poor. The median survival time for melanoma patients presenting with gastrointestinal invasion is less than one year [18,20]. The high mortality rate observed in these patients is associated with multiple metastases to other organs, such as the lung, liver, pancreas, spleen, endocrine glands, and the brain [21,22].

Pulmonary adenocarcinoma is one of the major types of primary lung cancers accounting for approximately one third of all primary pulmonary cancers. Metastasis is not uncommon in pulmonary neoplasms. The most common sites of pulmonal cancer metastases are:

adrenal glands (35% of cases), pancreas (up to 18% of cases), the skin (up to 12% of cases), CNS (up to 18% of cases) and the pleura (33% of cases) [23].

The lung cancers infrequently metastasize to the pancreas up to 0-18% in different

studies. The incidence of secondary pancreatic tumors has been reported in 15% of autopsy studies [24]. The majority of patients with pancreatic metastasis have small-cell lung cancer (10% cases), while among patients with adenocarcinoma only 2.3% cases [25]. Our patient had a lung adenocarcinoma.

The reported incidence of GI metastasis from lung cancer varies from 0.5%-10%, and mainly depends on the evaluation method used (endoscopy, surgical specimens, or autopsy) [26,27].

Gastric and/or duodenal metastases from lung cancer are very rare, and there are only a few cases of varying malignant cell types reported in the literature [28,29]. In contrast to the small bowel, the most common metastatic site of lung cancer is the GI tract [30,31], and there have been a few reports of lung cancer metastases to the colon, appendix, or anus [32-35].

GIT involvement with lung cancer is generally considered to be associated with a late or advanced stage of the disease. We report a case of advanced stage of pulmonary adenocarcinoma with multiple gastroduodenal, pleural, pancreatic and peritoneal metastases.

The typical presentations of GI metastases are abdominal pain, bleeding, obstruction, and perforation. Gastric and/or duodenal metastases from lung cancer exhibited symptoms of abdominal pain, anemia, chronic bleeding, melena, or hematemesis [28,29,36]. Small intestine involvement often leads to acute abdomal pain as a result of perforation or obstruction [26,30,37], whereas colon metastases usually result in vague symptoms.

In our cases of gastroduodenal metastases, patient had melena and unspecific abdominal pain.

Even with endoscopy, lung cancer involving the GIT has no specific features, appearing as a diffuse involvement of the mucosa and multiple nodules with or without mucosa ulceration [38]. An experienced pathologist might be able to conclude a metastatic tumor based on morphological study of tumor tissue from surgical resection. However, in most cases histological examination with immunostaining using cell type-specific markers is the only way to identify metastatic tumors of the GI tract. Several different CK and other protein markers are widely used to distinguish carcinomas of different origins. Rossi et al concluded that lung carcinomas usually demonstrate a CK7+/CK20- immunoprofile, whereas intestinal carcinomas have a different CK7-/CK20+ pattern [38]. Thus, CK7 is a good marker for distinguishing those cell types. In general, primary lung adenocarcinoma can be identified by CK7; however, studies have demonstrated that primary adenocarcinomas of the rectum or small intestine may also express

CK7 in a significant number of cases, and may even lose CK20 expression [39,40]. Therefore, to exclude a possibility like this, employing a more specific marker of lung tumor origin, such as TTF-1 [41], together with CK7 and CK20 could more effectively differentiate metastatic GI tumors from lung cancer.

Every type of lung cancer can result in GI metastasis. Berger et al reported that squamous cell carcinoma causes small bowel metastases more frequently than other lung tumor cell types [26]. Garwood et al reported that adenocarcinoma (23.7%) and squamous cell carcinoma (22.7%) were the most common histological types causing small bowel perforations. In our case squamous marker (CK5/6) was negative [30].

4. Conclusion

Gastroduodenal metastases are an unusual manifestation of malignant melanoma and lung cancer. Unspecific symptoms like abdominal pain, anemia, and gastrointestinal bleeding are highly suspicious for gastroduodenal metastases. Information on the patient's clinical history is useful for the correct diagnosis.

Diagnosis requires careful endoscopic examination of the mucosa for metastatic lesions and biopsy with special immunohistochemical stains.

Conflict of interest statement

Authors state no conflict of interest.

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