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Case report

A 64-year-old woman was hospitalized at an internal care unit, due to growing weakness, dizziness, lack of appetite, anemia and abdominal pain. In anamnesis: past myocardial infarction, post-operative hypothyroidism, type 2 diabetes insulin-dependent, stroke, left kidney cirrhosis, gout and anemia. The physical examination did not reveal pathological changes except for skin paleness. The biochemical tests showed iron deficiency anemia and elevated Ca 125 (54.5 U/ml) (normal range: 0.00–35.00). Other markers were normal. An abdominal CT revealed a bifocal infiltration of the small intestine. Due to the increasing obstruction symptoms, the patient was operated on. A bifocal small bowel tumor was found intra-surgically. A partial resection of the jejunum and distal ileum was made. The intestines were joined end to end. The histopathological diagnosis corresponded to metastases of malignant melanoma. The post-operative course was uncomplicated. She received two cycles of dacarbazine 1000 mg/day. Due to drug intolerance, the chemotherapy was discontinued. Now, she is receiving hospice care.

Key words: metastatic melanoma, unknown primary, mechanical obstruction.

Bifocal metastasis of melanoma to the small intestine from an unknown primary with intestinal obstruction – case report

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Introduction

Melanoma is a malignant tumor originating in neuroectodermal melanocytes. According to the AJCC (American Joint Committee on Cancer), metastatic melanoma of unknown primary (MUP) can be diagnosed when a histopathological examination confirms the metastatic nature of the melanoma and all diagnostic tests aiming to determine the primary site are negative [1]. Metastases of melanoma of unknown primary are a difficult diagnostic and therapeutic issue. The course of the disease and the survival time vary from long-term remission and cure to the patient's imminent death. Some researchers claim that patients with MUP have a better prognosis for survival than ones with known primary melanoma [2, 3].

The standardized incidence rate in Poland is 4 per 100,000, which corresponds to about 2200 cases a year – ca. 1000 in men and ca. 1200 in women. The median age is similar for both sexes and equals 51 years. The standardized mortality rate is 2 per 100,000 in men and 1.2 per 100,000 in women, which, in terms of the number of deaths from melanoma, corresponds to 500 in men and 400 in women [4].

The factors which significantly increase the risk of occurrence are:

- intense exposure to ultraviolet radiation (UV),
- constant mechanical or chemical irritation,
- low pigment content in the skin,
- genetic risk [5].

Case report

A woman, 64 years old, weight 55 kg, height 158 cm, was readmitted to the Internal Care Unit on 20.01.2011, because of growing weakness, dizziness, getting tired quickly, lack of appetite and anemia. Based on the medical history and the collected medical documentation, the following was stated: previous myocardial infarction, condition following PTCA of CX (two implants), post-operative hypothyroidism (the patient underwent surgery for toxic thyroid goiter), type 2 diabetes insulin-dependent, previous stroke, left kidney cirrhosis, gout and iron deficiency anemia. The physical examination did not reveal pathological changes except for skin paleness. Blood pressure 100/60, pulse 60/min, body temperature 36.5°C. During the patient's stay, having performed biochemical tests, the following was found: anemia, tumor markers CA, CEA, CA 19-9, Ca 15-3 (normal), elevated Ca 125 – 54.5 U/ml (normal range: 0.00–35.00), function of the right kidney (no deviation from the norm), urine culture and fecal occult blood test (negative).

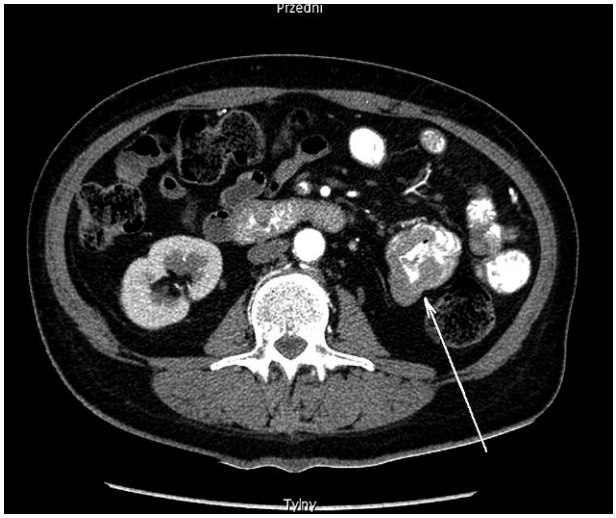

Fig. 1. CT abdomen following contrast. A tumor of the distal intestine (white arrow)

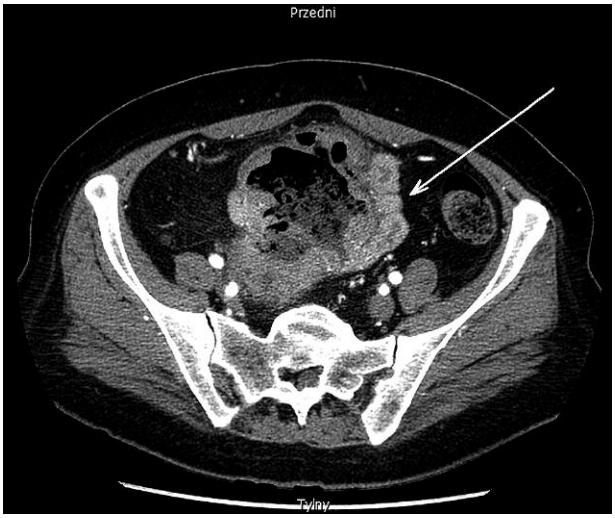

Fig. 2. CT abdomen following contrast media administration. A tumor of the jejunum (white arrow)

Ophthalmological consultation showed absence of pathology of the eyes.

The gynecological examination did not reveal any pathology. The gastroscopic examination and colonoscopy were without deviation from the norm. Because of colic-like abdominal pains abdomen CT was performed, which revealed in the minor pelvis a tumorous widening of the ileum and thickening of the wall, with the adjacent bowel loops surrounding. The lesion's approximate dimensions were about 12 × × 9 × 11.5 cm (wall thickness up to 2 cm) (Fig. 1). In addition, thickened wall of the jejunum was visible; in its initial section, on the left hand side, the wall thickness was up to 13 mm along up to 40 mm; it intensified following contrast media administration from ca. 36 jH to 69 jH (Fig. 2). The CT image suggests a bifocal neoplastic infiltration of the small intestine. The mesenteric lymph nodes slightly enlarged up to 10 mm. The stomach was distended, with thickening of the pyloric wall up to 12 mm. The liver, pancreas and spleen were not enlarged, with no focal changes. There was no lodgment in the gallbladder, and the bile ducts were not widened. The left kidney was small, cirrhotic. The right kidney was hypertrophic, the secretory function was maintained, and there were no focal changes, urinary retention or lodgment. The urinary bladder had smooth walls. The uterine appendages were without noticeable change. No dilation of the abdominal aorta or occurrence of atherosclerotic plaques was seen. The examination did not demonstrate significantly enlarged lymph glands, or existence of free abdominal fluid. The osseous structures showed no destruction foci.

The patient underwent operation on 2.02.2011. The following was found intra-surgically: one tumor in the middle of the jejunum, demonstrating subobstruction; another tumor, showing signs of necrosis, dragging the ileal loop, with characteristics of obstruction, featuring a perisigmoidal infiltration, but without obstruction and deficient blood supply to this section of the sigmoid. Having separated these from the sigmoid, both sections of the small bowel were excised and the intestine was joined end to end. The postoperative course

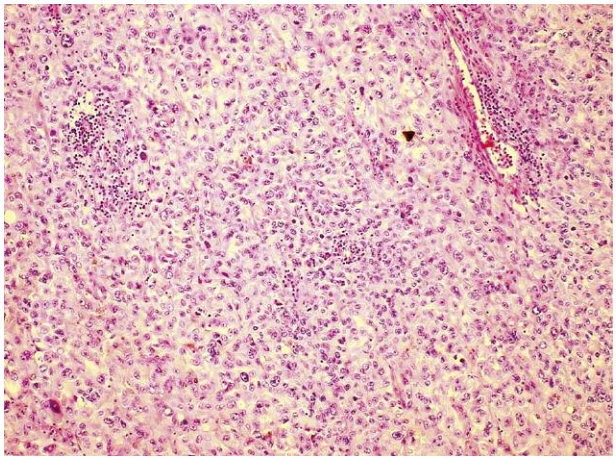

Fig. 3. The tumor of the small intestine – the melanoma cells with round and oval nuclei, some with visible, large nucleoli, pale, "epithelioid" cytoplasm, no creation of organoid, glandular structures. A few cells feature brown dye – melanin

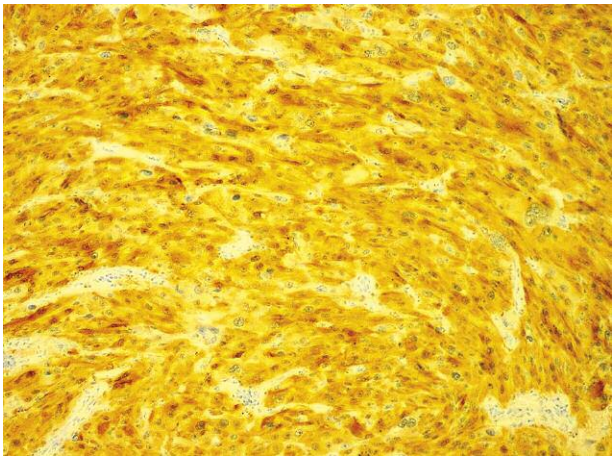

Fig. 4. Immunohistochemical staining (reaction for S-100), also positive in a majority of cells, confirms the diagnosis of melanoma

was uncomplicated. On the tenth day the patient was discharged from hospital and oncologic treatment was recommended. The histopathological examination no.: 8968/2011. The histopathological diagnosis based on the results of the immunohistochemical examination corresponds to metastases of malignant melanoma. The markers: CK(–), EMA(–), Vim(+), S100(+), CD34(–), CD117(+), Ki(–), LCA(–), SMA(–), HMB(+) (Figs. 3, 4). The mesenteric lymph nodes – lymphonodulitis. The edges of the intestinal resection were without neoplastic lesions.Following an oncologic consultation, the patient was qualified for chemotherapy; then she received two cycles of decarbazine, 1000 mg/day. The chemotherapy was discontinued due to drug intolerance. At present she is under the supervision of hospice care.

Discussion

Primary intestinal melanoma occurs extremely rarely because it develops from melanocytic cells, which do not occur in the intestine.

However, it may occur occasionally, as well as in the respiratory tract or in the lymph nodes, which may be a confirmation of the theory of primary melanoma in these organs [6, 7].

Melanocytes located in these organs originate from melanoblastic cells of the neural crest.

During embryogenesis they migrate to the organism through the umbilical-mesenteric canal and in the next stage diversify into specialized cells.

According to Mishima *et al*., an intestinal melanoma may develop from neuroblastic cells related to autonomous innervation of the intestine.

In the alimentary tract melanoblasts diversify to the APUD cell system and after cancer transformation may lead to gastrinoma, carcinoid and melanoma [8].

Intestinal metastases of melanoma are rare. They are most frequently observed in cases of malignant melanoma. In patients who died as a result of melanoma spread, intestinal metastases have been found in 43.5–86.3% of the cases. They have been the leading cause of death only in 1/3 of the patients, however [9]. Out of several theories, as suggested, explaining the causes of metastatic melanoma of unknown primary, the most popular one is the theory of regression of the primary site for immunological reasons. Among other causes, one may list neoplastic transformation of ectopic cells, pigmented cells, non-diagnosis of the melanoma during a physical examination or excision of moles without a histopathological examination [10].

From all types of cancers, metastases to all organs and systems are predominantly observed in melanoma.

Annual survival of patients with metastases of melanoma to the skin and subcutaneous tissue or distant group of lymph nodes is observed at the level of 59% and 57% in the group of patients with metastases to the lung. The lowest rate is observed in patients with metastases to other visceral organs (41%).

Patients who had single or multiple metastases removed have the longest survival [9].

Intestinal metastases of melanoma are diagnosed relatively seldom – in about 1.5 to 4% of cases. On the other hand, autopsies demonstrate a much more common occurrence of them – in as many as 58% of the cases. Intestinal metastases are most frequently to the small intestine (35%), and the large intestine (14.5%); metastatic tumors in the stomach are a relatively rare occurrence (7%) [10]. Clinical symptoms are non-characteristic. The following may occur: constipation, stomach ache, nausea, vomiting and weight loss. In some cases they may result in intestinal perforation, obstruction and/or bleeding. In cases where melanoma is located in the gastrointestinal tract, one may distinguish between three types of lesions: nodal, restricted and infiltrative ones. Infiltrative lesions are characterized by a higher risk of bleeding. More frequently metastatic melanoma are polypous, multitudinous and non-pigmented structures; due to their size, they may trigger obstruction, as in the case under discussion. The primary site is most often skin lesions, already diagnosed. In 4–12% of cases of intestinal metastases of melanoma, it is, however, impossible to determine the location and nature of the primary lesion[11].

Surgical treatment of gastrointestinal melanoma metastases was not long ago undertaken in life-threatening situations, such as bleeding, perforation or obstruction. The results of retrospective studies done over the last decade do not confirm the above principle [12–14].

Introduction of the planned surgery in order to perform a remedial resection of the primary lesion or gastrointestinal melanoma metastases has resulted in a statistically significant prolongation of patients' survival times, as compared to ones who are only treated pharmacologically or subjected to palliative surgery [11, 15–17].

The authors declare no conflict of interest.

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