MELANOMA OF UNKNOWN PRIMARY AS A CAUSE OF INTESTINAL OBSTRUCTION – A CASE DESCRIPTION

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Melanoma of unknown primary applies to 1-8% of all diagnosed melanomas, whereas primary melanoma of the small intestine is an extremely rare case. One of the melanoma characteristics is its capability of forming metastases in the small intestine which very often are diagnosed during autopsy. We present a case report of diagnosed melanoma of unknown primary, whose first symptom was intestinal obstruction. Before admission to the hospital cause of intestinal obstruction, the patient didn’t present any signs and symptoms. All typical localizations of primary melanoma were excluded during diagnostic procedure. Palliative right hemicolectomy and segmental small intestine resection were performed. There were no complications in the postoperative course. On the ninth day the patient was discharged from hospital.

Quick identification and radical resection of melanoma metastases in the alimentary tract may improve the survival rate in this group of patients. Resection, even if it is palliative by assumption, is not only the best method of elimination of persistent symptoms but it also gives hope for longer survival.

Key words: melanoma of unknown primary, intestinal obstruction

Melanoma is a malignant tumour of melanocytic origin. The primary focus of this cancer is usually diagnosed on the skin, eyeball or anus. Unfortunately, in spite of precise diagnostics it is impossible to locate the primary site of the tumour. Melanoma of unknown primary applies to 1-8% of all diagnosed melanomas (1, 2, 3). It is usually diagnosed when patients can observe clinical symptoms in the form of metastases. In order to make a definite diagnosis of melanoma of unknown primary it is necessary to confirm the presence of metastases histopathologically and to exclude all possible locations of the primary focus. There are several theories attempting to explain the aetiology of melanoma of unknown primary (2, 3). The first is a spontaneous regression of the primary focus as an effect of the immune system and the other is a malignant transformation of individual melanocytes, which enter a lymph node without forming a focus within any organ (2, 3). The biological behaviour of the tumour is similar to cases with known location of the primary focus. Some authors suggest that patients with metastases to lymph nodes without identified origin have better prognosis than patients with a known primary focus (3).

Primary small intestine melanoma is an extremely rare diagnosis of unknown aetiology. It is known that the melanoma develops as a result of numerous melanocytic mutations, which do not occur within the alimentary tract. Apart from that, the small intestine is not exposed to UV radiation. According to Mishima, an intestinal melanoma may develop from neuroblastic cells related with autonomous innervation of the intestine (4).

Another theory assumes the development of melanoma from melanoblastic cells, which during embryogenesis migrate from the neural crest to the intestine (5). However, regardless of the development of melanoma in the small intestine, it is very difficult to diagnose if it is a primary or metastatic intestinal melanoma.
In many situations it is impossible to differentiate. Some authors even think that primary intestinal melanoma does not exist (6, 7). The suggested criteria of diagnosis of primary intestinal melanoma are as follows: absence of another location of melanoma and atypical cutaneous naevi, a lesion located only within the small intestine, without distant metastases and the presence of a primary focus in the mucosa (8).

One of the melanoma characteristics is its capability of forming metastases in the small intestine. Due to the absence of clinical manifestation the metastases are often diagnosed on the basis of autopsy examinations. Having conducted autopsies on 216 patients with advanced melanoma, metastases in the small intestine were diagnosed in 35.6% (9). A similar analysis of autopsies on patients with advanced melanoma conducted at Memorial Sloan Kettering Cancer Center shows that metastases in the small intestine were identified in 58% of the patients (10). Only 1-4% of patients with melanoma metastases within the alimentary tract will have their clinical manifestation and intravital diagnosis. Patients with advanced melanoma and metastases in the alimentary tract may have the following symptoms: loss of body weight, blood in stool, anaemia. However, obstruction is an exceptional situation.

The aim of the study was a presentation of the case of melanoma of unknown primary, whose first symptom was intestinal obstruction.

CASE REPORT

A patient, 51, was admitted to the Department of Surgical Oncology and General Surgery due to intestinal obstruction. Over the last three months the patient had lost 8 kilograms. For three days he had been suffering from persistent vomiting. The patient did not report other symptoms. The anamnesis concerning cancers did not reveal clinical significance. The physical examination of the patient showed elements of dehydration. The patient’s skin was pale, without suspicious lesions. A lymph node package was palpable within the left armpit. No other deviations were found in the physical examination. A stomach probe was inserted; the patient was hydrated and received parenteral nutrition. The diagnostics was planned to begin after stabilisation of the patient’s general state. The patient underwent laboratory investigations, a chest X-ray and ultrasound of the abdominal cavity. The laboratory investigations and the assessed tumour markers CEA, CA19.9, LDH, AFP, CA 72.4 and Ca 15.3 were within normal limits. However, the ultrasound of the abdominal cavity revealed enlargement and dilation of the stomach and duodenum. Apart from that, two intussuscepted areas causing intestinal obstruction were found and an inhomogeneous hypoechoic focus with meta characteristics was diagnosed in segment VIII of the liver.

Due to the diagnostic difficulties and ambiguous image CT and PET/CT examinations were carried out. The CT confirmed the presence of intussusception of the terminal ileum in the colon, which stretched along 11 cm to the hepatic flexure, where a tumour of 45 mm in diameter infiltrating the wall was visible (fig. 1). Apart from that, on the left side of the abdominal cavity there was a jejunal intussusception stretching along about 16 cm with concomitant thickening of the intestinal wall with neo infiltration characteristics (fig. 2). Another intussusception of 4 cm could be seen distally several centimetres further. The intestinal wall was thickened there. There were numerous enlarged lymph nodes within the mesentery. Apart from the lesions visible in the CT, the PET/CT examination revealed hypermetabolic nodal masses in the left armpit, chest and abdominal cavity. There was an active metabolic focus within the liver and infiltrations with proliferative characteristics.

Fig. 1. CT – intussusception of the terminal ileum in the colon
in the intestines. Due to the intestinal obstruction, after stabilisation of the patient’s state a surgery was planned. The patient underwent diagnostic laparotomy. In the abdominal cavity, behind the ligament of Treitz an ileal intussusception and several metastases in the intestinal wall behind the intussusception were diagnosed (fig. 3). Another intussusception was diagnosed within the ileocaecal region with infiltration of the caecum (fig. 4). Apart from that, there were numerous enlarged lymph nodes within the mesentery. In the intraoperative examination the histopathologist diagnosed a tumour causing the intussusception to have the characteristics of a melanoma metastasis. Next, the patient underwent a right hemikolectomy and left axillary lymphadenectomy. The surgery had a palliative character. There were no complications in the postoperative course. On the ninth day the patient was discharged from hospital. After immunohistochemical tests the final result of the histopathological examination revealed 7 tumours in the small intestine, which were malignant melanoma infiltrations invading the vessels. Within the caecum and ascending colon there was a melanoma infiltration comprising the submucosal and muscle membrane. In the examination of the small intestine all the lesions were described as melanoma metastases.

The primary focus was not identified. In the specimen after axillary lymphadenectomy there were melanoma metastases found in 13 out of 24 resected lymph nodes. In spite of precise skin assessment, rectoscopy, laryngological and ophthalmological examinations the primary focus was not identified. The patient was qualified for a chemotherapy test combined with immunotherapy.

DISCUSSION

Melanoma of unknown primary applies to 1-8% of all diagnoses of this tumour. The diagnosis is made after all possible locations of the primary focus have been excluded. Having analysed their 33 years of experience in the treatment of melanoma Savoia et al observed that it was impossible to locate the primary focus in 88 out of 4881 patients. In 31 (35.3%) patients the first clinical presentation was metastases in the skin and subcutaneous tissue, in 48 (43.2%) patients the only symptom was an enlarged lymph node, whereas only in 15 patients (17%) dissemination of the neoplastic process to internal organs could be seen (11).
The literature describes cases of primary melanoma located in the alimentary tract, e.g. primary melanoma of the ascending colon or primary melanoma of the rectum. It is very difficult to diagnose primary melanoma of the alimentary tract. One of the suggested clinical criteria for diagnosis thereof is the absence of metastases in other locations. In the case under study the first clinical manifestation of the disease was intestinal obstruction. Distant metastases were identified in the patient. Especially the metastases in the left armpit could have indicated a focus in the left upper limb. Detailed examination and anamnesis of the patient did not confirm the presence of a focus in the left upper limb. After detailed analysis of all other possible locations the primary focus still could not be found. Therefore, melanoma of unknown primary was diagnosed in the patient.

In each case when melanoma metastases to the alimentary tract are suspected, appropriate imaging diagnostics should be carried out. The first basic stage of diagnostics is the abdominal cavity ultrasound, which is a non-invasive and inexpensive examination, which is widely available and does not require special preparation. The intussusception caused by melanoma metastases has a characteristic and evident ultrasound image. Another examination is computed tomography, whose sensitivity of identification of melanoma metastases in the alimentary tract is only 60-70%. In each case when metastases to the alimentary tract are clinically suspected it is necessary to carry out further diagnostics in spite of the negative CT examination. The PET/CT examination guarantees higher sensitivity than CT in the identification of melanoma metastases and it should be carried out if it is available. Furthermore, as some authors report, it is necessary to carry out the examination because it changes the decision concerning the range of surgery in 17-48% of cases. In the case under study all the examinations, i.e. the ultrasound, CT and PET/CT revealed metastases in the alimentary tract (12, 13).

At present there are no effective treatment methods for patients with melanoma dissemination regardless of the primary focus location. As one of few malignant cancers, this tumour is capable of forming metastases in the alimentary tract, especially in the small intestine. Letsch et al think that melanoma metastases to the small intestine are related with the expression of the C-C chemokine receptor 9 on the cellular surface. These receptors can be found in the small intestine and thymus and their expression level is significant in the formation of metastases. In about 50% of patients when melanoma metastases in the small intestine are diagnosed, there are also metastases in other locations. On average metastases develop in the small intestine within 3-6 years after resection of the primary melanoma (14).

However, sometimes they appear much sooner. In the case under study the metastases in the small intestine, which caused intestinal obstruction, were the first symptom the patient reported.

At present surgery is a method of choice in the treatment of patients with melanoma metastases in the alimentary tract. It is recommended to resect the lesion including an appropriate margin of the healthy intestine and to resect the mesentery in order to remove the lymph nodes. Due to resection of the organ with a metastasis it is possible to achieve a 5-year survival rate up to 40% and the disease-free period may extend up to 10 years (15). However, the average survival rate after resection of the organs is 15 months (16). The qualification for a surgery must allow for the patient’s age, their general state of health and presence of metastases in other organs. A radical resection enables improvement of the survival rate in this group of patients, as compared with the patients who have not undergone a surgery. The average survival rate of the patients who were operated on due to melanoma metastases in the alimentary tract was 48.9 months, whereas the survival rate of the patients who were not operated on was 5.7 months (17). In this group perioperative mortality was minimal. The procedure may be considered to be safe.

The most important negative prognostic factor in patients with melanoma metastases in the alimentary tract is the presence of dissemination in other organs. However, in spite of the presence of distant metastases, resection of possible segments of the alimentary tract remains the best form of palliative treatment in this group of patients. Simultaneously, resection of metastases gives a possibility to secure the patient from ailments and symptoms resulting from their presence. In the group of 65 patients with melanoma me-
tastases after surgical resection of the lesions in the abdominal cavity a 100% remission of the symptoms and ailments reported by the patients was achieved (18). Similar results come from John Wayne Cancer Institute, where 124 patients underwent a potentially radical resection or only a palliative surgery due to melanoma metastases in the alimentary tract. There was a 97% remission of the symptoms (17). In the case under study the patient was discharged from hospital in general good state without any symptoms of the disease.

CONCLUSIONS

The future of surgical oncology and improvement of treatment results assumes better understanding of the biology of tumours and identification of the mechanisms of metastatic formation. Quick identification and radical resection of melanoma metastases in the alimentary tract may improve the survival rate in this group of patients. Resection, even if it is palliative by assumption, is not only the best method of elimination of persistent symptoms but it also gives hope for longer survival.

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Received: 7.03.2012 r.
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