Metastatic Malignant Melanoma Causing Small Bowel Intussusception: A Case Report with 4-year Follow-up

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ABSTRACT Primary mucosal malignant melanoma of the small bowel is extremely rare. The small bowel is mostly affected by metastases of the primary malignant melanoma of the skin. Bowel obstruction is a rare complication of metastatic melanoma. We present a case of small bowel obstruction in a 49-year-old man with history of skin malignant melanoma. A segmental resection of the ileum with termino-terminal anastomosis was performed. Pathohistological examination showed metastatic melanoma. After 4 years of follow-up, the patient is still free of the disease.

KEY WORDS: intestinal melanoma; intussusception; malignant melanoma; small bowel metastases; surgery

INTRODUCTION

Gastrointestinal mucosa is a rare focus of primary melanoma because no melanocytes are present. Therefore, cutaneous malignant melanoma (MM) metastases to gastrointestinal mucosa occur more frequently than primary melanomas (1,2). These metastases are rarely detected clinically, only 2% to 4%, and are usually identified in the late phase of the disease when causing complications (3). Both primary and metastatic melanoma of the small bowel are associated with a more aggressive form of the disease, worse prognosis, and shorter survival compared with primary skin melanoma. According to a review of the related literature, the five-year survival rate for patients with small bowel metastatic melanoma is only 10% (4,5).

Surgery is the standard therapy choice for patients with resectable intestinal metastatic melanoma (6). Surgical treatment of bowel metastasis has a low morbidity and mortality rate (7,8). Preoperative lymphoscintigraphy and sentinel node biopsy is a safe, reliable, and essential procedure for staging the regional lymph node basin in patients with malignant melanoma (9).

Systemic therapy does not improve survival in patients with small bowel metastatic melanoma, and prognosis for these patients is poor. Patients with primary melanoma of the small bowel have a worse prognosis than patients with metastatic melanoma of the small bowel (6).

CASE REPORT

A 49-year-old man with a 3-year history of MM was admitted to the Department of Surgery of the University Clinical Hospital Mostar, with symptoms of abdominal pain, nausea, anemia, and recent weight

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loss. His past medical history included surgical resection of a cutaneous lesion on his back. Pathohistological examination revealed cutaneous melanoma, Clark 2, Breslow 3 (thickness 2.5 mm). Preoperative lymphoscintigraphy and sentinel node biopsy were negative. Surgical treatment was followed by 6 months of interferon-alpha therapy, which was stopped due to poor patient tolerance.

Abdominal radiography revealed irregular bowel passage with air-fluid levels. Abdominal multislice computed tomography (MSCT) showed a solid mass in the small bowel above the iliac bone crest infiltrating the ileal bowel wall.

Surgical treatment was indicated. An explorative laparotomy was performed after emergency preoperative preparation. A 20 cm long ileal bowel loop intussusception and increased mesenterial thickness were found (Figure 1). A resection of the 35 cm long ileum with termino-terminal anastomosis was performed. The resected bowel loop was explored, and a melanoma-like solid tumor mass measuring 3×2 cm was found (Figure 2).

The pathology report confirmed the presence of a yellowish-white tumor of the proximal ileum measuring 3×4×2 cm. The neoplasm extended up to the mucosa, causing focal areas of ulcerations. The histological examination showed that tissue was highly atypical, with an epithelial aspect.

Immunohistochemical analysis revealed that the tumor cells were highly reactive for human melanoma black-45 (HMB-45); melanA, and S100 (Figure 3). Extensive clinical and diagnostic examinations, including ophthalmological and dermatological consultation, were performed – no primary malignant melanoma was found. The small bowel tumor mass was considered to be a metastasis of previous cutaneous melanoma.

Intensive follow-up was recommended by an oncologist.

After 4 years of follow-up, the patient is still disease-free and in good health condition.

DISCUSSION AND CONCLUSIONS

While nodular melanoma (NM) is associated with worse outcomes compared with superficial spreading melanoma (SSM), tumor thickness, presence of ulceration, male sex, localization, high mitotic index, and histologic subtype of the primary cutaneous melanoma are risk factors for recurrence of the disease and distant metastases. There are three metastatic pathways of melanoma: 1) primary tumor, then satellite or in-transit metastases; 2) primary tumor, then regional lymph node metastases; 3) primary tumor, then distant metastases. About 50% of all patients with cutaneous MM and recurrence of disease first develop metastasis in regional lymph nodes. About 20% of them first develop satellite or in-transit metastasis, and about 30% develop metastases at distant sites directly. In the majority of cases, distant metastases may spread from the primary tumor individually and not through the lymph nodes. There are 7 important steps in the pathogenesis of cutaneous melanoma metastasis: proliferation, neovascularization, lymphangiogenesis, invasion, circulation, embolism, and tumor vascularity (10,11).

Metastatic melanoma in the gastrointestinal (GI) tract accounts for one third of all metastases to that region. Sites most often affected include the small bowel (75%), the large intestine (25%), and the stomach (16%) (12). Up to 60% of patients with MM have evidence of metastasis to the GI tract at autopsy (13). Nevertheless, only 2-4% of patients with MM have clinically detectable GI involvement that is diagnosed before death (14). Symptoms of small bowel melanoma metastasis include GI bleeding, obstruction, abdominal pain, nausea, vomiting, and weight loss (15). The time interval between the diagnosis of primary MM and the diagnosis of GI metastases ranges from 2 to 180 months (16). A careful evaluation and follow-up of all patients with a history of high-risk MM who have GI symptoms should be performed.

Primary small bowel melanoma is an extremely rare entity that is difficult to diagnose. The majority of

Figure 1. Resection specimen shows a 20 cm long ileal bowel loop intussusception.

Figure 2. Resection specimen shows a melanoma-like solid tumor mass measuring 3×2 cm.

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Figure 3. Immunohistochemical analysis shows tumor cells highly reactive to HMB-45, melanA, and S100.

these neoplastic lesions are metastases from primary skin lesions. It seems that a clear histological distinction between primary and metastatic small bowel melanoma is very difficult to determine. In most cases, metastatic melanoma of the small bowel is clinically unapparent. An acute presentation may rarely occur due to intestinal obstruction or intussusception (8). Compared with pediatric patients, intussusception is a rare condition in adults. In contrast to childhood intussusception, where 90% of the cases are idiopathic, adult intussusception has an underlying cause in 90% of the cases, with approximately 65% due to tumor growth. In most cases, adult intestinal obstruction occurs due to a benign tumor and due to malignant tumor in only 15% of the cases, with MM being by far the most common cause overall (17,18). Despite this, few cases of small bowel intussusceptions due to metastatic melanoma have been reported in the medical literature (18,19).

Our patient presented with a tumor mass in the small bowel three years after resection of primary cutaneous melanoma. Since clinical and pathohistological findings determined metastatic melanoma and excluded lymphatic pathways as a possible metastatic route, the only possible metastatic pathway was the bloodstream. Intravascular invasion and circulation of melanoma cells in the bloodstream play an important role in this type of metastatic process. The next step includes development of distant, unapparent micrometastasis that will finally progress into clinically detectable metastasis. It has been proposed that malignant melanoma stem cells (MMSC) may be responsible for disease initiation and progression (20). Additionally, there are inflammatory responses and associated products that have been involved in development of melanoma metastasis. It is hypothesized that some chemokine-releasing scaffolds may function as implantable traps for circulating metastatic cells (21). Recent studies have found an important correlation with the CCR9 chemokine receptor on melanoma cells, which facilitates metastasis to the small bowel where its ligand CCL25 is strongly expressed (14,22). This expression of chemokine receptors in melanoma cells was associated with the expression of the specific chemokine ligands in metastasis, which is an interesting finding that may prompt the development of new therapeutic options (10).

CONCLUSION

Metastatic malignant melanoma causing small bowel intussusception is a rare condition, and only a few cases have been reported in the literature. Prognosis for patients with small bowel metastatic melanoma is poor, and five-year survival is only 10%. Our patient is still on intensive follow-up and after 4 years he is still free of the disease and in good health condition.

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