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Clinical Case Report

Multiple gastrointestinal metastases of Merkel cell carcinoma

Eligijus Poškus [a], *Gediminas Platkevičius* [b], *Vilma Simanskaitė* [c], *Ernesta Rimkevičiūtė* [d], *Marius Petrulionis* [a,*], *Kestutis Strupas* [a]

[a] *Centre of Abdominal Surgery, Clinic of Gastroenterology, Nephrourology and Surgery, Vilnius University, Vilnius, Lithuania*
[b] *Faculty of Medicine, Vilnius University, Vilnius, Lithuania*
[c] *National Center of Pathology, Vilnius University, Vilnius, Lithuania*
[d] *Centre of Radiology and Nuclear Medicine, Vilnius University, Vilnius, Lithuania*

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ABSTRACT

Merkel cell carcinoma is an aggressive skin malignancy. Primary Merkel cell carcinomas are treated by wide radical excision with or without adjuvant radiotherapy, while benefits of adjuvant chemotherapy remain doubtful. There are only several cases of gastrointestinal metastases of Merkel cell carcinoma reported so far. We report a case of recurrent Merkel cell carcinoma with metastases to the stomach and the small intestines after wide excision of primary Merkel cell carcinoma.

1. Introduction

Merkel cell carcinoma (MCC) is a rare aggressive cutaneous malignancy, firstly described by Cyril Toker in 1972 [1]. The incidence of MCC is 0.6 per 100,000 [2]. It mostly affects the white population, with a rate 0.23 per 100,000 reported in the Caucasian race, compared to 0.01 per 100,000 in other groups [3]. MCC is twice as frequent in men as in women [4]. Ultraviolet radiation exposure, age >50 years, immunosuppression [5], and polyomavirus infection are the risk factors for MCC [6]. MCC clinically presents itself as a fast growing, painless, firm intracutaneous nodule and is most commonly found on a sun exposed surface of the skin. It is a highly aggressive tumor with a mortality rate of approximately 30% within 2-years and 50% within 5-years after diagnosis [7] and also relatively high recurrence rate after wide excision of primary tumor [8]. Prognosis of MCC depends on the original localization of the tumor, patient's sex, age and other co-morbidities. The presence of nodal distant metastases significantly lowers survival. Typical metastatic sites of MCC are liver, bone, brain and skin [5]. Median overall survival of patients

* *Corresponding author at*: Centre of Abdominal Surgery, Clinic of Gastroenterology, Nephrourology and Surgery, Santariškių 2, 08661 Vilnius, Lithuania.
E-mail address: marius.petrulionis@santa.lt (M. Petrulionis).
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with metastatic MCC is poor and reaches only about 22 months [9]. To the best of our knowledge, only a small number of cases of MCC have metastasized to the stomach have been reported as several more cases of metastasis to the intestines and mesentery, in most of these cases at first being confused as primary tumors of visceral organs [10–15]. Simultaneous metastatic MCC of the stomach and intestines has not been previously described. Therefore, we report a case of multiple gastrointestinal metastases after previous wide excision and local radiotherapy of a primary MCC occurring in sun non-exposed skin.

2. Case report

A 64-year-old Caucasian male was admitted to the Emergency Department with suspected gastrointestinal bleeding, presence of melena and severe anemia with hemoglobin level of 39 g/L. Other specificities of anamnesis was metabolic syndrome, adiposity grade III and history of histologically confirmed MCC skin tumor excised from his armpit 4 months ago with subsequent local radiotherapy. An esophagogastroduodenoscopy revealed a 3 cm × 4 cm diameter ulcer in the dorsal part of gastric corpus without active bleeding at the time of examination. Multiple biopsies were taken during the endoscopy procedure from the ulcer site as a primary gastric tumor was suspected. However, histological examination of the tissue specimens revealed a poorly differentiated MCC metastatic in the stomach, the diagnosis was confirmed by immunohistochemistry staining CK20 (++), Cam5.2 (++); chromogranin A (+/++), CD20/CD3 (−), Ki67 (+/++) and TTF1 (−) as described elsewhere [10,13,16,17]. Afterwards, the CT scan of the abdomen and the small bowel revealed a gastric tumor presenting as a 35 mm × 18 mm × 24 mm ulcerous formation in the middle third of the posterior wall (Fig. 1). The patient was operated on according to the decision of a multidisciplinary team. During the intraoperative exploration of visceral organs, four distant metastases in the loops of jejunum and ileum, previously undetermined in the CT scan, were found (Fig. 2). A radical gastrectomy type Billroth II, D2 lymphadenectomy and segmental resections of ileum and jejunum were performed. The histological analysis of all specimens confirmed a poorly differentiated metastatic CK20 positive (++) MCC in the stomach and small intestines, with suspected nodal and lymphovascular invasion (Fig. 3). The patient was released from the hospital on the 12th postoperative day. Six weeks after surgery he received the first of 6 planned chemotherapy courses, composed of intravenous infusion of cisplatin (80 mg/body skin m^2) and etoposide (100 mg/body skin m^2) from the first to third day in each course. However, one week after the second chemotherapy course a sudden heart attack and death of the patient were reported. At that time, no evidence of MCC further progression was determined.

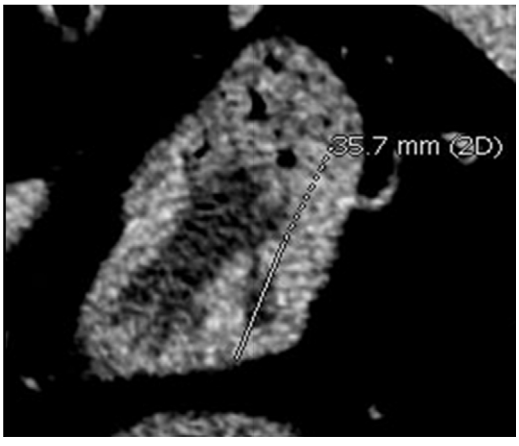

Fig. 1 – Abdominal CT scan represents a gastric tumor (white line) presenting as an ulcerous formation in the middle third of the posterior wall of stomach, histologically confirmed as MCC metastasis.

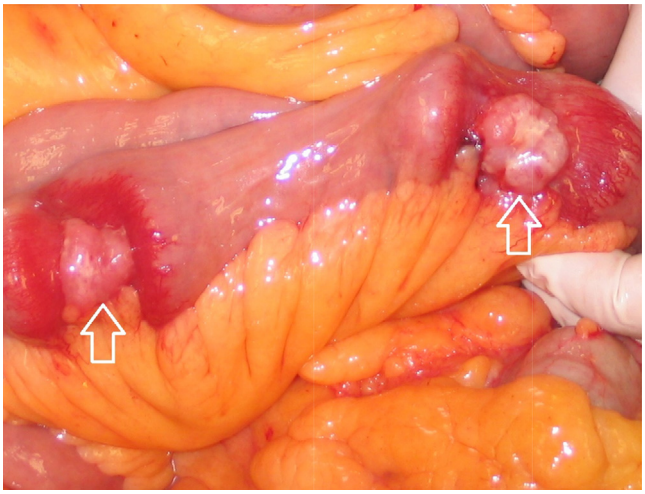

Fig. 2 – Intraoperative image of two MCC metastases in jejunum (white arrows), about 60 cm distally from the duodenojejunal fold.

3. Discussion

In our case, a primary MCC tumor originated in an uncommon area – the armpit. Despite wide primary tumor excision and subsequent local radiotherapy, metastatic MCC disease was diagnosed by esophagogastroduodenoscopy with histological analysis of multiple biopsies, performed after an episode of acute gastric bleeding and severe anemia. Metastatic gastrointestinal MCC was treated surgically with subsequent adjuvant chemotherapy. During the postoperative follow-up, the patient died due to a sudden heart attack 3 months after surgery. Only two courses of chemotherapy were performed. During a rather short postoperative period, no recurrence of MCC was found. Until now, none of several previously reported gastrointestinal MCC cases have described multiple metastases of MCC in the stomach and small bowel [10–15].

In the era of organ transplantation, immunosuppression as a predisposing factor for MCC is an important issue which turns posttransplant patients into a population with increased risk of MCC [5]. The role of immunosuppression has led to the search of possible infectious predisposing factors and interestingly the carcinogenesis of MCC has been linked to polyomavirus infection [6].

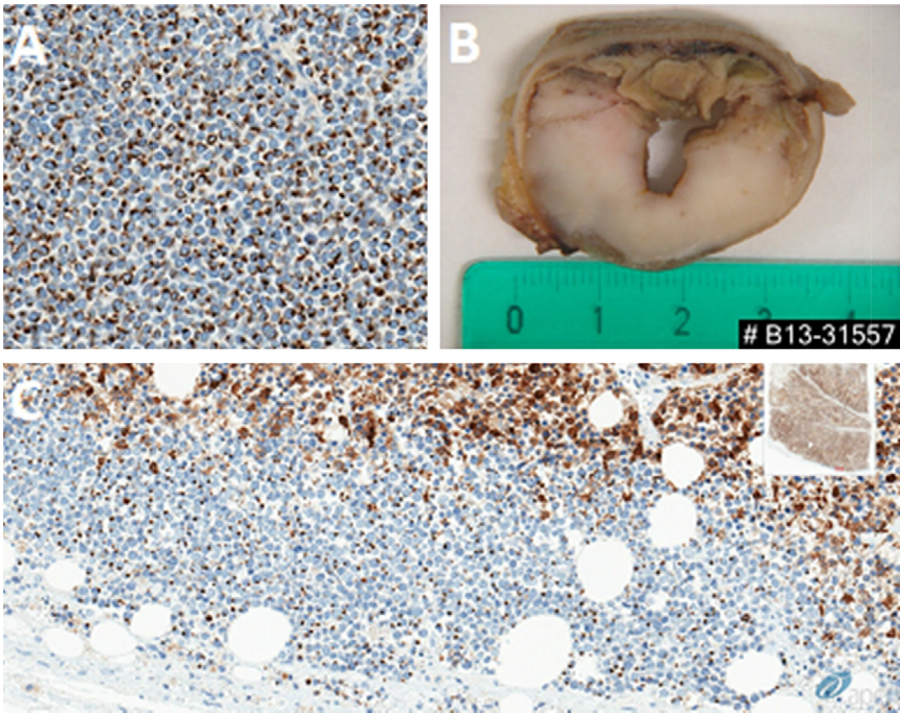

Fig. 3 – Histology images of Merkel cell carcinoma. (A) CK 20 positive staining of the metastatic MCC tumor; (B) macroscopic formalin-fixed MCC metastasis from the small intestine; (C) CK 20 positive staining of the primary MCC tumor, excised from the armpit of the patient 4 months before the metastatic disease was detected.

In general, the recommendations for a primary MCC tumor treatment is a wide excision with margins at least 1–2 cm and subsequent postoperative radiotherapy [18], as performed in our case. All borders of tissue specimen must be evaluated by a pathologist after tumor excision or Mohs micrographic surgery can achieve sufficient excision margins [19]. Roughly 32% of primary MCC patients with no nodal disease found by physical examination appeared to have nodal involvement, for this reason sentinel lymph node biopsy is recommended routinely even for those patients who had negative clinical and radiographic lymph node metastatic status [20]. Adjuvant radiotherapy decreases the rates of local and regional recurrences [21].

Relatively high recurrence rates are observed even after margin free primary MCC tumor excision [8] and long term follow-up after primary surgery is required. Complete skin and lymph node examination should occur every 3–6 months for 2 years and annually thereafter and imaging studies should be performed if recurrence is suspected clinically. When recurrence is detected, full radiologic diagnostics should be performed as suggested by the National Comprehensive Cancer Network [22]. According to previous studies, the benefits of chemotherapy or molecular-target therapy are doubtful [23].

Radiotherapy can be applied not only after excision of primary skin MCC, but also has been used to treat MCC metastases in the brain, bones, prostate, bladder and other organs [24]. In previously published gastrointestinal metastatic cases of MCC, palliative surgical treatment with subsequent chemotherapy or chemotherapy alone was applied [10–15]. However, treatment and follow-up recommendations for gastrointestinal progression of MCC are still scarce.

4. Conclusions

Wide radical excision and adjuvant radiotherapy are primary treatment options for primary cutaneous MCC, as the benefits of adjuvant chemotherapy are doubtful. Stomach and intestines are rare sites of MCC progression, while in general metastatic MCC disease is associated with poor prognosis. Our case highlights the importance of close follow-up after primary MCC tumor excision. In our opinion, surgery or modern radiotherapy methods should be considered for metastatic MCC treatment of various sites when applicable. Standardized follow up recommendations after excision of primary skin tumor and metastatic MCC management guidelines would be really appreciated, aiming to improve overall survival and outcomes.

Conflict of interests

The authors state no conflicts of interest.

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