Case Report
Radiotherapy for recurrent Merkel cell carcinoma in the head and neck—a case report

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Abstract: Merkel cell carcinoma (MCC) is a rare neuroendocrine skin tumor. The present report describes the case of an 80-year-old patient with MCC of the head and neck which continued to metastasize rapidly after surgery combined with chemotherapy. Then the patient was treated with radiation therapy using a conventional segmentation scheme (50 Gy provided in 2 Gy per fraction and five fractions per week) targeting the gross tumor. The treatment led to complete tumor remission. This case indicates that radiotherapy for recurrent MCC yielded excellent local and regional metastasis control results.

Keywords: Merkel cell carcinoma, lymph node metastasis, radiotherapy

Introduction

Merkel cell carcinoma (MCC) is a rare and highly malignant neuroendocrine skin cancer associated with viral etiology and a high rate of nodal metastasis. Its incidence has been increasing since it was described by Toker C in 1972 [1]. The incidence ranges between 0.15 and 0.79 cases per 100,000 individuals [2, 3]. Findings have revealed that MCC is extremely aggressive, with high locoregional metastasis and recurrence rates, and high lethality. Treatment is often multimodal, including surgery, chemotherapy, radiotherapy, and immunotherapy, with surgery usually being the preferred initial therapy option. The present report describes a case of recurrent MCC in which salvage radiotherapy yielded excellent local and regional control results.

Case report

An 80-year-old woman was admitted to the first affiliated hospital of Bengbu medical college 1 year after surgery for head and neck MCC, and presented with recurring and pain lasting for 2 months. The patient underwent surgery for swelling of the left frontal skin in September 2018. Histologically, there were sheets and narrow cords (trabeculae) of small, uniform, and oval cells, stained dark blue, and with scant cytoplasm and substantial mitosis (Figure 1A, 1B). Immunohistochemistry revealed positive staining for AE1/AE3, synaptophysin and CD56, and negative staining for neuroendocrine markers (melan-A), melanoma markers (HMB-45 and S-100) and myoepithelial markers (cytokeratin 5/6). The diagnosis was MCC with a Ki-67 labeling index of ~80%. Subsequently, the patient was given capecitabine for 14 days at a dose of 1 g twice a day. In February 2019, the patient had a mass in the left parotid gland area. Enhanced head, neck, and chest CT revealed node metastasis in the left neck. Subsequently, left parotid gland tumor radical surgery and radical left neck lymph node dissection were performed. Postoperative pathology confirmed metastatic MCC, and three of the four dissected neck lymph nodes were positive. Postoperative left peripheral facial paralysis with left ear hearing loss was observed. Between April and August 2019, the patient was given 120 mg/m² paclitaxel plus 200 mg/m² carboplatin as a 3-week regimen for 6 cycles of chemotherapy. In July 2019, the patient identified a gradually enlarged mass in the left parotid gland area with pain. Subsequently, the patient presented to our hospital.
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The patient had no history of other malignancies. On admission, physical examination revealed painful facial features, the left frontal striations had disappeared, left eyelid closure was incomplete, the left nasolabial groove had become shallow, and left hearing was decreased. A bluish-red fused mass with a diameter of ~4 cm was visible in the left parotid gland area, with hard and fixed quality, and the local skin was thin and tender. The results of accessory examinations after admission were as follows: Tumor markers (α-fetoprotein, carcinoembryonic antigen, and carbohydrate antigen 153, 199, and 125) were negative, and doppler ultrasound revealed multiple lymph nodes in the left neck with abnormal structure and hepatic hypoechoic nodules, indicating possible metastasis. Head and neck localization CT demonstrated an abnormal density shadow in the left parotid gland area (Figure 2A), and multiple enlarged lymph nodes in the IV and V areas of the left neck (Figure 2B).

No radiotherapy contraindications were observed, and intensity-modulated radiotherapy was started in September 2019. The left parotid gland area and the target area of the lesion in the left neck were described as follows: The gross target volume for primary disease (GTVnx), including visible lesions; the gross target volume for involved lymph nodes (GTVnd), including the IV and V area visible lymph nodes; and the clinical target volume (CTV), including the Ib, II, III, IV, V and VIII area lymphatic drainage areas. The planning target volume (PTV), defined as the GTV or CTV plus a margin of 3 mm, were PGTVnx, PGTVnd, PTV. The 95% PGTVnx irradiation received was 66 Gy/33 fractions (F; 2.0 Gy/F; one session/day; five sessions/week). The 95% PGTVnd irradiation received was 60 Gy/33 F (1.82 Gy/F; one session/day; five sessions/week). The 95% PTV irradiation received was 50 Gy/33 F (1.52 Gy/F; one session/day; five sessions/week). The dose distribution in the target area was reasonable, and the dose to normal organs was within the range limit (Figure 3A-C).

After 20 fractions of radiotherapy involving 40 Gy, mild pigmentation appeared on the local skin (I-degree radiodermatitis) with an I-degree
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oral mucosal reaction. CT examination of the head and neck revealed that the lesions had been markedly reduced (Figure 2C, 2D). Considering that the patient’s lesions had been completely relieved, the radiotherapy was stopped when the dose was 50 Gy. At present, the patient has been followed for 6 months and the tumor in the left parotid region has not recurred.

Discussion

MCC is a rare neuroendocrine tumor that manifests on the head/neck (29%) and upper limbs (24%) in skin that is exposed to sunlight. The skin lesion can present as painless, rapidly growing, cutaneous, firm, non-tender, and shiny, and often as a reddish or purple intracutaneous nodule [4]. Typical risk factors, other than exposure to ultraviolet radiation, are immunosuppression (human immunodeficiency virus or organ transplants), advanced age (50 years; median, 75 years), fair skin, virus involvement (Merkel cell polyomavirus) and previous tumors [5]. Prognostic factors include age >75 years, male sex, and tumor diameter >2 cm [6]. The numbers of head and neck metastases are also associated with poor survival and are sometimes positively associated with local recurrence [7]. MCC is microscopically characterized by small cells with round nuclei that are monomorphic and exhibit basophilic nuclei associated with high mitotic index and apoptotic bodies [8]. MCC is positive for neuroendocrine markers, such as synaptophysin, chromogranin A and CD56 [9]. However, the specificity of these markers is low. In the present case, the cells were positive for synaptophysin and CD56.

The National Comprehensive Cancer Network guidelines recommend extensive primary tumor and sentinel lymph node biopsy. Lymphadenectomy and adjuvant radiotherapy may subsequently be performed based on histopathological findings and stages of the results [10]. In metastatic MCC, the most commonly used cytotoxic chemotherapy includes anthracycline, platinum, or etoposide. Lack of molecular specificity and early resistance to chemotherapy limit their efficacy, and chemotherapy is currently considered to have only palliative action in MCC [11]. Studies report that adjuvant radiotherapy can decrease locoregional recurrence and increase overall survival in MCC. Yusuf M [12] performed a retrospective analysis of 805 MCC patients and found that adjuvant radiotherapy was associated with a decreased hazard of death for patients with localized MCC of the head and neck. Bishop AJ [13] demonstrated that radiotherapy provides excellent area control for head and neck MCC. Jouary T [14] reported a marked reduction in regional recurrence rates in patients receiving regional radiotherapy. Cheraghhol S [15] reported that in cases with a high lymph node ratio (>0.31), surgery and adjuvant radiotherapy may have an improved survival benefit. In lymph node-positive MCC, radiotherapy is recommended at a minimum dose of 50-55 Gy, with a single dose of 2 or 2.5 Gy [16]. Antibody immunotherapy for programmed cell death protein 1 or programmed cell death ligand 1, such as avelumab, pembrolizumab, and nivolumab, is an effective option for metastatic MCC [10, 17].

In the present case, the patient completed the surgical excision as well as chemotherapy. In the head and neck, wide surgical margins can result in marked cosmetic and functional deformities due to the proximity of important organs. The surgical margin and scope are often limited. The scope of surgical resection is insuffi-
cient and the efficacy of chemotherapy is limited, which leads to postoperative recurrence. The current radiotherapy showed good sensitivity. Taking into account the patient’s advanced age and economic reasons, immunotherapy was not used in the present case.

In conclusion, primary skin MCC rapidly progressed even after surgery and chemical treatment. However, radiation treatment showed good sensitivity and regional control.

Disclosure of conflict of interest

None.

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References


