Radiotherapy in Merkel cell carcinoma of facial skin with lymph node recurrence

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Abstract

Introduction: Merkel cell carcinoma (MCC) is an aggressive cutaneous neuroendocrine tumour. Although surgical resection is a treatment choice, it often occurs in the head and neck and occurs mainly in the elderly, making surgery impossible. Radical radiation therapy may be an alternative to surgery in these patients. In addition, radiation treatment may be performed even after recurrence after surgery.

Methods: An 82-year-old MCC patient had cT2N0M0, stage IIA MCC on the left cheek that metastasised to lymph node 2 months after surgery. She was treated with radiation monotherapy with a hypofractionation schedule (39 Gy at 3 Gy per fraction).

Results: The patient achieved complete remission after radiotherapy without severe toxicities.

Introduction

Merkel cell carcinoma (MCC) is an aggressive neuroendocrine malignancy of skin associated with lymph node (LN) involvement, distant metastasis and disease recurrence. It is prevalent among the white elderly population and is associated with sun exposure, immunosuppression and a Merkel cell poliovirus.¹ The recommended treatment is a wide local excision of the primary site with 1–2 cm margins and sentinel LN dissection by National Comprehensive Cancer Network guidelines.² However, definitive radiation monotherapy is an alternative to surgery for patients who are poor surgical candidates or in those for whom surgery would result in functional compromise. As reviewed, MCC is a radiosensitive tumour, and when definitive radiotherapy is performed, local control is considerably high, about 75–85%.³ Also, a retrospective study revealed that radiation monotherapy as regional treatment for positive LN involvement has similar efficacy and excellent local control comparable to complete lymphadenectomy.⁴

Radiation therapy recommends a 60–66 Gy administered in 30–33 fractions and five fractions per week,⁵ but frequent visits to the hospital can be burdensome for elderly patients. Also after treatment, some problems such as fibrosis after head and neck treatment are seen. In the case of small lesions, it is a reality that there are few reports of adequate radiation dose. Therefore, in this report, small LNs were treated with a 39 Gy/13 fraction. The treatment led to complete remission (CR) with well-tolerated toxicities.

Case Report/Case Presentation

An 82-year-old woman presented with a skin coloured papule on her left cheek area (Figure 1). An excisional biopsy was performed in the Dermatology Department, and MCC was diagnosed by histopathology. The patient was referred to the Plastic Surgery Department of our hospital for further evaluation and treatment. Computed tomography (CT) was performed preoperatively to evaluate the extent of the primary tumour and to detect metastases. The CT scan revealed no evidence of a metastatic lesion in the neck area. For insurance reasons, positron emission tomography (PET)-CT was not taken, but chest and abdominal pelvis CT was taken, and no metastases were observed in other organs. A wide excision was completed during the plastic surgery. The defect was reconstructed by full-thickness skin graft using right periauricular skin. Histopathologic examination revealed a 3 cm sized mass with a 1.0 cm invasion depth, focal invasion of muscle, presence of lymphovascular invasion and clear resection margin. Immunohistochemical analysis of the biopsied specimen showed positivity for CK20 (with a paranuclear dot-like pattern), synaptophysin and negativity for CD56. Two months after surgery, a nodule was palpated on the left cheek below the operation site. Neck CT showed a 1.16 cm sized new soft tissue lesion which was suspected to originate from a metastasis to the subcutaneous LN (Figure 2a). As the patient was old, she refused any further surgery and was treated with radiation monotherapy. The patient received radiation therapy with a total dose of 39 Gy administered in 13 fractions (five fractions per week). Electrons (6 MeV) were delivered to the gross tumour with a margin of 2–3 cm using a 5 mm thickness tissue equivalent...
bolus with immobilisation using thermoplastic mask. The treatment was well tolerated; the patient experienced grade 1 dermatitis. A CR was observed on the CT and was followed up 3 months later (Figure 2b). One year after radiotherapy, the patient developed three small LN metastases in the left submental region (Figure 2c). The metastatic nodes were treated with radiation (39 Gy in 13 fractions) using intensity-modulated radiation therapy. The treatment led to clinical CR of the irradiated lesion with no evidence of metastasis for another 4 months.

Discussion
MCC is an uncommon tumour and is characterised by aggressive spread. It occurs mainly in old patients and patients with poor immunity, so radiation therapy is performed for local lesions as an alternative treatment to surgery.1,6 The local response to radiotherapy is very good, and the literature suggests 60 Gy/30 Fr, but there is no clear standard for radiation dose. There are also case reports with good treatment results with hypofractionation.7,8

In this case, the patient refused to receive surgery again when the cancer recurred after surgery due to her old age. Therefore, radiotherapy was performed only at the local recurrence site with a salvage aim. Even when the neck node relapsed at 1 year and only radiation therapy was performed; the response to the radiation therapy was good and it was well tolerated without complications. Although the follow-up period is short, radiation therapy is effective for local lesions in old patients. At the time of relapse, elective nodal irradiation might have been considered in this case, but radiation treatment was performed only at the recurring site with the patient’s consent considering the treatment’s morbidity. The radiation dose of 39 Gy per 3 Gy daily is 50.7 and 97.5 Gy, respectively, when calculated as BED10 (biologically equivalent dose with an a/b ratio of 10) and BED2 (biologically equivalent dose with an a/b ratio of 2). This is the dose that shows late toxicity of about 50 Gy at 2 Gy when viewed with an a/b ratio 2. Long-term toxicity (skin fibrosis, lymphedema, etc.) rates are expected to be low, particularly with doses of 50 Gy. The radiation dose also has the advantage of reducing the number of treatments with hypofractionation, and even at 39 Gy, if there is no recurrence in the treatment area.

Conclusion
The radiation dose of 39 Gy per 3 Gy daily is recommended when the area is not large in MCC. The results of this study may be useful in determining the radiation schedule in the case of a small tumour burden in the elderly and medically inoperable MCC patients.

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References
1. Bichakjian C K, Lowe L, Lao C D et al. Merkel cell carcinoma: critical review with guidelines for multidisciplinary management. Cancer 2007; 110: 1–12.
2. Bichakjian C K, Olencki T, Aasi S Z et al. Merkel cell carcinoma, version 1.2018, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2018; 16: 742–774.

3. Gunaratne D A, Howle J R, Veness M J. Definitive radiotherapy for Merkel cell carcinoma confers clinically meaningful in-field locoregional control: a review and analysis of the literature. J Am Acad Dermatol 2017; 77: 142–148e141.

4. Fang L C, Lemos B, Douglas J, Iyer J, Nghiem P. Radiation monotherapy as regional treatment for lymph node-positive Merkel cell carcinoma. Cancer 2010; 116: 1783–1790.

5. Tello T L, Coggshall K, Yom S S, Yu S S. Merkel cell carcinoma: an update and review: current and future therapy. J Am Acad Dermatol 2018; 78: 445–454.

6. Harms K L, Healy M A, Nghiem P et al. Analysis of prognostic factors from 9387 Merkel cell carcinoma cases forms the basis for the new 8th edition AJCC staging system. Ann Surg Oncol 2016; 23: 3564–3571.

7. Matsui T, Okano N, Kawamura H, Oike T, Ohno T. Mild hypofractionated radiation therapy for Merkel cell carcinoma. Cureus 2020; 12: e6786.

8. Petrov A, Kraleva S, Kubelka-Sabit K, Petrova D. Treatment of a patient with Merkel cell skin carcinoma using radiation therapy—a case report. Open Access Maced J Med Sci 2018; 6: 669–672.