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Case Report

Cancer of the External Auditory Canal with Extensive Osteoradionecrosis of the Skull Base after Re-Irradiation with Particle Beams: A Case Report

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Keywords
Osteoradionecrosis · Skull base · Re-irradiation · Particle beams · Head and neck cancer

Abstract
Re-irradiation with X-rays and particle beams can be used to treat localized recurrence of unresectable head and neck cancer after initial irradiation therapy. However, re-irradiation therapy increases the risk of severe and late sequelae by 4-to 8-fold. It can also result in fatal outcomes, such as rupture of the carotid artery and cerebral necrosis or abscess. A 41-year-old woman was diagnosed with squamous cell carcinoma of the external auditory canal. The patient was initially treated with X-ray irradiation. However, the patient underwent re-irradiation with heavy particle beams and neutron rays for a recurrent tumor. The patient developed necrosis of the skull base involving the facial skin and temporal bone 2 months after the last session of re-irradiation therapy. The tissue in the parapharyngeal and masticatory regions also became completely necrotic, resulting in extensive exposure of the brain parenchyma. Although the patient underwent conservative and surgical treatment, necrosis of the tissue progressed, and a large part of the brain was exposed. Approximately 2.5 years later, although the brain is still exposed, the patient is alive without disease. Although the tumor had subsided and long-term survival was achieved, our patient developed serious osteoradionecrosis of the skull base with extensive brain exposure. For patients who are not candidates for surgery, re-irradiation alone is an option, albeit with poor prospects. This approach should be discussed with the patient while balancing the potential survival gain against the burden of treatment and the risk of complications.

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Introduction

Chemotherapy is the standard treatment for localized recurrence of unresectable head and neck cancer after irradiation therapy. However, re-irradiation may occasionally be an alternative therapy. Among patients with locally recurrent head and neck cancer, mainly nasopharyngeal carcinoma, who have undergone X-ray re-irradiation, 5-year survival is observed in 10–30% cases [1–3].

Since recurrence within the irradiation field is primarily considered radiation-resistant cancer, particle beams, which are believed to be effective for radiation-resistant cancer, can be a potential treatment option. In a previous study including 229 patients treated with heavy particle beam re-irradiation for head and neck cancer, the median survival time was 26.1 months [4]. In another study, the 2-year survival rate for patients treated with boron neutron capture therapy (BNCT) for recurrent head and neck cancer was approximately 20% [5].

However, re-irradiation therapy increases the risk of severe and late complications. The incidence of such complications is <5% with initial X-ray irradiation, but it increases to approximately 20–40% with re-irradiation [1]. The incidence of necrosis of the jaw associated with fractures is 11.3% after X-ray re-irradiation [6] and that of cranial neuropathy involving dysphagia requiring permanent gastrostomy is 11–14% [2, 3]. Furthermore, fatal outcomes, such as carotid artery rupture or carotid blowout syndrome, have been reported in approximately 4–15% of re-irradiation cases [1, 3, 7]. Herein, we report a case of extensive osteoradionecrosis of the skull base that developed due to re-irradiation with heavy particle beams and neutron rays for a recurrent tumor after initial X-ray irradiation therapy.

Case Report/Case Presentation

This case report was approved by the Institutional Review Board of Kyushu University (Reference number: 29-43). This case has been reported in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

A 41-year-old woman was diagnosed with squamous cell carcinoma of the external auditory canal (T4N0M0) and was treated with X-ray irradiation therapy (dose: 60 Gy). However, 5 months after the initial irradiation therapy, the tumor recurred. Therefore, lateral temporal bone resection and reconstruction using a free tissue flap (anterolateral thigh flap) were performed. A second recurrent tumor was treated with heavy particle beam re-irradiation (dose: 52.8 Gy) 8 months after the surgical treatment of the first recurrent tumor. A third recurrent tumor was treated with paclitaxel (80 mg/m^2/week) and cetuximab (250 mg/m^2/week) 7 months after heavy particle beam re-irradiation. After 12 months, as the residual tumor continued to grow (Fig. 1), the treatment regimen was switched to nivolumab (240 mg/body/once every 2 weeks), and BNCT was used for re-irradiation.

One month later, the patient developed a small facial skin fistula that grew rapidly. Two months after BNCT, the mandible was extensively exposed. Six months after BNCT, most soft tissues in the parapharyngeal and masticatory regions and the right temporal lobe were necrotic. Surgical debridement was not feasible because of the risk of vessel rupture (Fig. 2). During this period, there were no complications, such as fatal hemorrhage or cerebral abscess; however, cerebrospinal fluid leakage occurred multiple times, which resolved with conservative treatment (a rest-cure and antibiotics).

Nineteen months after BNCT, the defects in the skull base and parapharyngeal region were repaired with a free flap obtained from the anterolateral region of the thigh (Fig. 3).

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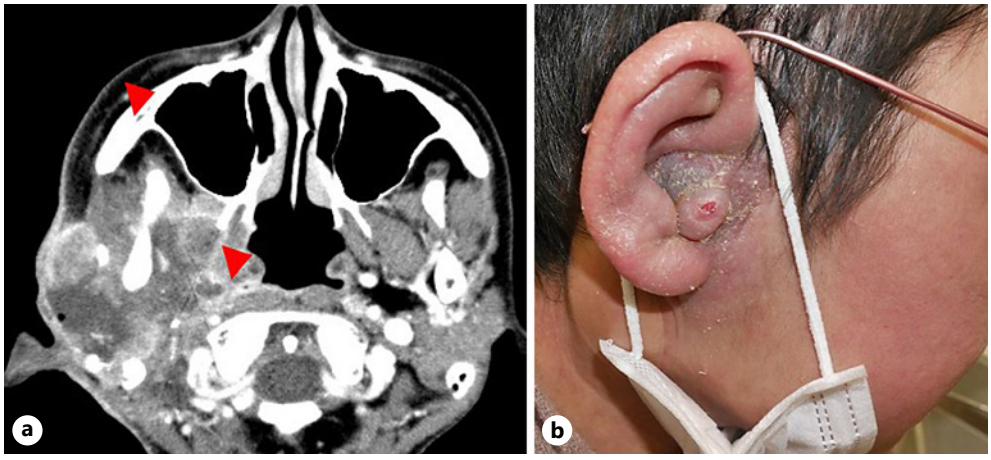

Fig. 1. a Computed tomography findings of a third recurrent tumor. **b** Gross appearance of the third recurrent tumor.

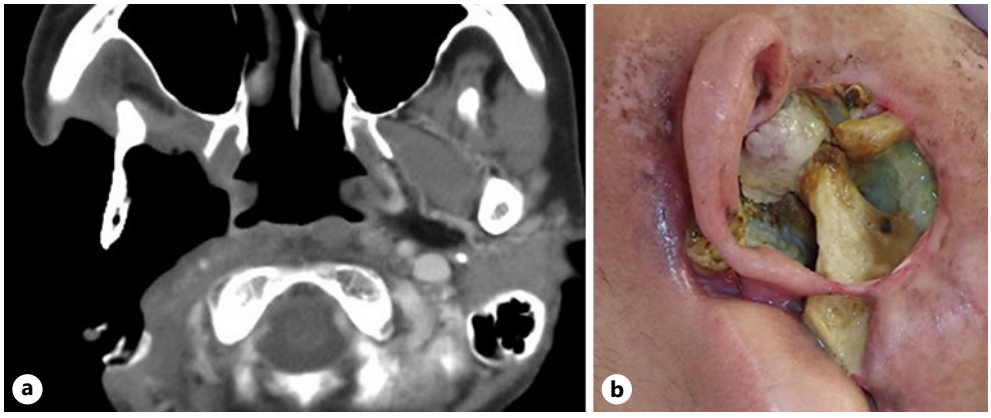

Fig. 2. a Computed tomography findings of necrosis of the skull base and the parapharyngeal soft tissues. **b** Gross appearance of necrosis of the skull base and the parapharyngeal soft tissues.

However, the flap on the skull base did not engraft, and the necrosis of the temporal bone and skull base progressed even further. The subsequent gradual removal of the necrotic parts of the skull base resulted in extensive exposure of the brain parenchyma.

Thirty-eight months after BNCT, necrosis in most tissues and bones had resolved, and epithelialization of the skin over the brain parenchyma was observed (Fig. 3). The patient has been asymptomatic for approximately 2.5 years, despite extensive exposure of the brain. Furthermore, in spite of the development of this severe complication, the tumor subsided, and the patient is alive without disease.

Discussion/Conclusion

Radiation-induced temporal lobe/brain necrosis is a late complication that occasionally develops after radiation therapy for head and neck cancer. The incidence of brain necrosis with initial X-ray irradiation treatment for nasopharyngeal carcinoma is 3%, whereas that with re-irradiation treatment is 17% [8].

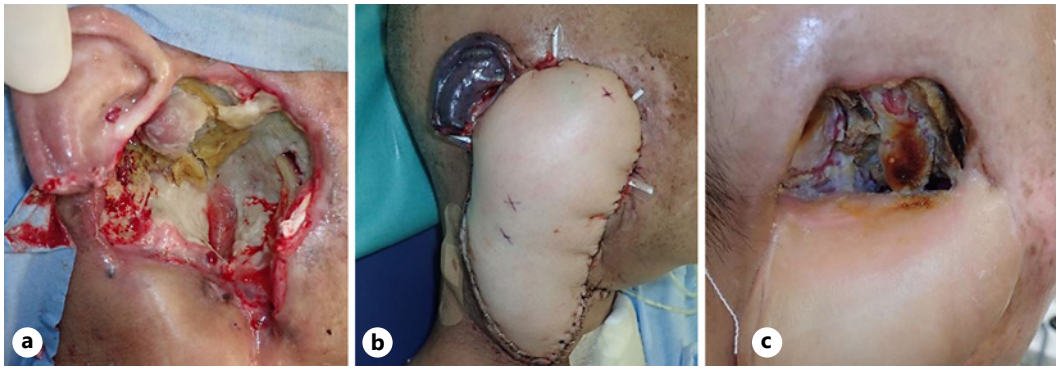

Fig. 3. a Necrotomy of the skull base and parapharyngeal region. **b** Repair of the defect with an anterolateral free flap. **c** Epithelialization of the skin over the brain parenchyma.

Osteoradionecrosis of the temporal bone (ORNTB) is also a late complication of radiation therapy for head and neck cancer. Its incidence is lower than that of radiation-induced brain necrosis. In a previous study on parotid cancer, the incidence of ORNTB after irradiation therapy was reported as 1.9% [9]. Yuhan et al. [10] reported that irradiation therapy for nasopharyngeal carcinoma, parotid gland cancer, and cancer of the external auditory canal accounted for approximately 75% of ORNTB cases. They also mentioned that the median radiation dose was 58 Gy, and the mean duration from irradiation to the onset of ORNTB was approximately 9 years. In the current case, serious ORNTB developed 3.5 years after the initial X-ray irradiation therapy. This could be attributed to the application of 2 cycles of re-irradiation with particle beams, suggesting that re-irradiation can occasionally cause unprecedented and extremely serious complications.

ORNTB can be classified according to its severity. Some studies have categorized ORNTB into 2 types (localized/diffuse), while others have categorized it into 5 types (I: erosion of the external auditory canal skin without bony involvement, II: erosion of the external auditory canal skin with bony necrosis, III: involvement of the middle ear space and/or mastoid, IVa: cranial nerve involvement, and IVb: skull base involvement) [11]. The treatment plan is based on the severity of ORNTB [11, 12].

The treatment for ORNTB generally consists of conservative therapy, such as debridement, antibiotic therapy, steroid therapy, and hyperbaric oxygen therapy. Surgical therapy should be considered when symptoms worsen. Surgical options include mastoidectomy or lateral temporal bone resection, depending on the extent of necrosis, and petrosectomy can occasionally be performed. After surgical resection, local or free flap reconstruction is performed to reconstruct the defective areas [10, 11]. In a study by Yuhan et al. [10], 60.9% ORNTB cases required surgical treatment, 33.9% required only mastoidectomy, 40.9% required lateral temporal bone resection, and 12.8% required petrosectomy. Moreover, reconstruction using a free flap with abundant blood flow has a lower ORNTB relapse rate than local flap reconstruction [11, 13, 14].

In the present case, debridement was performed slowly owing to the progression of necrosis. Although we tried to perform reconstruction using a free flap, the range of the necrosis expanded, and we were unable to fill the defect and achieve engraftment with the surrounding tissue. It is difficult to estimate the progression of necrosis in cases treated with re-irradiation therapy, as in this case.

Serious complications of ORNTB include internal carotid artery rupture, meningitis, brain abscess, and sigmoid sinus thrombosis. The incidence of internal carotid artery rupture, meningitis, and brain abscess is 1.9, 3.1, and 3.8%, respectively, and the mortality rate from

ORNTB is 3.0% [10]. During the 2.5 years of brain exposure, our patient experienced several instances of cerebrospinal fluid leakage; however, the leakage resolved with conservative treatment and did not lead to other fatal complications.

We encountered a case in which, despite extensive exposure of the brain due to serious ORNTB, long-term survival was achieved without any complications. For patients who are not candidates for surgery, re-irradiation alone is an option, albeit with poor prospects. This approach should be discussed with the patient while balancing the potential survival gain against the burden of treatment and the risk of complications.

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Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. This case report was approved by the Institutional Review Board of Kyushu University (reference number: 29-43). This case has been reported in accordance with the principles of the Declaration of Helsinki.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Mioko Matsuo and Sei Yoshida conceived of the presented idea. Mioko Matsuo and Ryuji Yasumatsu developed the theory. Jiroumaru, Kazuki Hashimoto, Takahiro Wakasaki, and Takashi Nakagawa encouraged Mioko Matsuo and Sei Yoshida to investigate and supervised the findings of this work. All the authors revised the manuscript, approved the manuscript to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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