

Case Report

A Case of Photoimmunotherapy for Nasopharyngeal Carcinoma Requiring Emergency Tracheostomy

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Keywords

Photoimmunotherapy · Nasopharyngeal carcinoma · Tracheostomy · Airway emergency

Abstract

Introduction: Photoimmunotherapy (PIT) is a treatment wherein intravenous cetuximab sarotalocan sodium is administered followed by laser light irradiation. This treatment exhibits a specific antitumor effect if in tumors expressing the epidermal growth factor receptor, regardless of the carcinoma [Mitsunaga et al.: Nat Med. 2011;17(12):1685–91, Sato et al.: ACS Cent Sci. 2018;4(11):1559–69, Nakajima et al.: Cancer Sci. 2018;109(9):2889–96]. The current indications are unresectable, locally advanced, or locally recurrent head and neck cancer. If standard treatments, such as radiotherapy and chemotherapy, are available, they are given priority. However, a significant concern in PIT is the occurrence of airway emergencies related to pharyngeal edema. Prophylactic tracheostomy is often performed in cases of PIT involving the root of the tongue, hypopharynx, or larynx. **Case Presentation:** In this study, we administered transoral PIT to a patient diagnosed with radiation-induced nasopharyngeal carcinoma (squamous cell carcinoma (SCC) cT1N0M0 stage I). Although previous case reports and our own experiences did not report airway emergencies following PIT for nasopharyngeal carcinoma, a unique case occurred in our study [Omura et al.: Auris Nasus Larynx. 2023; 50(4):641–5, Kushihashi et al.: Int J Otolaryngol Head Neck Surg. 2022;11(5, Sep):258–65]. The patient experienced poor oxygenation and a decreased level of consciousness early in the morning following the laser irradiation. Nasal endoscopy revealed airway narrowing due to upper airway edema, and intubation was challenging. Consequently, we performed emergency

bedside tracheostomy and the patient's condition improved. **Conclusion:** Therefore, it is crucial to note that airway emergencies can be life-threatening and should be diligently monitored as a potential complication of PIT.

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Introduction

Photoimmunotherapy (PIT) is an innovative treatment that targets various carcinomas expressing epidermal growth factor receptor [1–6]. Cetuximab arotarocan sodium was administered intravenously, followed by laser light 24 h later under general anesthesia. Given the prevalence of epidermal growth factor receptor expression in head and neck cancer, Japan approved PIT in January 2021, making it available ahead of other countries. The approved indications are “unresectable locally advanced or locally recurrent head and neck cancer,” and standard treatment is preferred when available. If the lesion invaded the carotid artery, the PIT was considered off-label [7].

Serious complications associated with PIT include bleeding due to tumor necrosis and airway emergencies associated with pharyngeal edema. Therefore, prophylactic tracheostomy is recommended when performing PIT in areas such as the root of the tongue, the hypopharynx, and the larynx. However, unlike at these sites, no airway emergencies have been reported for PIT in the nasopharynx, leading to the omission of prophylactic tracheostomy.

In the present study, we administered transoral laser irradiation to a patient with radiation-induced nasopharyngeal carcinoma. The patient exhibited poor oxygenation and decreased consciousness the day after the procedure. Emergency tracheostomy was performed after nasal endoscopy revealed airway stenosis. Fortunately, the patient's recovery progressed uneventfully and she was discharged on the 12th day post-surgery. Thus, this case underscores the potential for airway emergencies in PIT irrespective of the laser irradiation site, emphasizing the importance of vigilant monitoring and follow-up care.

Case Report

The patient was a 34-year-old female who had a history of rhabdomyosarcoma of the parapharyngeal space (received radiation alone at the age of 10 years; specific radiation details unknown). There is no family or psychosocial medical history. The patient reported a sore throat around X-1. In year X, her sore throat worsened, and she consulted a family otorhinolaryngologist. During this visit, irregular mucous membrane of the nasopharynx was identified. Subsequently, she sought evaluation at a university hospital, where a tissue biopsy confirmed the diagnosis of nasopharyngeal cancer and she was referred to our center for further treatment.

Upon initial assessment nasal endoscopy revealed mucosal irregularities from the posterior wall of the nasopharynx to the right and left lateral walls and canopy (Fig. 1a). The hematochemical findings were within normal ranges except for elevated LDH levels. CT showed no obvious neoplastic lesions in the nasopharynx (Fig. 1b). MRI was consistent with CT findings (Fig. 1c). However, PET/CT showed abnormal accumulation (SUVmax:15.6) localized in the nasopharynx, with no distant metastases (Fig. 1d). Based on the above findings, she was diagnosed with nonkeratinizing squamous cell carcinoma, specifically, radiation-induced nasopharyngeal carcinoma (SCC, cT1N0M0, Stage I).

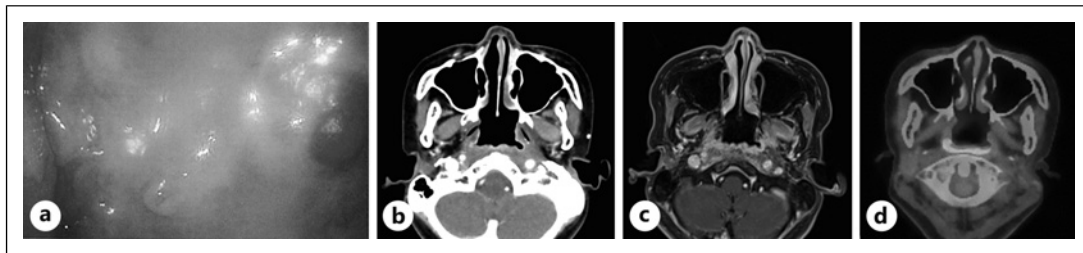


Fig. 1. **a** Initial nasal endoscopy findings – Coarse mucosal irregularities observed throughout the nasopharynx. **b** Initial CT imaging findings – No tumor lesions detected in the nasopharynx. Absence of apparent cervical lymph node metastasis. **c** MRI findings [T1 contrast] – no evident neoplastic lesions, consistent with cervical contrast CT findings. **d** PET/CT findings – localized abnormal SUV max 15.6 accumulation in the nasopharynx. No indications of distant metastasis.

The Raystation software was utilized to create treatment plans. The simulation confirmed the need for four irradiation sites with a 30 mm frontal diffuser to cover the tumor (Fig. 2). Sarotarocan sodium (640 mg/m^2) was administered the day before laser irradiation. The procedure was performed under general anesthesia. Neraton tubes inserted through both nasal passages. The soft palate repositioned anteriorly and cephalad to provide a working space. The lesion was irradiated with a 20 mm frontal diffuser, deviating from the planned 30 mm, owing to sufficient coverage.

Postoperatively, the initial local pain alleviated with analgesics. The patient was stable upon return to the room. However, on the first postoperative day (6:00 a.m.), the nurse noted sluggish patient response and reduced blood oxygen saturation. A nasal endoscopy diagnosed an airway emergency due to upper airway edema and emergency bedside tracheostomy was performed due to difficulties with oral intubation (Fig. 3a). Consciousness and oxygenation improved promptly post the procedure. The tracheal cannula replaced with retina on the third postoperative day. On the sixth postoperative day, the light patch test revealed no symptoms of hypersensitivity to sunlight, and the light shielding was removed. The patient was discharged on postoperative day 12 with a tracheostomy and the retina in place, with the exception of nasopharyngeal crusting (Fig. 3b). The CARE Checklist has been completed by the authors for this case report, and attached as supplementary material (for all online suppl. material, see <https://doi.org/10.1159/000537898>).

Discussion

Nasopharyngeal carcinoma poses surgical challenges owing to its anatomical features [8, 9]. Therefore, radiotherapy or chemoradiotherapy is the preferred treatment approach in most cases [10]. The patient presented with radiation-induced nasopharyngeal carcinoma, rendering traditional radiotherapy or combined chemoradiotherapy ineffective as a curative treatment. This case shared similarities with nasopharyngeal carcinoma recurring locally after radiotherapy, which typically has a poor prognosis as standard therapies become less viable [11].

However, as per the abovementioned indications for PIT, radiation-induced nasopharyngeal carcinoma, owing to its unresectable nature and lack of alternative standard treatments, is an excellent candidate for PIT. Prior to the advent of PIT as a treatment option, patients in such situations could only receive palliative care. However, PIT also offers a curative approach.



Fig. 2. Preoperative simulation irradiation of a single site with a 30-mm frontal diffuser does not cover the entire tumor; irradiation at four sites is necessary to encompass the entire tumor.

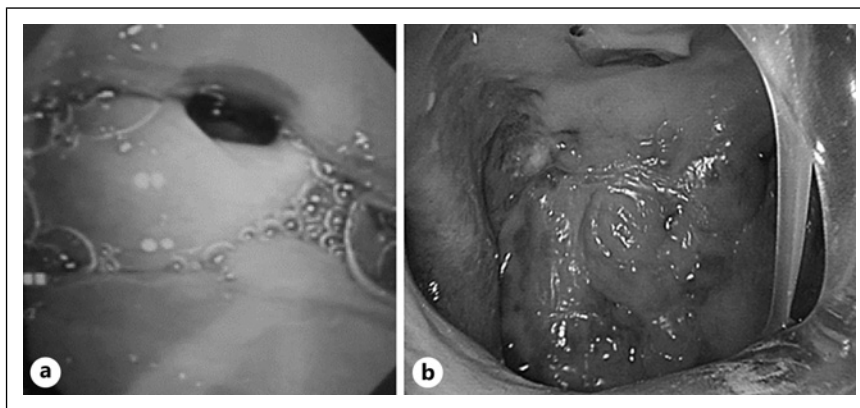


Fig. 3. a Postoperative day 1 nasal endoscopy findings – significant edema observed from the root of the tongue to the epiglottis. **b** Postoperative day 12 nasal endoscopy findings – crust formation observed, corresponding to the laser-irradiated area.

For PIT, cetuximab sarotarocan sodium was administered intravenously. This was followed by laser irradiation under general anesthesia after an interval of approximately 24 h. Laser irradiation systems include cylindrical diffusers for the internal irradiation of voluminous tumors and frontal diffusers for the external irradiation of superficial tumors. Therefore, the choice of the device or combination thereof depends on the specific case. In this case, given the superficial nature of the lesion, we opted for a frontal diffuser. Adequate preoperative planning for laser irradiation is crucial considering the primary site, tumor shape, and spread. We conducted preoperative simulations based on preoperative CT scans. Our simulation indicated that irradiating the entire tumor from four locations with a 30-mm frontal diffuser would suffice. However, inserting the frontal diffuser via the nasal cavity may hinder device maneuverability and prevent precise control of the laser irradiation range. Consequently, we determined that pulling the soft palate as far anteriorly and cephalad as possible and inserting the frontal diffuser transorally would offer better access to irradiate the soft palate, as simulated. However, during the procedure, we adapted and switched to a 20 mm frontal diffuser because the

planned 30 mm one led to significant overlap with the posterior wall and canopy area. Prophylactic tracheostomy was deemed unnecessary in this case because of the confined nature of the nasopharyngeal lesion, which led to the discernment that airway emergencies were unlikely.

Although the exact mechanism underlying mucosal edema, a known PIT complication, remains unknown, we speculate that its occurrence is based on the following rationale: PIT induces tumor cell necrosis, releasing damage-associated molecular patterns (DAMPs), which stimulate cytokine production and trigger an inflammatory response. The subsequent increase in vascular permeability is believed to contribute to edema [12, 13].

Despite the physical separation of the nasopharynx from the hypopharynx and larynx, which typically prevents airway emergencies following laser irradiation for nasopharyngeal cancer, our case raises concerns. Excessive laser irradiation, particularly near the soft palate, may cause extensive edema and airway complications. While laser irradiation through the nasal cavity maintains an appropriate distance between the frontal diffuser and the lesion, transoral insertion poses challenges owing to soft palate obstruction. In particular, the canopy behind the soft palate and above the lateral wall is problematic. To mitigate this, a potential preventive measure involves creating an incision in the soft palate to establish an irradiation hole for laser treatment. However, such measures cannot guarantee the complete prevention of airway emergencies. Although the notion of performing prophylactic tracheostomy in all PIT cases may be controversial, our center is considering adopting this policy in the future.

PIT is used as a treatment modality for radiation-induced nasopharyngeal carcinoma. However, on the first postoperative day, the patient experienced a critical airway emergency necessitating emergency tracheostomy. Thus, while PIT demonstrates substantial promise as a treatment option for locally recurrent nasopharyngeal cancer following radiotherapy or radiation-induced carcinoma, it underscores the importance of a thorough postoperative airway assessment and preparedness for potential airway emergencies, as in our case.

Moreover, whether prophylactic tracheostomy should be universally adopted for all patients undergoing PIT remains debatable. Nevertheless, our center is actively considering the implementation of prophylactic tracheostomy as a standard procedure for all patients given the inherent risks associated with this treatment approach.

As the number of PIT cases continues to increase in Japan, there is a growing need for comprehensive data analysis based on accumulated clinical experience. Such an analysis will contribute to a deeper understanding of the nuances of treatment and potential complications, guide future practices, and improve patient outcomes.

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Statement of Ethics

The Ethics Review Committee of International University of Health and Welfare, International University of Health and Welfare did not require ethics approval for the case report. Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Yukiomi Kushihashi, Tatsuo Masubuchi, Isaku Okamoto, and Chihiro Fushimi for their work on the paper and on PIT. Morio Yamazaki, Hisashi Asano, Reo Aoki, Shota Fujii, and Yukiko Asako were involved in PIT. Yuichiro Tada was involved in the preparation of the paper.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its supplementary material files. Further inquiries can be directed to the corresponding author.

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