

Photoimmunotherapy for Local Recurrence of Nasopharyngeal Carcinoma: A Case Report

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Abstract

Photoimmunotherapy (PIT), developed by the National Cancer Institute, involves Cetuximab sarotalocan sodium infusion followed by laser irradiation. PIT exerts specific antitumor effects on a variety of carcinomas that express epidermal growth factor receptors. PIT is a new cancer treatment option approved by Japan ahead of other countries worldwide. As of 2022, PIT is indicated in “unresectable, locally advanced, or locally recurrent head and neck cancer, with priority given to standard treatments such as chemotherapy when available”. The conventional treatment for unresectable locally advanced or locally recurrent head and neck cancer is palliative. Whether photoimmunotherapy can be curative for unresectable locally advanced head and neck cancers depends on the case. Herein, we report a case of locally recurrent nasopharyngeal carcinoma, treated with photoimmunotherapy via the nasal cavity, along with a literature review. Preoperative simulation provided considerable information on device selection, numbers of devices, and availability of working space. As a result, a complete response was obtained following a cylindrical diffuser puncture. Cases of local recurrence of nasopharyngeal carcinoma are considered a good indication for PIT. However, since the follow-up period after treatment was short in this case, we will continue to conduct strict follow-ups and accumulate more cases.

Keywords

Photoimmunotherapy, Nasopharyngeal Carcinoma, Head and Neck Carcinoma, Cetuximab Sarotalocan Sodium

1. Introduction

Photoimmunotherapy (PIT) was developed by the National Cancer Institute. It

exerts specific antitumor effects on various carcinomas that express epidermal growth factor receptor (EGFR) [1] [2] [3]. Since EGFR is expressed in many head and neck cancers [4], insurance approval was granted for PIT in Japan on January 1, 2021, ahead of all other countries. As of 2022, the indication for PIT is “unresectable, locally advanced, or locally recurrent head and neck cancer, with preference given to standard treatments such as chemotherapy when those treatments are available”. Moreover, cases in which invasion of large blood vessels is observed are considered for off-label treatment [5]. The nasopharynx is a difficult site for radical resection due to its complex anatomy. Therefore, we considered local recurrence of nasopharyngeal carcinoma to be a very good indication for PIT. In this report, we describe a complete response to PIT in a patient with locally recurrent nasopharyngeal carcinoma. This is the first case in the world in which puncture was performed using a cylindrical diffuser.

2. Case Report

A 57-year-old man underwent chemoradiotherapy (from nasopharynx to right neck: 40 Gy irradiation + weekly Carboplatin: 25 mg/body) for cervical lymph node metastasis of nasopharyngeal cancer 21 years ago. The patient subsequently underwent right radical neck dissection, and chemoradiotherapy (nasopharynx: 20 Gy + weekly Carboplatin: 25 mg/body) was administered postoperatively. Post-treatment tissue biopsy confirmed complete response. In 202x (data blinded to protect patient’s identity), the patient consulted an otolaryngologist and was suspected of having rhinosinusitis. Nasal endoscopy was performed, during which a nasopharyngeal tumor was incidentally detected. The patient was referred to our center for further examination.

Endoscopic findings at initial visit: The tumor about the size of a fingernail with a rough surface was found anterior to the Eustachian tube on the right side of the nasopharynx (**Figure 1(a)**).

Initial computed tomography (CT) imaging findings: The tumor was confined to the right lateral wall of the nasopharynx, with no invasion into the skull base (**Figure 1(b)**). There was no evidence of metastasis to the lateral retropharyngeal (Rouviere) or cervical lymph nodes.

Magnetic resonance imaging (MRI) findings: A tumor measuring approximately 18 mm was seen around the right Eustachian tube (**Figure 1(c)**).

Positron Emission Tomography (PET)/CT findings: Abnormal accumulation of SUVmax: 6.9 was observed in a tumor around the right Eustachian tube (**Figure 1(d)**). No accumulation was observed in other distant tissues.

Histopathological findings: A nonkeratinizing squamous cell carcinoma (SCC) was observed (**Figure 2**).

Clinical diagnosis: Local recurrence of nasopharyngeal carcinoma (SCC, rT1N0M0 Stage I).

Treatment plan: The patient had a local recurrence of nasopharyngeal carcinoma in the lateral wall, and surgical resection was not indicated; therefore, PIT

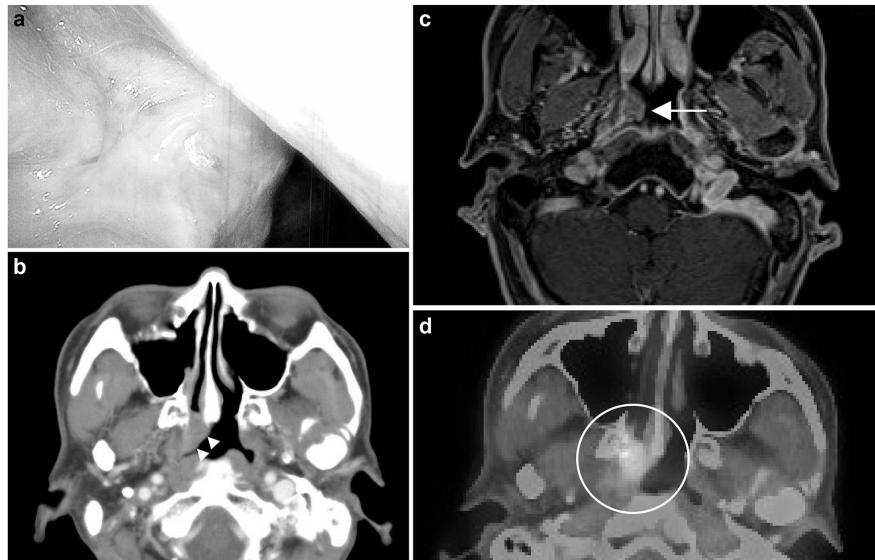


Figure 1. Local recurrence of nasopharyngeal carcinoma before treatment. (a) Recurrent tumor with a rough surface around the Eustachian tube. (b) Contrast CT (axial): Recurrent tumor with pale contrast effect localized to the right side of the nasopharynx with no invasion into the skull base (arrowheads). (c) Contrast-enhanced MRI (axial): Approximately 18-mm tumor located on the lateral wall of the nasopharynx (arrow). (d) PET/CT (axial): The accumulation was localized to the tumor (circle).

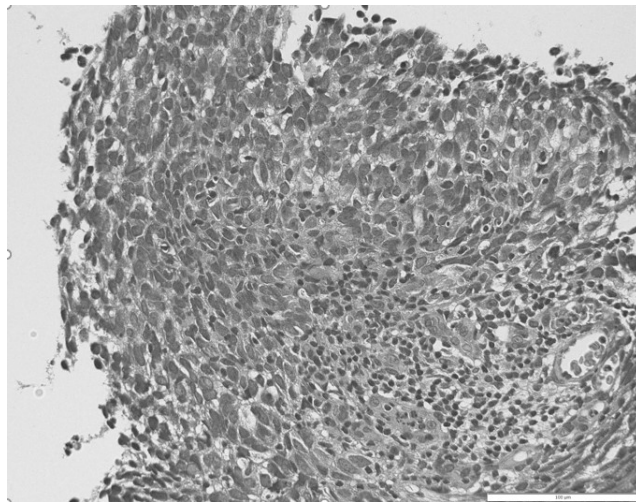


Figure 2. Histopathological findings: A nonkeratinizing squamous cell carcinoma (SCC) was observed.

was planned. Because the lesion was elevated rather than a superficial lesion of the nasopharyngeal mucosa, it was punctured with a cylindrical diffuser (Bio Brade[®] cylindrical diffuser; Rakuten Medica, Tokyo, Japan).

Preoperative simulation: Preoperative treatment planning was performed using RayStation software (Hitachi, Ltd., Tokyo, Japan). Treatment plans were developed with the cooperation of a medical radiographer. Simulation results confirmed that two cylindrical diffuser punctures were sufficient to treat the tumor (**Figure 3(a)**). Since the working space in the nasal cavity is narrow, we decided

to resect the inferior turbinate bone first and then perform an accurate puncture. If the tumor is located in the posterior wall of the nasopharynx, either a frontal or cylindrical diffuser can be selected depending on the thickness of the tumor.

If the tumor is located on the lateral wall, only cylindrical diffusers are indicated.

The frontal diffuser can only beam the laser forward from the tip of the device. Therefore, it is not possible to beam to tumors located in the lateral wall. Cylindrical diffusers, on the other hand, emit the laser in a cylindrical shape with a radius of 10 mm around the long axis of the device.

Preoperative procedures: Cetuximab sarotalocan sodium (640 mg/m^2) was administered intravenously over 2 h.

Operative findings: First, the right inferior turbinate bone was endoscopically resected from the base using an ultrasonic coagulation incision device. After careful hemostasis, the tumor was observed endoscopically, and a single cylindrical diffuser was punctured. Intraoperative CT imaging was performed after the puncture for comparison with the simulation and to confirm that there were no problems (**Figure 3(b)**). Using the first puncture as a reference, a second puncture was made parallel to the first puncture on the medial-inferior side. Intraoperative CT was performed again to confirm that the puncture position was the same as in the simulation (**Figure 3(c)**). Finally, the surgery was terminated by simultaneous light irradiation of the two areas using a laser (Bio Brade laser; Rakuten Medical).

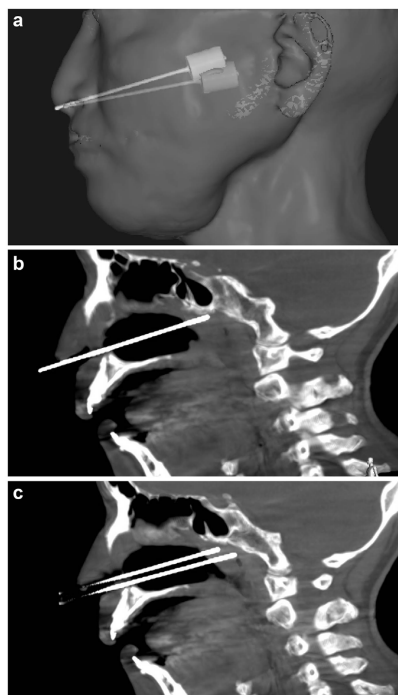


Figure 3. Preoperative simulation and intraoperative CT. (a) Sagittal section of preoperative simulation. (b) Intraoperative CT findings after puncture of one cylindrical diffuser. (c) Intraoperative CT findings after two cylindrical diffusers have been punctured.

Postoperative course: On the first postoperative day, the patient's nasal cavity was swollen, which made endoscopic observation of the tumor difficult. On the fourth postoperative day, swelling in the nasal cavity reduced, and the wound became visible. The base of the inferior turbinate bone was covered with crusts, and the wound had a raw surface with thin crusts and blood clots (**Figure 4(a)**). On the seventh postoperative day, marked shrinkage of the tumor was observed (**Figure 4(b)**). A patch test was performed on the same day, and light shielding was removed since no hypersensitivity symptoms to sunlight were observed. On the 12th postoperative day, the patient was discharged from the hospital with only a thin crust on the wound and no adverse events. Six months after surgery, both endoscopic (**Figure 4(c)**) and MRI findings (**Figure 4(d)**) were satisfactory, and a complete response was maintained.

3. Discussion

Surgical resection of nasopharyngeal carcinoma is difficult because of its anatomical features [6] [7]. Even when surgery is indicated, chemoradiotherapy is the curative treatment of choice in many cases because of the invasive nature of the surgery [8]. Therefore, once a local recurrence occurs, the choice of treatment is difficult. Relief surgery and re-irradiation are treatment options for locally recurrent nasopharyngeal carcinoma, but their indications are very limited [9]. Therefore, cases of local recurrence of nasopharyngeal carcinoma may have a poor prognosis [10]. Curative treatment is impossible with unresectable, locally advanced, or locally recurrent head and neck cancer, and palliative treatment is indicated in such cases. The indication for PIT is "unresectable, locally advanced,

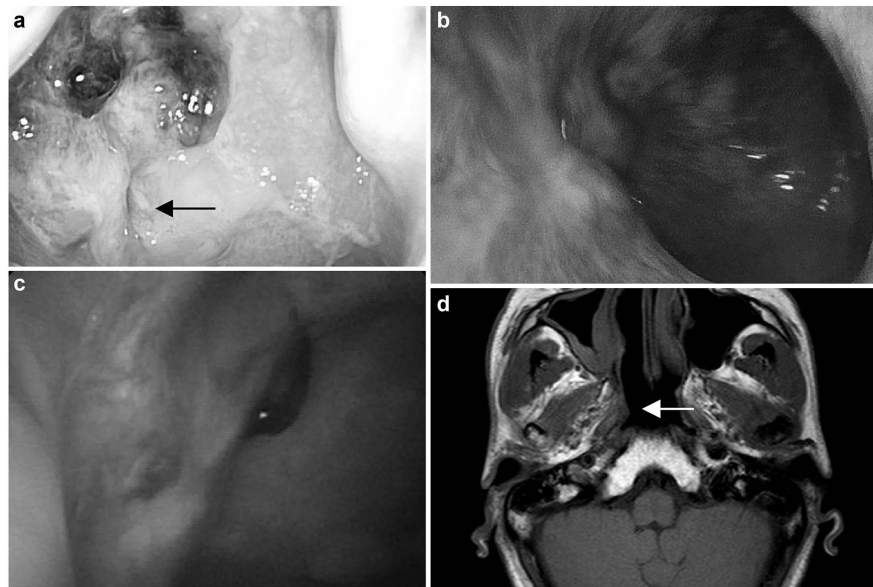


Figure 4. Postoperative course. (a) Findings of the wound on the fourth postoperative day. Arrow points to Eustachian tube. (b) Wound findings on the seventh postoperative day. (c) Wound findings on the 141st postoperative day. (d) MRI findings on the 141st postoperative day. Complete response is observed (arrow).

or locally recurrent head and neck cancer, with priority given to standard treatments such as chemotherapy when these treatments are available". T1 cases of nasopharyngeal carcinoma with local recurrence after chemoradiotherapy confined to the nasopharynx are considered a very good indication for PIT. Thus, curative treatment is now possible with PIT in cases of local recurrence of nasopharyngeal carcinoma confined to the nasopharynx.

PIT involves treatment with intravenous cetuximab sarotalocan sodium, followed by laser light irradiation. Two types of devices exist for laser beam irradiation: cylindrical diffusers and frontal diffusers (Bio Brade frontal diffuser). The cylindrical diffuser is a device that performs intratumoral irradiation by puncturing tumors with a thickness of at least 10 mm. The frontal diffuser is a device that provides superficial external radiation to tumors that are less than 10 mm in thickness. The decision to use a cylindrical diffuser, a frontal diffuser, or a combination of the two, depends on the tumor's nature and recurrence site.

Preoperative planning for light irradiation is extremely important owing to the complex anatomy of the head and neck region. This case had a recurrent tumor around the Eustachian tube in the nasopharynx. Because the tumor was elevated and the broad base was located around the Eustachian tube, it was determined that the frontal diffuser would not provide uniform irradiation to the tumor. Preoperative simulation showed that if two cylindrical diffusers were punctured, the entire tumor could be sufficiently irradiated. To puncture the tumor in the lateral wall of the nasopharynx transnasally with a cylindrical diffuser, it was necessary to resect the inferior turbinate bone at the base to provide the working space. The advantages of preoperative simulation are the ability to determine: 1) the type of device needed (cylindrical diffuser, frontal diffuser, or both); 2) the number of devices needed; and 3) working space and body position during irradiation. Instead of finalizing the treatment plan in the operating room on the day of surgery, the treatment can be facilitated by simulating it in advance. The type and number of devices may be somewhat predictable without simulation. However, to determine the working space and body position, the simulation provides useful information. In this case, it was known preoperatively that the inferior turbinate bone would obstruct because of the location of the nasal cavity and the tumor. The anatomical features of the nasopharynx make it difficult to directly visualize the tumor. Therefore, it is very important to determine the choice of device and how it will be irradiated in advance. Careful simulation allows the determination of a specific treatment plan, shortens the operation time, and reduces patient burden. Furthermore, the use of extra devices during surgery is expected to decrease, thereby reducing the burden on the health care economy.

The challenge for the future is to accurately reproduce the treatment plan determined in the simulation in an actual operating room. We ensured the reproducibility of treatment by performing intraoperative CT imaging; however, further methods need to be explored. Moreover, only two types of devices (*i.e.*, cy-

lindrical diffusers and frontal diffusers) currently exist. The development of new devices would greatly expand the scope of treatment, and we look forward to further developments in this area.

PIT is the first new treatment approved by insurance in Japan, and to our knowledge there are no reports of complete response using cylindrical diffusers for local recurrence of nasopharyngeal carcinoma. Therefore, this is a very valuable case report, and we need to continue to monitor the patient's progress carefully in the coming months and years. PIT is a new treatment and there is no accumulated data yet. Therefore, we cannot say on the basis of evidence which cases it is effective. However, we believe that PIT is very effective in the treatment of local recurrence of nasopharyngeal cancer that is difficult to resect surgically. In the future, it is necessary to accumulate data not only on nasopharyngeal cancer cases, but also on the therapeutic efficacy of PIT for other recurrent head and neck cancers. If we can demonstrate the efficacy of PIT for recurrent head and neck cancer, we believe that we can expect to expand the indication to early-stage cancer in the future.

4. Conclusion

Here, we report a case of complete response to PIT in a patient with a local recurrence of nasopharyngeal carcinoma. Local recurrence of nasopharyngeal carcinoma is a good indication for PIT. Preoperative simulation is very useful for the actual treatment. We will continue to accumulate more cases for further studies.

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Statement of Ethics

This study protocol was reviewed and the need for approval was waived by the Ethics Committee of the International University of Health and Welfare. Prior written consent was obtained from the patient for the publication of the patient's medical information and accompanying images.

Author Contributions

Yukiomi Kusihashi designed the study. Yukiomi Kushihashi wrote the main manuscript and prepared the figure. Yukiomi Kushihashi, Tatsuo Masubuchi, and Isaku Okamoto developed a treatment plan and performed the PIT. Yukiomi Kushihashi, Tatsuo Masubuchi, Chihiro Fushimi, Kenji Hanyu, Mayu Yamauchi, Yuichiro Tada, and Koki Miura were responsible for the treatment of this patient. All authors discussed the results of the case report, made comments on the manuscript, and approved the final version to be published.

Data Availability Statement

All data generated or analyzed in this study are included in this article. Further inquiries can be directed to the corresponding authors.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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