

Case Report

Preparatory endonasal surgical modification to create a functional corridor for effective photoimmunotherapy in residual nasopharyngeal carcinoma: a case report

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ABSTRACT

Delivering effective photoimmunotherapy (PIT) in the anatomically constrained nasopharynx is technically challenging. Optimizing laser access is essential for achieving complete tumor illumination and maximizing treatment efficacy. A man in his fifties with refractory residual nasopharyngeal carcinoma (NPC) underwent preparatory endonasal surgical modification consisting of endoscopic resection of the posterior nasal septum and inferior turbinates. This procedure created a straight transnasal functional corridor and provided an adequate standoff distance for frontal diffuser placement. PIT was subsequently administered using intravenous cetuximab sarotalocan sodium, according to the standard protocol. The newly established functional corridor enabled stable and uniform laser illumination of the nasopharyngeal lesion. The procedure was completed without intraoperative or postoperative complications. Endoscopy and biopsy performed seven weeks after PIT confirmed a complete response, and the patient remained disease-free at 12 months of follow-up. Preparatory endonasal surgical modification can overcome anatomical barriers and facilitate safe and effective PIT delivery for residual NPC. By simplifying laser access and reducing technical demands, this minimally invasive approach may facilitate broader clinical use of PIT in anatomically constrained nasopharyngeal regions.

Keywords: Photoimmunotherapy, Nasopharyngeal carcinoma, Endoscopic surgery, Functional corridor, Head and neck cancer

INTRODUCTION

Nasopharyngeal carcinoma (NPC) poses a therapeutic challenge because residual or recurrent lesions after chemoradiotherapy are often difficult to manage.¹⁻³ Photoimmunotherapy (PIT) is a novel treatment that combines a tumor-targeting monoclonal antibody conjugated to a photosensitizer with local 690-nm light irradiation to selectively destroy cancer cells.⁴ A first-in-

human, phase I/IIa clinical trial for unresectable, locally recurrent head and neck squamous cell carcinoma began in the United States in 2015, followed by a Japanese phase I trial in 2018.^{5,6} In 2021, Japan became the first country to approve PIT, using the combination of the monoclonal antibody cetuximab and the photosensitizer sarotalocan, for treating unresectable, locally advanced, or recurrent head and neck cancers (HNC) in cases refractory to standard treatments.⁶ Early clinical results have demonstrated favorable efficacy and safety profiles.^{4,5}

In the study by Okamoto et al, it was reported that patients who underwent PIT exhibited improved quality of life and demonstrated a satisfactory level of local control.⁶ Furthermore, PIT may contribute to prolonged survival in patients with HNC.⁷ Several case reports have described the effectiveness of PIT in treating recurrent NPC.⁸⁻¹⁰ However, successful PIT requires precise and sufficient illumination of the target, which is technically challenging in the nasopharynx due to its deep and narrow anatomy.

Here, we present a case of residual NPC that was successfully treated with PIT following preparatory endonasal surgical modification after chemoradiotherapy. This procedure is designed not for tumor resection, but rather to create a "functional corridor," which facilitates optimal laser access for PIT. This approach enables effective PIT delivery with fewer technical demands than complex endoscopic resections and could expand the therapeutic applicability of PIT, potentially in combination with immune checkpoint inhibitors.^{11,12}

CASE REPORT

A man in his fifties was diagnosed with left nasopharyngeal squamous cell carcinoma (non-keratinizing) and staged as cT1N1M0 (stage II) according to the eighth edition of the UICC classification. He received induction chemotherapy with paclitaxel, carboplatin, and cetuximab, followed by radiotherapy totaling 60 Gy.¹³ Despite these treatments, residual disease persisted in the nasopharynx. Additional systemic therapy with cetuximab plus carboplatin and two cycles of nivolumab produced no further response. An endoscopic biopsy confirmed the presence of residual squamous cell carcinoma. The lesion appeared thin and superficial on endoscopy and indistinct on MRI, consistent with a localized surface lesion (Figures 1a and b).

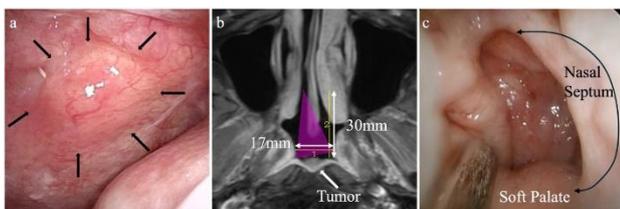


Figure 1: Preoperative findings (a) endoscopic view showing a residual tumor (arrows) on the left posterior nasopharyngeal wall; (b) MRI demonstrating that the laser irradiation pathway to the residual tumor was restricted by the posterior nasal septum and inferior turbinate; and (c) the posterior nasal septum required partial resection to secure an adequate standoff distance for photoimmunotherapy (PIT).

Due to the technical difficulty of conventional surgery and the patient's preference for a minimally invasive option with a rapid recovery time, PIT was planned. This involved the administration of intravenous cetuximab sarotalocan

sodium (Akalux®, Rakuten Medical, Tokyo, Japan), followed by near-infrared (690 nm) laser illumination using a frontal diffuser (BioBlade®, Rakuten Medical).⁸ Cetuximab sarotalocan sodium was infused 24 hours before illumination at the standard dose of 640 mg/m².⁴ The patient remained in a dark room during the 24-hour interval, and no infusion-related adverse events occurred.

The frontal diffuser requires a standoff distance of approximately 1.7 times the illumination-spot diameter. Achieving the necessary 30 mm distance for the 17 mm beam was difficult in the narrow nasopharyngeal space (Figures 1b and c). Endonasal surgical modification was performed to secure adequate exposure, under general anesthesia immediately before PIT (Figure 1c). Using electro-surgical and powered instruments under endoscopic guidance, the posterior nasal septum and posterior portions of both inferior turbinates were resected. After posterior septectomy, the tumor and torus tubarius were exposed. Additional partial resection of the inferior turbinates improved maneuverability. A soft rubber Nelaton catheter was passed transnasally to retract the soft palate and enhance visualization of the nasopharynx. This modification created a direct working functional corridor, which increased the distance and angulation for laser application (Figure 2a).

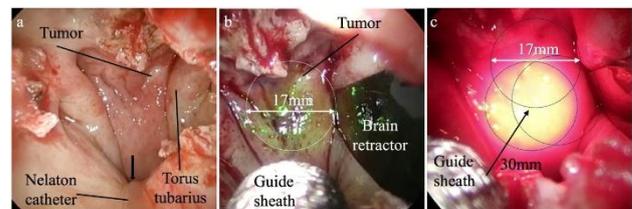


Figure 2: Endonasal surgical modification and laser irradiation technique to create a functional corridor for PIT (a) exposure of the nasopharyngeal tumor after resection of the posterior nasal septum and inferior turbinates; (b) a 17-mm circular irradiation field was established through the transnasal corridor using a frontal diffuser; and (c) three overlapping 17-mm circular irradiations were delivered with an approximate standoff distance of 30 mm.

Then, a brain retractor was used to gently retract the torus tubarius, providing an unobstructed view of the lesion in the left Rosenmüller fossa. Approaching from the right nasal cavity allowed for visualization of the left Rosenmüller fossa and enabled safe margin-based broad irradiation. A transnasal guide sheath created a stable, linear pathway for the frontal diffuser probe (Figure 2b). PIT was then performed transnasally using a 17 mm illumination spot in three overlapping fields, which covered the entire lesion and a safety margin. The frontal diffuser was kept 30 mm from the target via the newly created functional corridor (Figure 2c). The procedure was conducted in a darkened operating room to prevent unintended photoactivation, and it was completed without technical difficulties or intraoperative complications.

Tracheostomy was not required. Due to the potential for airway edema and pain after PIT, the patient was monitored in the intensive care unit for two days. Analgesia included continuous intravenous fentanyl and acetaminophen. The patient recovered uneventfully, without laryngeal edema or acute complications, and was discharged seven days after surgery.

Three weeks after PIT, endoscopy revealed a thick eschar adhering to the treated site (Figure 3a), indicating effective tumor necrosis. At seven weeks after PIT, the crust detached, revealing complete epithelialization without residual mass (Figure 3b). Biopsies from the treated area showed only scar tissue, with no viable carcinoma. MRI performed seven weeks after PIT confirmed the absence of residual tumor and demonstrated a widened nasopharyngeal space, reflecting preparatory endonasal resection (Figure 3c). Twelve months after PIT, the patient remained disease-free with no recurrence or treatment-related complications.

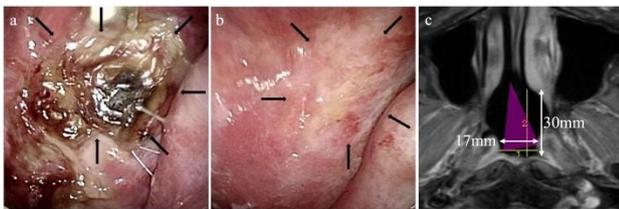


Figure 3: Post-treatment findings after PIT (a) Eschar formation observed at the treated site three weeks after PIT; (b) complete epithelialization without evidence of residual or recurrent diseases even weeks after PIT; and (c) MRI showing disappearance of the nasopharyngeal carcinoma and a persistently widened functional corridor seven weeks after PIT.

DISCUSSION

NPC poses a therapeutic challenge when residual or recurrent disease remains after chemoradiotherapy. Salvage strategies such as re-irradiation, endoscopic resection, and systemic therapy all have significant limitations.² According to NCCN guidelines, there is limited evidence supporting salvage surgery (category 2A: "considered in selected patients").¹⁴ However, in practice, anatomical constraints, radiation-induced fibrosis, and proximity to critical structures often preclude complete resection. Consequently, surgery is reserved for highly select cases at expert centers and is not considered standard.

Several factors supported the choice of PIT in the present case. Endoscopic evaluation revealed the resection margin was unclear, and technically, doubts arose about the feasibility of achieving complete resection. The lesion was superficial on MRI, indicating its suitability for PIT with a frontal diffuser. Furthermore, the patient strongly preferred a minimally invasive approach with a quick recovery time. Taken together, these factors made PIT a reasonable alternative.

This case underscores the importance of optimizing PIT delivery in anatomically complex regions, such as the nasopharynx. Effective treatment requires secure physical access to ensure uniform laser illumination. Previous reports have emphasized the difficulty of securing an optimal illumination path for nasopharyngeal PIT.⁸⁻¹⁰ In this case, the posterior nasal septum and inferior turbinates initially obstructed the visual field. Endoscopic resection of these structures created an adequate functional corridor, enabling the required standoff distance for frontal diffuser application. Approaching from the right nasal cavity allowed visualization of the left Rosenmüller fossa and enabled safe, margin-based, broad irradiation under endoscopic guidance. This approach ensured uniform activation of the photosensitizer throughout the lesion. This surgical modification provides a simple and effective solution. A frontal diffuser is suitable for superficial lesions (rT1), as in this case. A cylindrical diffuser (BioBlade®, Rakuten Medical, Tokyo, Japan) may be appropriate for deeper rT2-4 lesions. Enlarging the posterior nasal cavity facilitates flexible light delivery and accommodates various diffuser types. Unlike corridors created for tumor resection, this functional corridor is designed specifically to optimize illumination rather than tissue removal, which could expand the applicability of PIT.

In our patient, PIT proactively addressed anatomical limitations and achieved complete remission of residual NPC. The modified transnasal approach enabled effective laser delivery and achieved durable local control, with no recurrence at 12 months. This case demonstrates that PIT is oncologically effective and technically simpler than endoscopic resection, which is challenging after radiotherapy. In specific cases, this strategy may make PIT as effective as conventional salvage therapy.

Unlike endoscopic resection, PIT selectively targets tumor cells that express the epidermal growth factor receptor while sparing normal tissue.⁶ Although endoscopic resection is less costly, it lacks this selective mechanism and cannot guarantee negative margins. Similarly, endoscopic ablation with a plasma knife is less expensive and technically feasible. However, margin assessment remains difficult, and the mechanism differs fundamentally from that of PIT. Although PIT is resource-intensive, its ability to achieve local control without extensive resection or prolonged recovery makes it advantageous for carefully selected patients. Additionally, PIT offers the benefit of repeated irradiation at the same site, which is advantageous for managing recurrent carcinoma.⁶ Furthermore, the clinical efficacy of PIT in combination with immune checkpoint inhibitors has been reported, and recent clinical data in the United States (ASP-1929; Photoimmunotherapy with Pembrolizumab) may reveal its potential to become a global standard for select patients with recurrent HNC.^{11,12}

PIT is gaining regulatory approval and clinical application in multiple regions.^{6,12} However, it cannot substitute for salvage surgery in terms of histologic margin

assessment.¹⁵ The cost and limited availability of specialized equipment restrict its widespread adoption. Therefore, while this case study demonstrates that PIT can provide effective local control, its long-term oncologic adequacy in recurrent NPC remains to be determined. Further studies are necessary to clarify the procedure's long-term safety and efficacy and to determine which patients are best suited for it. This case underscores the importance of surgical preparation in maximizing the therapeutic potential of PIT for NPC.

CONCLUSION

Preparatory endonasal surgical modification to establish a functional corridor enabled the effective and uniform delivery of PIT in residual NPC. This strategy achieved durable remission without complications and could be a valuable addition to the management of anatomically challenging nasopharyngeal carcinoma.

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