

## Case Report

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# Lemierre's Syndrome after Head and Neck Photoimmunotherapy for Local Recurrence of Nasopharyngeal Carcinoma

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### Keywords

Head and neck photoimmunotherapy · Lemierre's syndrome · Head and neck carcinoma ·  
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### Abstract

**Introduction:** Head and neck photoimmunotherapy (HN-PIT) uses a combination of drugs and laser illumination to specifically destroy tumor cells. Lemierre's syndrome is an infectious disease with severe systemic symptoms caused by prior infection in the pharyngeal region, leading to thrombophlebitis. Here, we report a case of Lemierre's syndrome that developed after HN-PIT for recurrent nasopharyngeal carcinoma. **Case Presentation:** A 68-year-old male with nasopharyngeal carcinoma (squamous cell carcinoma) underwent HN-PIT after local recurrence with chemoradiation therapy. Three months after HN-PIT, the patient developed fever and neck pain, which led to a diagnosis of Lemierre's syndrome. The patient was treated with antibiotics and anticoagulants for at least 1 month. The patient's general condition and inflammatory findings on blood sampling showed gradual improvement, and a follow-up cervicothoracic computed tomography imaging showed that the venous thrombus had been obscured and the patient was doing well. **Conclusion:** HN-PIT is a high-risk procedure for the development of Lemierre's syndrome due to irradiation-induced mucositis, and anticipating the development of Lemierre's syndrome during HN-PIT is important.

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## Introduction

Head and neck photoimmunotherapy (HN-PIT) is a treatment in which cetuximab sarotalocan sodium is administered, followed by illumination with red light at 690 nm to specifically destroy tumor cells. HN-PIT is indicated for unresectable, locally advanced, or locally recurrent head and neck cancer [1, 2]. Chemoradiotherapy is the standard treatment for nasopharyngeal carcinoma [3]. However, salvage surgery is difficult in cases of local recurrence and is considered a good indication for HN-PIT [4]. We encountered a case of Lemierre's syndrome, which developed after HN-PIT for recurrent nasopharyngeal carcinoma. Lemierre's syndrome is an infection of the pharyngeal region that leads to thrombophlebitis in the internal jugular vein and other jugular veins. The infection can be complicated by abscesses in remote organs, causing severe systemic symptoms [5]. HN-PIT causes mucositis due to illumination and is consequently associated with a high risk of developing Lemierre's syndrome. Therefore, we report this case, along with a review of the relevant literature.

## Case Report

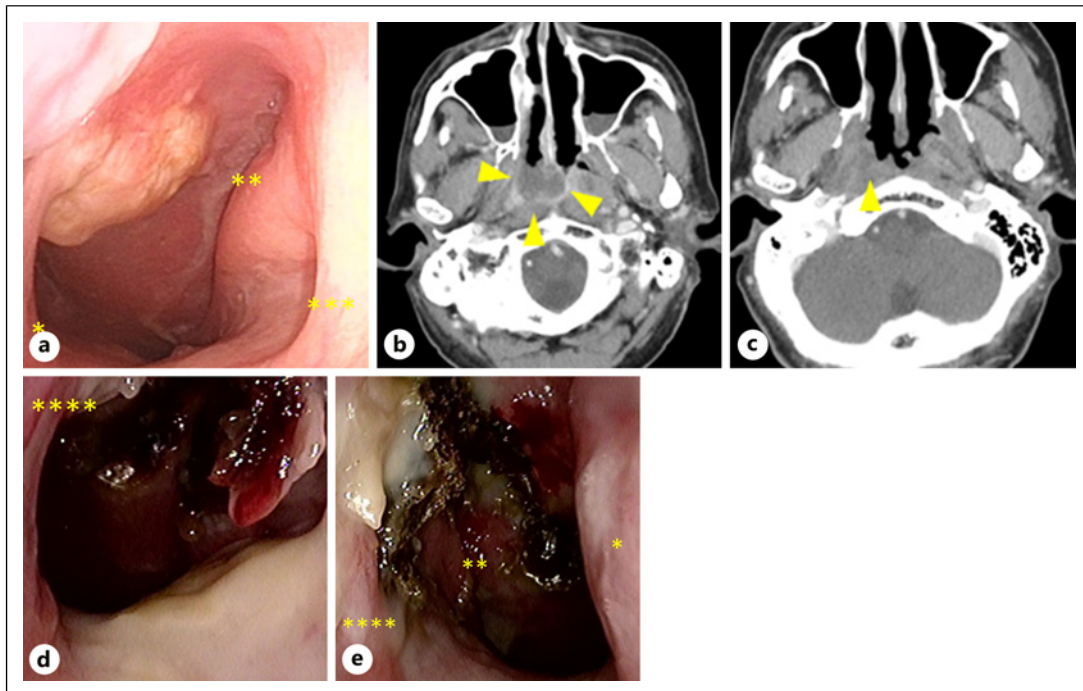
A 68-year-old patient was treated with chemoradiotherapy in March 2022 for nasopharyngeal cancer (squamous cell carcinoma of the right wall, cT2N2M0 stage III). The primary tumor and cervical lymph node size did not change significantly, and the effect of the treatment was judged to be poor. In July 2022, the patient underwent HN-PIT after cervical lymph node dissection (shown in Fig. 1a–d). After HN-PIT, mucositis in the nasopharynx persisted but became mild after 3 months. The primary lesion showed a tendency to shrink after treatment. In October 2022, the patient complained of anorexia, neck pain, and headache and was admitted to the hospital as an emergency.

Physical findings on admission of the patient revealed clear consciousness, a temperature of 38.4°C, blood pressure of 123/67 mm Hg, pulse of 101/min, and a respiratory rate of 16 breaths/min. The patient experienced spontaneous pain on both sides of the neck with no skin redness.

Nasopharyngeal endoscopy revealed mucosal redness and crusting (shown in Fig. 1e). Blood tests yielded the following results: white blood cell count, 33,000/ $\mu$ L (98% neutrophil fraction); hemoglobin, 7.2 g/dL; platelets,  $1.5 \times 10^5$ / $\mu$ L; BUN, 31.3 mg/dL; Cre, 1.17 mg/dL; CRP, 24.24 mg/dL; PT-INR, 1.11; D-dimer, 2.30  $\mu$ g/dL; fibrinogen, 608 mg/dL; and FDP, 7.3  $\mu$ g/dL.

Contrast-enhanced computed tomography (CT) of the cervicothoracic region revealed the following: the thrombus spreads bilaterally to the vertebral veins, bilateral brachiocephalic veins, right internal jugular vein, and pterygoid venous plexus. The vessel wall was ring-shaped, a finding that was suspicious for thrombophlebitis. No abscesses were observed in the lung field or other organs (shown in Fig. 2).

In-hospitalization disease course of the patient was as follows: abnormally high white blood cell count and leftward shift, fever of 38°C or higher, and the heart rate of over 90 beats/min. The symptoms fulfilled the criteria for systemic inflammatory response syndrome [6]. The patient did not have acute disseminated intravascular coagulation [7]. He was diagnosed with Lemierre's syndrome based on the symptoms of mucositis and CT findings of thrombophlebitis after HN-PIT for nasopharyngeal carcinoma. Ampicillin/sulbactam was initiated on the day of admission. After admission, the patient was switched to ceftriaxone, vancomycin, and metronidazole for central migration. On day 6 of hospitalization, *Fusobacterium necrophorum* and *Prevotella denticola* were detected in one set of blood culture anaerobic bottles; therefore, vancomycin was discontinued, and after confirming drug sensitivity, treatment with ceftriaxone and metronidazole was continued. The patient's general condition and inflammatory findings on blood sampling showed gradual improvement. Cervicothoracic



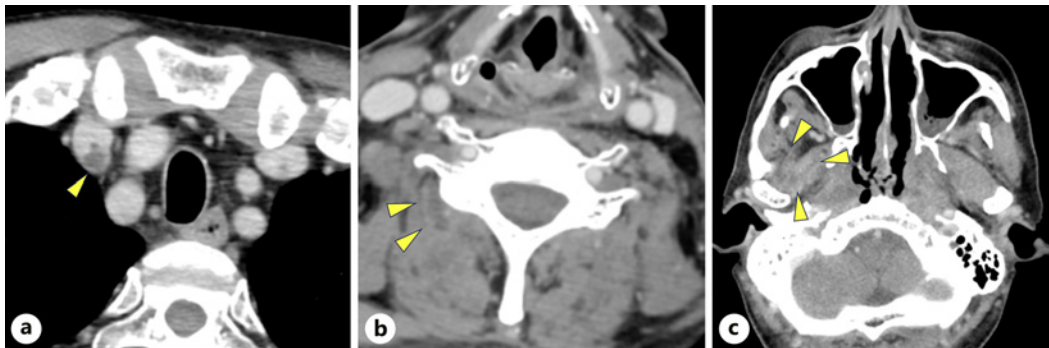
**Fig. 1.** **a** Endoscopic view prior to head and neck photoimmunotherapy (HN-PIT). **b** Enhanced CT before HN-PIT: contrast-enhanced tumor with low internal absorption on the right wall of the nasopharynx. **c** Enhanced CT after 1 month of HN-PIT: the nasopharyngeal tumor showed shrinkage. **d** Mucosal findings on day 18 after HN-PIT. **e** Endoscopic view on the day of admission: reddening of the mucosa of the lateral wall of the nasopharynx is observed. \*Nasal septum, \*\*fossa of Rosenmüller, \*\*\*eustachian tube opening, \*\*\*\*lateral wall.

CT on days 11 and 24 of hospitalization showed no worsening of the thrombus (shown in Fig. 3). A cervicothoracic CT at 1 year later showed that the venous thrombus had been obscured and the patient was doing well. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

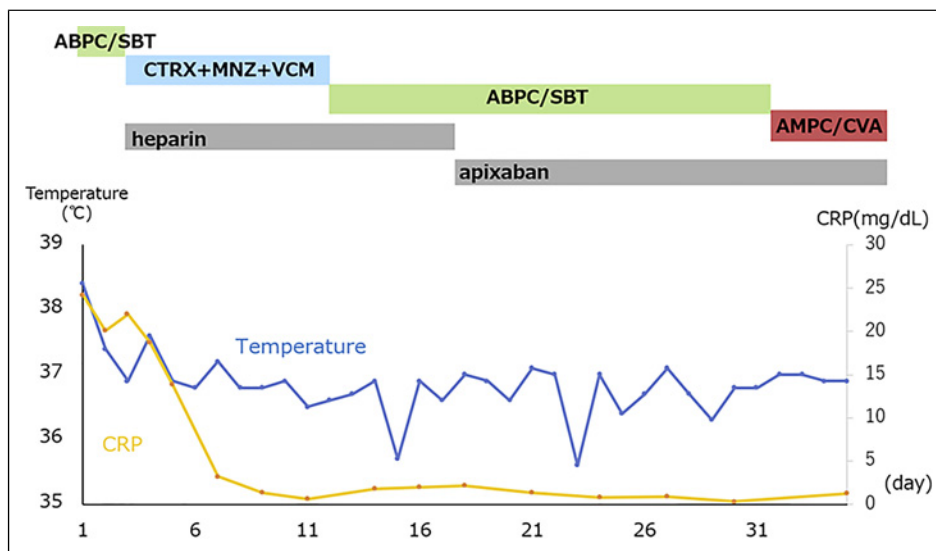
## Discussion

Although scattered clinical reports on HN-PIT exist, Lemierre's syndrome triggered by HN-PIT has not been reported [4, 8–12]. Patients treated with HN-PIT are prone to mucosal infection of the head and neck region due to the nature of the treatment, and the development of Lemierre's syndrome is a high-risk event that requires caution. *Fusobacterium necrophorum*, which was also detected in this case, is the most common causative organism; *Fusobacterium*, *Streptococcus*, *Bacteroides*, *Staphylococcus aureus*, and *Prevotella* have also been reported [13].

Sinave's diagnostic criteria for Lemierre's syndrome include (1) infection of the oropharyngeal region by a preceding anaerobic organism, (2) sepsis with at least one positive blood culture, (3) infectious thrombosis of the internal jugular vein, and (4) one or more distant sites of infection [14]. However, no completely established definition of this syndrome exists. In the present case, three criteria were met, and a diagnosis of Lemierre's syndrome was made. With the development of imaging tests and antimicrobial therapy, Lemierre's syndrome has become relatively uncommon; however, its fatality rate is high, and early diagnosis and treatment are important.



**Fig. 2.** **a** Thrombus in the internal jugular vein to the brachiocephalic vein. **b** Thrombus in the peri-vertebral vein. **c** Poor contrast areas of suspected thrombus in the pterygoid venous plexus.



**Fig. 3.** Progress of treatments.

HN-PIT was performed using intravenous cetuximab sarotalocan sodium followed by laser therapy. This treatment has been covered by medical insurance in Japan for “un-resectable locally advanced or locally recurrent head and neck cancer” since January 2021. Intravenous cetuximab sarotalocan sodium infusion is a complex of cetuximab, a chimeric monoclonal antibody that binds to the human epidermal growth factor receptor, and the light-sensitive dye IR700. After drug administration, a 690 nm laser light was used to specifically damage tumor cell membranes, leading to necrotic cell death. Human epidermal growth factor receptor-targeted therapy for squamous cell carcinoma, a common type of head and neck cancer, minimizes damage to tumor cells and surrounding normal tissue but is highly tissue-destructive and frequently causes mucosal and skin damage.

The lesion was located in the right lateral wall of the nasopharynx. There was no distant metastasis, and neck dissection and HN-PIT were selected for local control. Cylindrical diffusers were inserted into the tumor, and light illumination was performed. Several days after HN-PIT, mucositis appeared and persisted for a long time after the surgery. As the laser illumination area bordered the pterygoid muscle, it was believed that the inflammation progressed upward from the pterygoid plexus vein to the cavernous sinus and downward

through the parapharyngeal space to the internal jugular vein. Malignant head and neck tumors, radiation therapy, and inflammatory diseases of the pharynx may increase the risk of potential thrombosis of the vein [15]. In this case, the patient was treated with HN-PIT after radiotherapy and surgery, which was conducive to thrombus formation. We believe that venous endothelial damage caused by inflammatory spillover to the area surrounding the treated site leads to thrombus formation over time, resulting in infection. The fragile mucosa around the previously treated recurrent lesion and poor wound healing may have created a portal of entry for oral bacteria, thereby increasing the risk of Lemierre's syndrome. HN-PIT is a good indicator of recurrence after surgical or radiotherapy treatment; however, care for mucositis is essential [12]. Although oral care was provided in this case, the nasopharynx is anatomically difficult to treat directly for mucositis, and we believe that prolonged postoperative mucositis is one of the causes of Lemierre's syndrome. Considering the condition of postoperative mucositis, adequate oral care and antimicrobial measures are important.

HN-PIT is associated with severe mucositis to necrosis. The risk of Lemierre's syndrome is high for HN-PIT in the nasopharynx as well as in the oropharynx and oral cavity. It is possible that some patients diagnosed with sepsis after HN-PIT may have Lemierre's syndrome. Lemierre's syndrome has a high fatality rate, and early diagnosis and treatment are important and should be recognized as knowledge by all surgeons involved in HN-PIT.

## Conclusion

HN-PIT is highly tissue-destructive, and mucositis caused by this treatment is considered likely to promote the development of Lemierre's syndrome. Care for mucositis is important for maintaining the barrier function of the mucosa. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see <https://doi.org/10.1159/000535597>).

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## Statement of Ethics

As this was a case report, approval from the Ethics Committee of Tokyo Medical University was not required. This retrospective review of patient data did not require ethical approval in accordance with national guidelines. Written informed consent was obtained from the patient for the publication of the details of their medical case and any accompanying images.

## Conflict of Interest Statement

Isaku Okamoto received lecturer fees from Rakuten Medical KK. The authors have no conflicts of interest to declare.

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### Author Contributions

Midori Nishimura and Isaku Okamoto designed the case report. Midori Nishimura and Tatsuya Ito wrote the manuscript and prepared figures. Isaku Okamoto, Kiyooki Tsukahara, and Kunihiko Tokashiki performed the photoimmunotherapy. Isaku Okamoto, Tatsuya Ito, and Kunihiko Tokashiki treated the patient. All authors discussed the results of the case report, commented on the manuscript, and approved the final version for publication.

### Data Availability Statement

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

### References

- 1 Mitsunaga M, Ogawa M, Kosaka N, Rosenblum LT, Choyke PL, Kobayashi H. Cancer cell-selective in vivo near infrared photoimmunotherapy targeting specific membrane molecules. *Nat Med*. 2011;17(12):1685–91.
- 2 Tahara M, Okano S, Enokida T, Ueda Y, Fujisawa T, Shinozaki T, et al. A phase I, single-center, open-label study of rm-1929 photoimmunotherapy in Japanese patients with recurrent head and neck squamous cell carcinoma. *Int J Clin Oncol*. 2021;26(10):1812–21.
- 3 National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology, head and neck cancers. cited Oct 18, 2023 version 3.2021. Available from: [https://www.nccn.org/professionals/physician\\_gls/pdf/head-and-neck\\_blocks.pdf](https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck_blocks.pdf).
- 4 Omura G, Honma Y, Matsumoto Y, Shinozaki T, Itoyama M, Eguchi K, et al. Transnasal photoimmunotherapy with cetuximab sarotalocan sodium: outcomes on the local recurrence of nasopharyngeal squamous cell carcinoma. *Auris Nasus Larynx*. 2023;50(4):641–5.
- 5 AL. On certain septicemias due to an-aerobic organisms. *Lancet*. 1963;227:701–3.
- 6 Bone RC, Balk RA, Cerra FB, Dellinger RP, Fein AM, Knaus WA, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM consensus conference committee. American college of chest physicians/society of critical care medicine. *Chest*. 1992;101(6):1644–55.
- 7 Gando S, Iba T, Eguchi Y, Ohtomo Y, Okamoto K, Koseki K, et al. A multicenter, prospective validation of disseminated intravascular coagulation diagnostic criteria for critically ill patients: comparing current criteria. *Crit Care Med*. 2006;34(3):625–31.
- 8 Okamoto I, Okada T, Tokashiki K, Tsukahara K. Quality-of-life evaluation of patients with unresectable locally advanced or locally recurrent head and neck carcinoma treated with head and neck photoimmunotherapy. *Cancers*. 2022;14(18):4413.
- 9 Kushihashi Y, Masubuchi T, Okamoto I, Fushimi C, Hanyu K, Yamauchi M, et al. Photoimmunotherapy for local recurrence of nasopharyngeal carcinoma: a case report. *Int J Otolaryngol Head Neck Surg*. 2022;11(05):258–65.
- 10 Nishikawa D, Suzuki H, Beppu S, Terada H, Sawabe M, Hanai N. Near-infrared photoimmunotherapy for oropharyngeal cancer. *Cancers*. 2022;14(22):5662.
- 11 Okamoto I, Okada T, Tokashiki K, Tsukahara K. A case treated with photoimmunotherapy under a navigation system for recurrent lesions of the lateral pterygoid muscle. *vivo*. 2022;36(2):1035–40.
- 12 Okamoto I, Okada T, Tokashiki K, Tsukahara K. Photoimmunotherapy for managing recurrent laryngeal cancer cervical lesions: a case report. *Case Rep Oncol*. 2022;15(1):34–9.
- 13 Johannesen KM, Bodtger U. Lemierre's syndrome: current perspectives on diagnosis and management. *Infect Drug Resist*. 2016;9:221–7.
- 14 Sinave CP, Hardy GJ, Fardy PW. The Lemierre syndrome: suppurative thrombophlebitis of the internal jugular vein secondary to oropharyngeal infection. *Med*. 1989;68(2):85–94.
- 15 Hahn J, Nordmann-Kleiner M, Hoffmann TK, Greve J. Thrombosis of the internal jugular vein in the ENT-department- Prevalence, causes and therapy: a retrospective analysis. *Auris Nasus Larynx*. 2019;46(4):624–9.