

Three Cases of Carcinoma of the Hypopharynx Developing as Metachronous Second Primary Cancers after Total Laryngectomy with Radiotherapy for Carcinoma of the Larynx

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Abstract

We describe 3 cases of metachronous hypopharyngeal cancer developing after laryngeal cancer had been treated with both radiotherapy and total laryngectomy.

All 3 patients were men, 2 were 89 years old, and 1 was 65 years old. All patients had undergone total laryngectomy and radiotherapy for cancer for the glottis more than 20 years earlier. All patients underwent total hypopharyngectomy with jejunal free flap reconstruction. Surgery was complicated by scars from previous cancer treatment, and highly sophisticated surgical skills are needed, especially for preparing the recipient vessels. The postoperative period was largely uneventful and without fatal complications, however, 2 of the 3 patients died of distant metastasis 22 months and 31 months after surgery.

(J Nippon Med Sch 2011; 78: 261–266)

Key words: hypopharyngeal cancer, salvage surgery, second primary cancer, radiation induced malignancy

Introduction

Outcomes of radiotherapy for early stage laryngeal carcinomas are generally good. However, when radiotherapy fails for a small number of primary lesions, salvage surgery with total laryngectomy is effective and yields better results. Furthermore, because of improvements in public health and general medical practices, patients are surviving longer after treatment for laryngeal carcinoma.

However, such surgery and radiotherapy can

complicate subsequent surgery of the neck. To perform safe and successful salvage surgery, advanced knowledge and highly-sophisticated surgical skills are required¹.

We herein report on 3 patients with hypopharyngeal cancer developing after radiotherapy and total laryngectomy for laryngeal cancer. These patients underwent surgical treatment. The results should help salvage surgery after chemoradiotherapy and highlight the role of head and neck surgeons in chemoradiotherapy for head and neck cancers.

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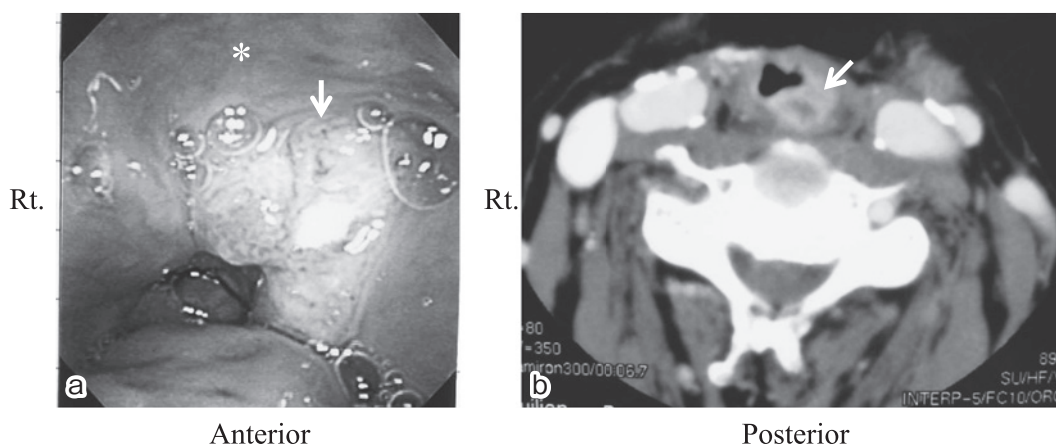


Fig. 1 Preoperative evaluation of case 1

A necrotic tumor was present in the posterior wall of the hypopharynx. **a:** Findings of fiberoptic laryngoscopy. **b:** CT findings. **Arrow:** tumor; *****: Posterior wall of the hypopharynx.

Case Reports

Case 1

An 89-year-old man was referred to Nippon Medical School Hospital with a 2-month history of dysphagia and odynophagia. He had been treated for laryngeal cancer by means of radiation and surgery. Twenty-five years earlier, when he was 64 years old, T1bN0 carcinoma of the glottis had been diagnosed, and initially treated with radiotherapy (60 Gy). Recurrence of the primary lesion was treated with salvage total laryngectomy 1 year after radiotherapy. The course after surgery was favorable, and no recurrence was found.

At admission, fiber-optic laryngoscopy revealed a necrotic mass in the left posterior wall of the hypopharynx (**Fig. 1a**). Biopsy showed squamous cell carcinoma. Computed tomography (CT) of the neck revealed a contrast-enhanced mass in the hypopharynx; however, the margin of the tumor was unclear (**Fig. 1b**).

The patient underwent total hypopharyngectomy with right-sided neck dissection. The anterior wall of the hypopharynx was adherent to the subcutaneous tissue of the neck skin; however, the skin of the anterior neck could be preserved when the flap was elevated (**Fig. 2a**). The right lobe of the thyroid gland was adherent to the pharyngeal wall, and en-bloc resection could not be avoided (**Fig. 2b**). First, the pharyngotomy was performed at the level of the

hyoid bone, which was recognized by the scar of the pharyngeal suture at the site of the previous total laryngectomy. The inferior incised margin was determined with palpation and direct observation of the pharyngeal mucosa (**Fig. 2c**). The inferior margin was placed just above the tracheal stoma. The hypopharyngeal mucosa could not be preserved. Additional resection of the trachea was unnecessary. The circumferential defect of the hypopharynx was reconstructed with a free jejunal flap (**Fig. 3a**). The right superior thyroid artery and the right internal jugular vein were selected as recipient vessels. In fact, these vessels must be confirmed before resection of the hypopharynx. Because the neck skin was congested at the end of the operation, it was partially resected and reconstructed with a deltopectoral flap (**Fig. 3b**).

The pathological diagnosis was moderately differentiated squamous cell carcinoma. The surgical margin was free of cancer. The neck skin and the thyroid gland also showed no cancer invasion. For more than 12 months postoperatively, there has been no evidence of local recurrence or distant metastasis.

Case 2

An 89-year-old man admitted to the Nippon Medical School Hospital with complaints of deteriorating esophageal phonation for 3 months, and dysphagia for 2 months. Twenty-eight years earlier, when the patient was 61 years old,

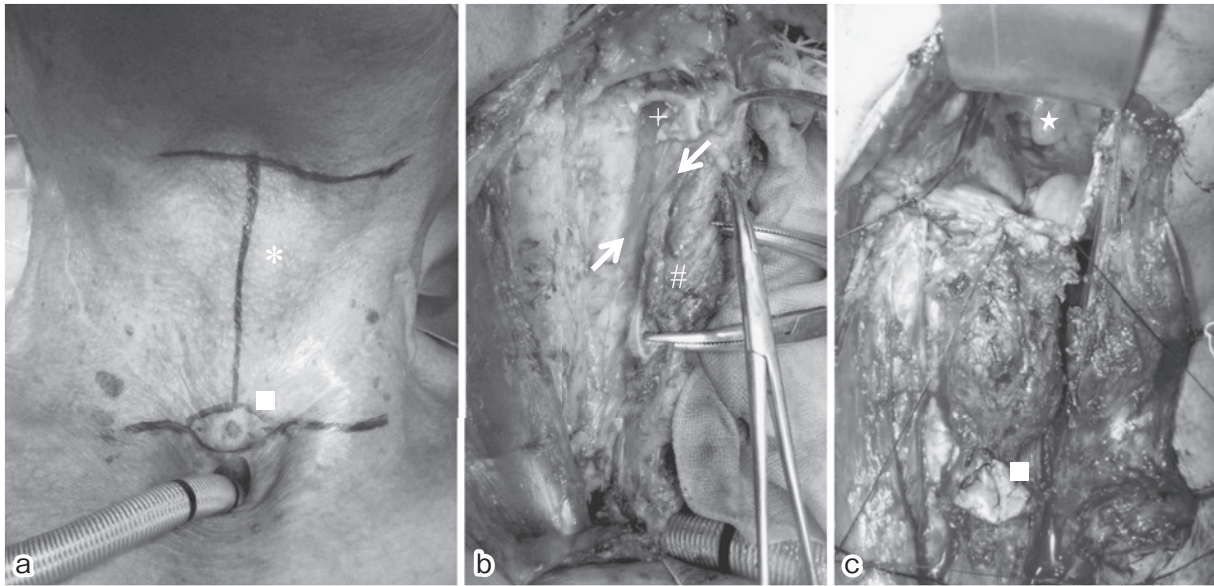


Fig. 2 Intraoperative findings of case 1

a: Skin incision of the neck. **b:** The pharyngeal wall was adherent with scar to the surrounding structures (**arrows**). **c:** Pharyngotomy, *: tumor, ■: tracheoesophageal shunt for phonation, resected. +: Superior thyroid artery. #: Right lobe of thyroid gland. ★: Uvula

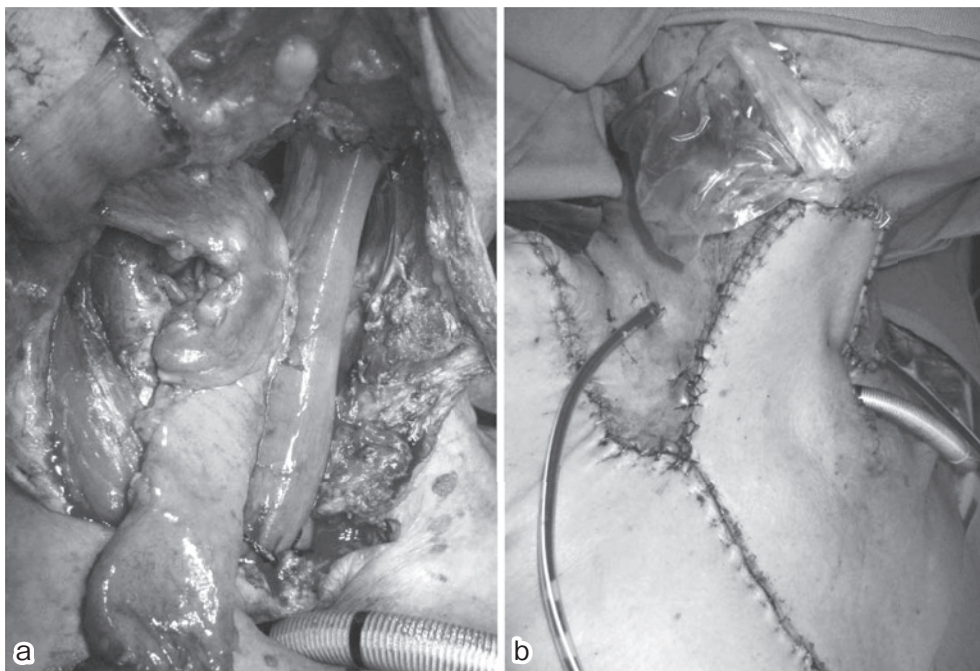


Fig. 3 Reconstructive surgery of case 1

a: The circumferential pharyngeal defect was reconstructed by means of free jejunal transfer. **b:** The defect of the skin of the anterior aspect of the neck was reconstructed with a deltopectoral flap.

hoarseness had led to a diagnosis of T2N0 carcinoma of the glottis. Radical radiotherapy (60 Gy) was performed. However, the disease recurred at the site of the primary tumor 13 months after radiotherapy. Salvage total laryngectomy was performed. The

post-operative course was good with no recurrence of disease.

At admission, a 3-cm-diameter mass was palpable at the front neck (**Fig. 4**). Fiber-optic laryngoscopy and pharyngography revealed severe stenosis of the

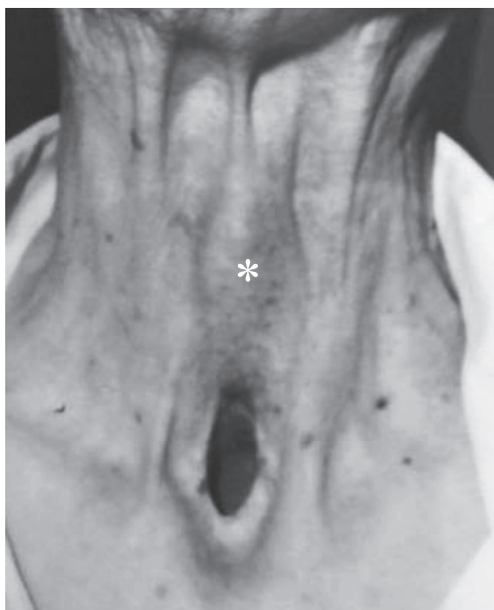


Fig. 4 Preoperative view of case 2
The pharyngeal tumor was palpable at the front of the neck.
*: Tumor

hypopharynx. A biopsy showed squamous cell carcinoma.

The patient underwent total hypopharyngectomy with bilateral dissection of the neck. The neck skin and the thyroid gland were adherent to the primary lesion, and en-bloc resection could not be avoided. The surgical margin was determined by means of palpation. The inferior incision was made at the level of the tracheal stoma without additional resection of the trachea. At neck dissection, the bilateral superior thyroid arteries and the bilateral transverse cervical arteries were identified and judged to be too thin for micro-vascular anastomosis; therefore, the right facial artery was prepared as the recipient artery. The circumferential defect of the hypopharynx was reconstructed with a free jejunal flap. The external jugular vein was used as a recipient vein. The defect of the anterior neck skin was covered with a deltopectoral flap.

The pathological diagnosis was moderately differentiated squamous cell carcinoma, without extrapharyngeal spread. No lymph node metastasis was detected. The postoperative course was good and without complications. However, 7 months after operation, radiography revealed multiple metastases to the lung. When the patient died of these distant

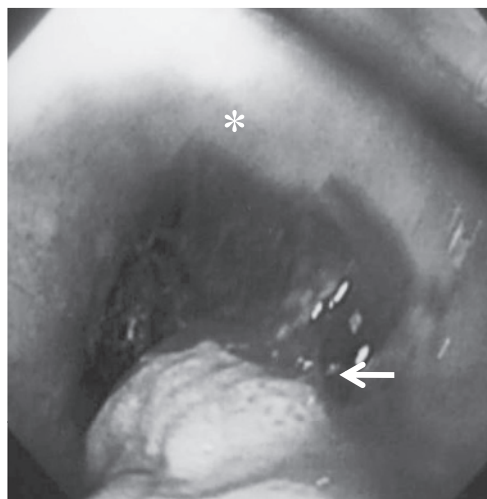


Fig. 5 Findings of fiberoptic laryngoscopy in case 3
Fiberoptic laryngoscopy revealed a stenotic lesion with blood clot in the hypopharynx. **Arrow:** tumor.
*: Posterior wall of the hypopharynx.

metastases 22 months after surgery, no locoregional recurrence was detected. He died at home.

Case 3

A 65-year-old man was referred to the Nippon Medical School Hospital, complaining of oral bleeding for 2 days. He also complained of having dysphagia for 1 year. Twenty-three years earlier, when he was 42 years old, hoarseness had led to a diagnosis of T3N1 carcinoma of the glottis. Preoperative radiotherapy (40 Gy) was followed by total laryngectomy with left sided neck dissection and postoperative radiotherapy (20 Gy). The course after treatment was good, with no recurrence of disease.

At admission, fiberoptic-laryngoscopy revealed a massive tumor with a blood clot as the cause of the esophageal stenosis (**Fig. 5**). CT of the neck revealed a contrast-enhanced mass with unclear margins. Metastasis to lymph nodes of the neck was not found. The pathological diagnosis was squamous cell carcinoma.

The patient underwent total hypopharyngectomy with right sided neck dissection. Because the skin of the neck and the right lobe of the thyroid gland were not strongly adherent to the primary lesion, they could be preserved. After neck dissection, the primary lesion was resected. Both the upper and lower surgical margins were determined only by means of palpation. Because the tumor was located

at a lower level in this case than the other 2 cases, the cervical esophagus was also ablated without additional tracheal resection. The circumferential defects of the hypopharynx and the cervical esophagus were reconstructed with a free jejunal flap. The transverse cervical artery and vein on the right side were used for microvascular anastomosis. These vessels could be prepared relatively easily and sufficiently enough.

The neck skin flap was congested for 2 weeks postoperatively; however, the edema resolved without marginal necrosis of the skin flap. The pathological diagnosis was well-differentiated squamous cell carcinoma, with a negative surgical margin. No lymph node metastasis was detected. The postoperative course was largely uneventful and without complications, except for a small hematoma of the neck, which was treated by conservatively. However, 9 months after the operation, radiography revealed multiple metastases to the lung. When the patient died of distant metastases 31 months after surgery, no locoregional recurrence was detected. He died at home.

Discussion

Numerous studies have suggested that multiple primary cancers often develop in the head and neck. However, management remains controversial. In particular, metachronous second primary cancers are more difficult to treat because of limitations arising from previous cancer treatments, including radiotherapy and surgery¹. If the first cancer was treated with radiation, the second cancer can rarely be treated with radiation. In surgically treated cases, scar formation can complicate subsequent treatment in the same surgical field. In the present report, we focused on such difficulties, especially on reconstructive surgery by means of free tissue transfer after the ablation of cancers.

Radiotherapy is often performed for laryngeal cancer. Especially in the early stage, radiotherapy has been the treatment of first choice. However, late adverse events must not be neglected. In addition, recurrence in the primary site after radiotherapy for the laryngeal cancer has been treated with salvage

total laryngectomy. However, scar formation around the pharyngeal wall is severe after both radiotherapy and total laryngectomy. From these points of view, if patients with the laryngeal cancer treated with these 2 modalities have metachronous second primary hypopharyngeal cancer, salvage surgery might be difficult¹. Because the number of such patients has increased, as treatments for laryngeal cancer have advanced and general medical practices and public health have improved in the last 30 years, surgeons must know how to treat these patients. Our analysis of these 3 cases might also help to improve salvage surgery after concurrent chemoradiotherapy, which is often performed for head and neck cancer.

One of the most difficult points of these surgeries is selecting the reconstructive strategy. In other words, the selection and preparation of recipient vessels in areas of scarring is difficult¹. The pedicled flap is not ideal for reconstructing circumferential defects²; however, it is not so easy to determine whether reconstruction with a free jejunal flap is possible¹⁻³. For reconstructing circumferential defects of the hypopharynx, the use of a free jejunal flap would be a standard strategy⁴. However, it is absolutely essential to prepare ideal recipient vessels for free-tissue transfers. This preparation is sometimes complicated in the patients who have undergone surgery or radiotherapy.

The superior thyroid artery was selected as the recipient artery for head and neck reconstruction in our series of previously untreated cases⁵. This artery is ideal for head and neck reconstruction because of its abundant blood flow and its course after arising from the external carotid artery^{5,6}. However, this artery was selected in only 1 of the present 3 cases. In these 3 cases, including a case in which the superior thyroid artery was used for microvascular anastomosis, adhesion around this artery was unexpectedly severe, likely because of both radiotherapy and dissection from the pharyngeal constrictor muscle during total laryngectomy. In 1 case, the transverse cervical artery was used instead of the superior thyroid artery and was easily prepared, despite being within a scar from the previous neck dissection. In another case, the facial

artery was selected as the recipient vessel, because both the superior thyroid artery and the transverse cervical artery were too thin. The facial artery was not in the dissected field and was thought to be outside the radiation field.

Selecting the recipient vein is easier. In these 3 cases, the internal jugular vein, the external jugular vein and the transverse cervical vein were used. Any vein in the surgical field can be chosen, but at least 1 vein must be prepared for free-tissue transfer. A serious problem is that the recipient vein cannot be selected preoperatively, except in the case of the internal jugular vein, which is easily detected with contrast-enhanced CT of the neck¹. This vein can be easily anastomosed with the end-to-side method, even if there are adhesions around the vein, if the vein is detected with contrast-enhanced CT¹. Because the preservation of the vein depends upon the previous surgery, neck dissection must be conservative, and unnecessary dissection must be avoided⁷.

These hypopharyngeal cancers might be metachronous second primary cancers. For this diagnosis, recurrence of the first cancer must be ruled out. Doing so is often very difficult, because the hypopharynx is adjacent to the larynx. Dual cancers of the hypopharynx and the larynx can be diagnosed only with different pathological diagnosis⁸. However, few cases can meet all criteria. The present 3 cases also did not meet all the criteria. However, more than 20 years would be a sufficient period to eliminate the possibility that the primary cancer had recurred. The second hypopharyngeal cancers might be diagnosed as a radiation-induced cancer. Radiation-related malignancy must develop in a previous radiation field, and at least 3 years are necessary between the occurrences of the 2 kinds of cancer. Ideally, each pathological diagnosis is distinct⁸. In our 3 patients, both hypopharyngeal cancer and laryngeal cancer were squamous cell

carcinomas. However, more than 20 years is enough time to determine that these cases were metachronous second primary hypopharyngeal cancers and also radiation induced-malignancies^{9,10}.

It is difficult to evaluate whether the surgical management of these 3 patients was appropriate or not. However, surgical treatment is needed to maintain oral food intake and to allow the patient to die at home.

References

1. Yokoshima K, Nakamizo M, Shimada K, et al: Free tissue transfer to the head and neck for patients with a history of prior neck surgery (Japanese). *Jap J Head Neck Surg* 2005; 15: 55-60.
2. Shah JP, Haribhakti V, Loree TR, Sutaria P: Complications of the pectoralis major myocutaneous flap in head and neck reconstruction. *Am J Surg* 1990; 160: 352-355.
3. Shah JP, Shemen L, Spiro RH, Strong EW: Selecting variants in pharyngeal reconstruction. *Ann Otol Rhinol Laryngol* 1984; 93: 318-321.
4. Chu PY, Chang SY: Reconstruction of the hypopharynx after surgical treatment of squamous cell carcinoma. *J Chin Med Assoc* 2009; 72: 351-355.
5. Nakamizo M, Yokoshima K, Yagi T: Use of free flaps for reconstruction in head and neck surgery. *Auris Nasus Larynx* 2004; 31: 269-273.
6. Urken ML: Recipient vessel selection in free tissue transfer to the head and neck. In *Atlas of regional and free flaps for head and neck reconstruction* (Urken ML, Cheney ML, Sullivan MJ, Biller HF, eds), 1995; pp 331-337, Raven Press, New York.
7. Gavilan J, Herranz J, DeSanto LW, Gavilan C: Conceptual approach to functional and selective neck dissection. In *Functional and selective neck dissection*, 2001; pp 55-62, Thieme, New York.
8. Ferlito A: Double primary synchronous and metachronous cancer of the larynx and hypopharynx with dissimilar histology. *Arch Otorhinolaryngol* 1980; 229: 107-119.
9. Lawson W, Som M: Second primary cancer after irradiation of laryngeal cancer. *Ann Otol Rhinol Laryngol* 1975; 84: 771-775.
10. Aanesen JP, Olofsson J: Irradiation-induced tumors of the head and neck. *Acta Otolaryngol* 1979; 360: 178-181.

(Received, February 7, 2011)

(Accepted, April 21, 2011)