

A case of advanced hypopharyngeal cervical esophageal cancer with management of tracheoesophageal fistula and complete resection

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Case Report

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Abstract

Background: Advanced esophageal cancer with tracheal invasion is fatal due to airway narrowing, and due to the possibility of tracheoesophageal fistula formation during the treatment process. If a tracheoesophageal fistula develops, palliative care is often chosen, and curative resection is very rarely achieved.

Case Presentation: A 71-year-old man presented with dysphagia. He was diagnosed hypopharyngeal and cervical esophageal cancer with severe airway stenosis (cT4b [main bronchus, thyroid] N3 M0 cStageIIIC); we initially created a tracheostomy. He received induction chemotherapy (docetaxel, nedaplatin and S-1: DGS). After one course of DGS therapy, he developed a tracheoesophageal fistula due to tumor shrinkage. We managed both the airway route and nutrition strictly under continuous suctioning over the cuff of the tracheal cannula, prohibited swallowing saliva, and provided enteral nutrition using a nasogastric tube. Three courses of DGS therapy were performed. A clinical complete response was achieved. We then performed pharyngo-laryngo-esophagectomy. The postoperative course was uneventful. His response was evaluated as a pathological complete response (pretreatment effect grade 3) and we achieved R0 resection. Two courses of DGS therapy were administered as adjuvant chemotherapy. He is currently alive without recurrence at 9 years after treatment.

Conclusions: In the case of upper tracheoesophageal fistula caused by advanced hypopharyngeal cervical esophageal cancer, chemotherapy under strict airway and nutritional management after tracheostomy may facilitate radical surgery.

Background

Advanced esophageal cancer with tracheal invasion is fatal due to airway narrowing and the possibility of tracheoesophageal fistula (TEF) formation during the treatment process. Palliative care is often chosen for patients with TEF due to its poor prognosis.[1] We herein report the case of a patient with advanced hypopharyngeal cervical esophageal cancer who developed TEF during chemotherapy but who was successfully treated with complete resection under appropriate airway and nutritional management.

Case Presentation

A 71-year-old man consulted his previous doctor with a chief complaint of dysphagia, which had persisted for three months. His symptoms had developed and eating had become difficult. He visited an otolaryngologist, and a hypopharyngeal tumor was detected by laryngoscopy. Evaluation of a biopsy specimen revealed squamous cell carcinoma. Contrast-enhanced CT (CECT) and position emission tomography (PET)-CT revealed a tumor located from the hypopharynx to the upper thoracic esophagus, with entire circumferential wall thickening and no distant metastasis (Fig. 1). He developed dyspnea during a detailed examination and was rushed to his previous hospital. Esophageal stricture and airway stricture due to the tumor were observed, and he was intubated and placed on a ventilator on the same

day. Four days later, he was tracheotomized and transferred to our hospital for further treatment. On admission to our hospital, he was breathing spontaneously and his vital signs were stable. A laboratory analysis showed a slightly elevated white blood cell count (12,800/mm³) and c-reactive protein (CRP) level (2.61 mg/dL). His tumor marker levels, which were not increased, were as follows: CEA (1.3 ng/mL), CA19-9 (13.3 U/mL), CYFRA (0.9 ng/mL), and AFP (2.0 ng/mL). CECT showed a tumor from the epiglottis to the thoracic esophagus, which invaded the trachea in the hypopharyngeal cervical esophagus (Fig. 2). There were several enlarged lymph nodes, but there was no evidence of distant lymph node metastasis or distant metastasis. The preoperative diagnosis of the tumor was T4b [main bronchus, thyroid] N3 M0 cStageⅢC according to the International Union Against Cancer Tumor–Node–Metastasis Classification of Malignant Tumors (7th edition).[2] We initiated DGS (docetaxel, nedaplatin and S-1) therapy as induction chemotherapy[3, 4], intravenous hyperalimentation (IVH) from a right internal jugular vein catheter and enteral feeding from a nasogastric tube. After one course of DGS therapy, although esophageal stricture was improved by the tumor shrinkage, CECT revealed a suspected cervical TEF (Fig. 3). We confirmed the fistula by upper endoscopy and bronchoscopy and made a diagnosis of TEF (Fig. 4). Nutritional management consisted of a combination of IVH and enteral feeding at the onset of TEF, with a gradual increase of enteral feeding after confirming the absence of nausea and vomiting, and finally, a transition to enteral feeding only. Airway management consisted of cuffing the tracheal cannula, continuous suctioning over the cuff, and constant upper body positioning to prevent aspiration. We managed the airway and nutrition strictly and three courses of DGS therapy were administered. He had a clinical complete response. Chemotherapy-related side effects included grade 3 neutropenia. Granulocyte-colony stimulating factor was used. We performed pharyngo-laryngo-esophagectomy, three-field lymphadenectomy, subtotal stomach reconstruction via the posterior mediastinal route, jejunostomy, total thyroidectomy, and permanent tracheostomy using a delto-pectoral flap as conversion surgery. The postoperative course was uneventful. Enteral feeding was started on postoperative day (POD) 2, the patient was weaned from the ventilator on POD 4, oral intake was started on POD 12, and the patient was discharged on POD 30. A histopathological examination revealed no residual viable tumor cells in the primary tumor or lymph nodes. The outcome was evaluated as a pathological complete response (pCR) (pretreatment effect grade 3), with the achievement of R0 resection. The patient was then given two courses of DGS therapy as adjuvant chemotherapy. At the time of writing this report, the patient is alive without recurrence at 9 years after treatment.

Discussion And Conclusions

The esophagus is in close proximity to surrounding vital organs and vessels, such as the trachea, aorta, and pulmonary veins. Advanced esophageal cancer frequently involves the trachea, with 20-36.6% of patients developing tracheal invasion[5, 6] and 5–10% developing TEF,[7] a potentially fatal complication. TEFs are generally more likely to occur after chemoradiotherapy for advanced esophageal cancer,[8] and once completed, they have an extremely poor prognosis, with an average survival time of approximately 1 month.[9]

The most difficult aspect of TEF management is the management of digestive fluids that flow into the trachea through the fistula. Most have a fatal course with repeated aspiration pneumonia during the course of management.

There have been a few cases of TEFs due to benign or postoperative complications that have been cured by innovative surgical procedures, such as the use of a muscle flap[8] or three-step surgery;[10] however, TEFs due to esophageal cancer are more complicated to treat because the patient is also receiving cancer treatment.

The treatment of TEF in esophageal cancer is a combination of chemotherapy or chemoradiation therapy (CRT) for the tumor and stenting, esophageal bypass, or the use of a muscle flap for TEF, all of which are often performed as palliative—rather than curative—treatments.

Esophageal stents and airway-esophageal double stents are often selected for TEF, especially to close the fistula and improve the quality of life.[11, 12] Although there are reports of improved survival,[13, 14] it is considered to be a palliative treatment, and associated disadvantages include the possibility of fistula enlargement and difficulty in surgical manipulation due to stenting. Surgical treatment may be an option, but most patients undergo esophageal bypass surgery[15, 16] or muscle flap coverage[9, 17] as a palliative treatment. There are reports of two-step surgery for TEF caused by lung cancer[18] and TEF caused by malignant lymphoma that was closed after continued chemotherapy;[19] however, we were unable to find any reports of radical surgery for TEF caused by esophageal cancer.

In the present case, the patient developed an upper TEF; however, prior tracheostomy allowed for the continuation of chemotherapy under strict airway and nutrition management, and successful chemotherapy enabled the *en bloc* resection of the TEF by pharyngo-laryngo-esophagectomy and R0 resection as conversion surgery. Currently, this patient remains alive without recurrence at 9 years after treatment.

To safely administer chemotherapy, it is necessary to reduce the risk of aspiration and pneumonia as much as possible by preventing the backflow of digestive fluids into the fistula and collecting digestive fluids that have entered the trachea through managements such as continuous suctioning over the cuff of a tracheal cannula, prohibiting saliva swallowing, and maintaining constant upper body positioning (Fig. 5). Generally, the creation of a permanent tracheostomy is considered if the trachea can be dissected cephalad of the suprasternal margin.[20] Before surgery, biopsy is performed at the level of the tracheal incision by bronchoscopy through the tracheostomy site and the tracheal incision level is determined based on the confirmation of negative biopsy results. This ensures the achievement of complete resection of the tumor. Sakai et al.[21] also reported no difference in the recurrence pattern in patients undergoing laryngeal cancer surgery, even when tracheotomy was performed first. If the TEF caused by the tumor is located caudal to the suprasternal margin, the tracheal cannula may not be long enough or a permanent tracheostomy may not be safely created, in which case stenting to close the fistula or esophageal bypass may be considered.

In this case, tracheostomy was performed first due to the presence of severe airway stenosis. Even in the absence of airway stenosis, however, creating a tracheostomy prior to other treatments is advantageous as it facilitates confirmation of the fistula site, allows for better management of aspiration and pneumonia, and facilitates biopsy to determine the level of the tracheal incision before surgery. When a patient with advanced esophageal cancer with tracheal invasion develops TEF, we believe that it is useful to create a tracheostomy before performing other treatments.

In patients with advanced hypopharyngeal and cervical esophageal cancer with upper TEF, the strict management of TEF by tracheostomy may facilitate subsequent treatment with chemotherapy and curative surgery.

Abbreviations

docetaxel

nedaplatin and S-1

DGS

tracheoesophageal fistula

TEF

Contrast-enhanced CT

CECT

positron emission tomography

PET

c-reactive protein

CRP

intravenous hyperalimentation

IVH

postoperative day

POD

pathological complete response

pCR

chemoradiation therapy

CRT

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for the publication of this case report and accompanying images.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

SO drafted the manuscript. YK and YT performed the operation, YK, YT, ME, YS, NM, NO and TT provided academic advice. All authors read and approved the final manuscript.

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References

1. Reed MF, Mathisen DJ. Tracheoesophageal fistula. *Chest Surg Clin N Am.* 2003;13:271–89.
2. Sobin LH, Gospodarowicz MK, Wittekind C. *TNM Classification of Malignant Tumours.* 7th ed. Oxford, UK: Wiley-Blackwell; 2011.
3. Tanaka Y, Yoshida K, Tanahashi T, Okumura N, Matsushashi N, Yamaguchi K. Phase II trial of neoadjuvant chemotherapy with docetaxel, nedaplatin, and S1 for advanced esophageal squamous cell carcinoma. *Cancer Sci.* 2016;107:764–72.
4. Tanaka Y, Yoshida K, Osada S, Yamaguchi K, Takahashi T. Docetaxel, nedaplatin, and S-1 (DGS) chemotherapy for advanced esophageal carcinoma: a phase I dose-escalation study. *Anticancer Res.* 2011;31:4589–97.
5. Alexander EP, Trachiotis GD, Lipman TO, Wadleigh RG. Evolving management and outcome of esophageal cancer with airway involvement. *Ann Thorac Surg.* 2001;71:1640–4.
6. Goh KJ, Lee P, Foo AZX, Tan EH, Ong HS, Hsu AAL. Characteristics and outcomes of airway involvement in esophageal cancer. *Ann Thorac Surg.* 2021;112:912–20.
7. Sharma A, Rehman MU, Cowen ME. Management of a difficult malignant tracheoesophageal fistula. *Interact Cardiovasc Thorac Surg.* 2003;2:665–7.

8. Hürtgen M, Herber SCA. Treatment of malignant tracheoesophageal fistula. *Thorac Surg Clin*. 2014;24:117–27.
9. Kim HS, Khemasuwan D, Diaz-Mendoza J, Mehta AC. Management of tracheo-oesophageal fistula in adults. *Eur Respir Rev*. 2020;29:200094.
10. Khan A, Hashim Z, Neyaz Z, Agarwal A, Mohindra S, Nath A. Dual airway and esophageal stenting in advanced esophageal cancer with lesions near carina. *J Bronchology Interv Pulmonol*. 2020;27:286–93.
11. Fermi M, Lo Manto A, Ferri G, Ghirelli M, Mattioli F, Presutti L. Surgical management of benign cervical tracheoesophageal fistulas: A single-tertiary academic institution experience. *Am J Otolaryngol*. 2021;42:103091.
12. Sato Y, Tanaka Y, Suetsugu T, Takaha R, Ojio H, Hatanaka Y, et al. Three-step operation for esophago-left bronchial fistula with respiratory failure after esophagectomy: a case report with literature review. *BMC Gastroenterol*. 2021;21:467.
13. Herth FJ, Peter S, Baty F, Eberhardt R, Leuppi JD, Chhajed PN. Combined airway and oesophageal stenting in malignant airway–oesophageal fistulas: a prospective study. *Eur Respir J*. 2010;36:1370–4.
14. May A, Ell C. Palliative treatment of malignant esophagorespiratory fistulas with Gianturco-Z stents. A prospective clinical trial and review of the literature on covered metal stents. 1998;93:532–5.
15. Seto Y, Yamada K, Fukuda T, Hosoi N, Takebayashi R, Chin K, et al. Esophageal bypass using a gastric tube and a cardiostomy for malignant esophagorespiratory fistula. *Am J Surg*. 2007;193:792–3.
16. Meunier B, Stasik C, Raoul JL, Spiliopoulos Y, Lakehal M, Champion JP, et al. Gastric bypass for malignant esophagotracheal fistula: a series of 21 cases. *Eur J Cardiothorac Surg*. 1998;13:184–8.
17. Kremer T, Gazyakan E, Maurer JT, Ott K, Gerken A, Schmittner M, et al. Intra- and extrathoracic malignant tracheoesophageal fistula—A differentiated reconstructive algorithm. *Cancers (Basel)*. 2021;13:4329.
18. Watanabe I, Takamochi K, Oh S, Suzuki K. Salvage surgery for lung cancer with tracheo-oesophageal fistula during concurrent chemoradiotherapy. *Interact Cardiovasc Thorac Surg*. 2019;29:641–3.
19. Hayashi T, Nakashima Y, Nishimoto M, Nanno S, Naka R, Gyobu K, et al. High-dose chemotherapy with autologous stem cell transplantation in a case of refractory peripheral T cell lymphoma with tracheoesophageal fistula: a case report. *Transplant Proc*. 2022;54:189 – 92.
20. Yamasaki M, Makino T, Tanaka K, Yamashita K, Doki Y. Surgery for cervical esophageal cancer. *J Jpn Surg Soc*. 2020;121:429–34.
21. Sakai A, Yokoshima K, Nakamizo M, Inai S, Sakanushi A, Kato T, et al. Negative impact of tracheotomy prior to total laryngectomy for patients with advanced laryngeal cancer. *Head and Neck Cancer*. 2020;46:334–9.

Figures

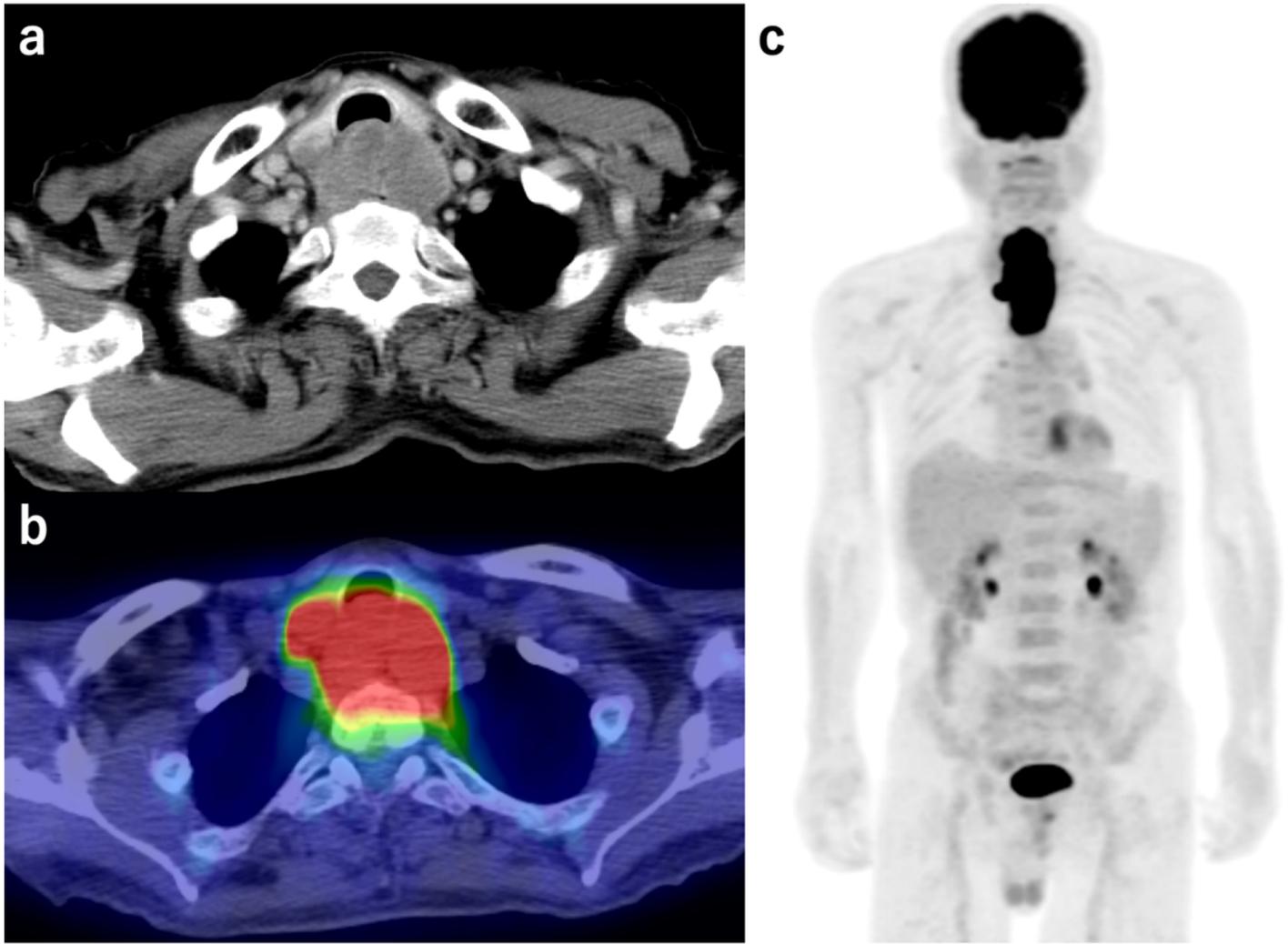


Figure 1

CECT and PET-CT at the previous hospital.

(a,b) The tumor in the cervical esophagus compressed the trachea and showed a high degree of FDG accumulation.

(c) A high degree of FDG accumulation was observed in the cervical region with no evidence of distant metastasis.

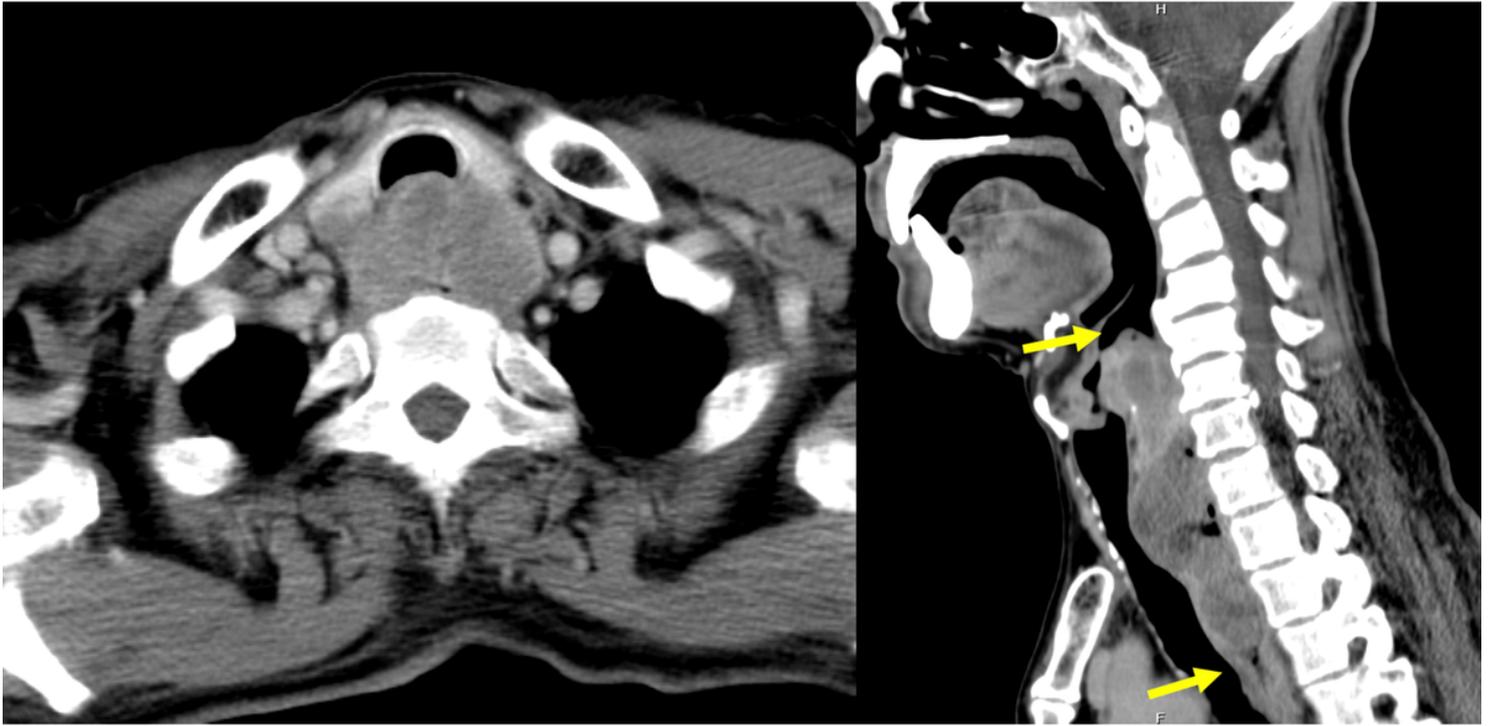


Figure 2

CECT on admission to our hospital

CECT showed a tumor from the epiglottis to the thoracic esophagus, which invaded the trachea in the hypopharyngeal cervical esophagus.

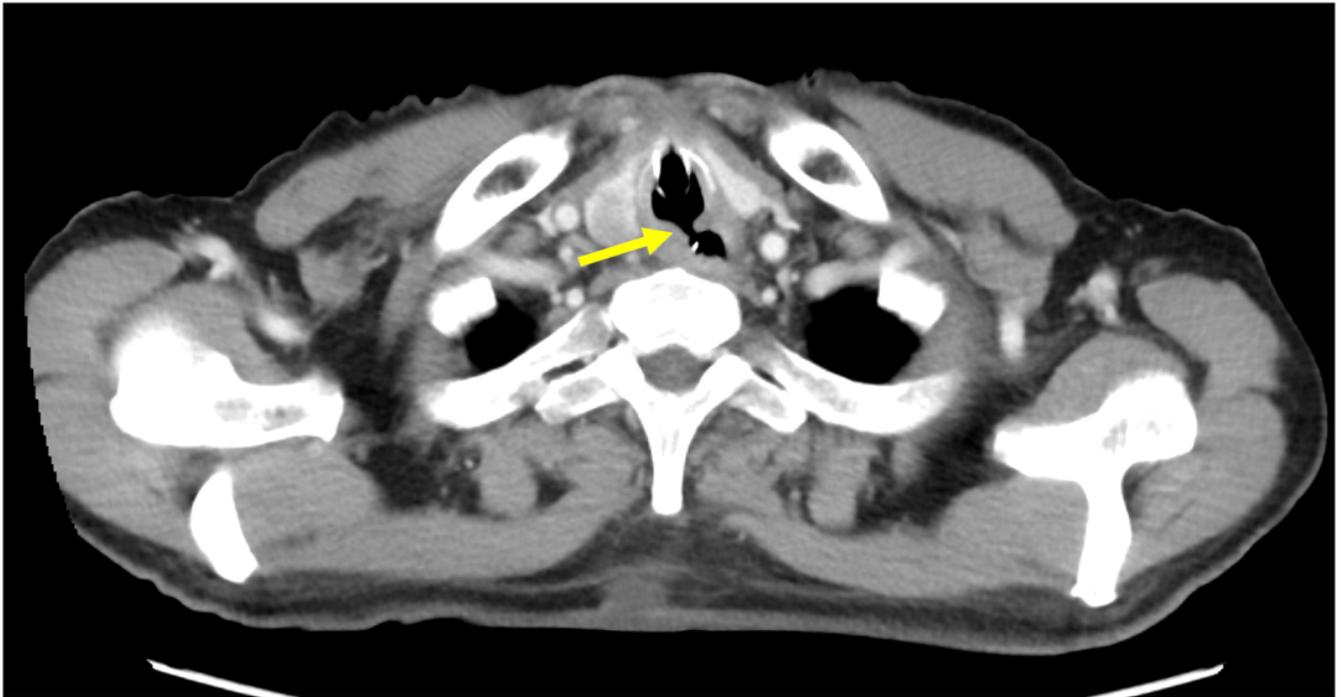


Figure 3

CECT showing cervical TEF after one course of DGS therapy.

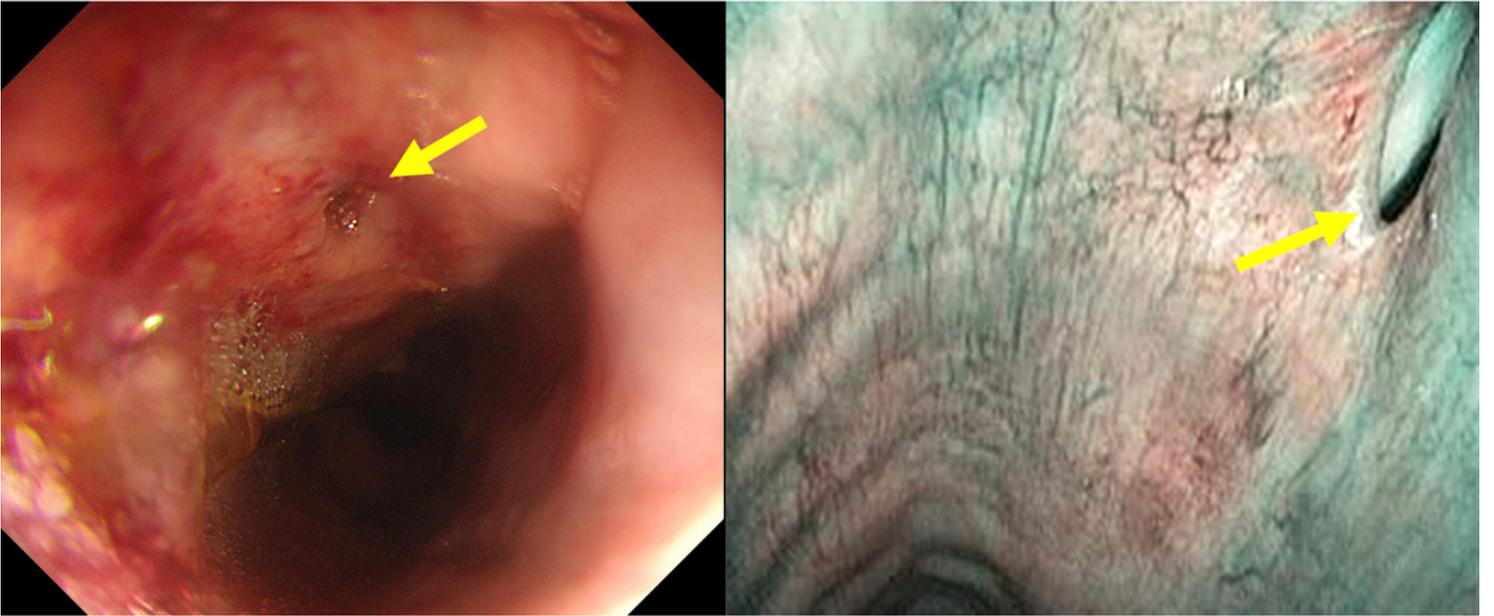


Figure 4

Upper endoscopy and bronchoscopy showing cervical TEF.

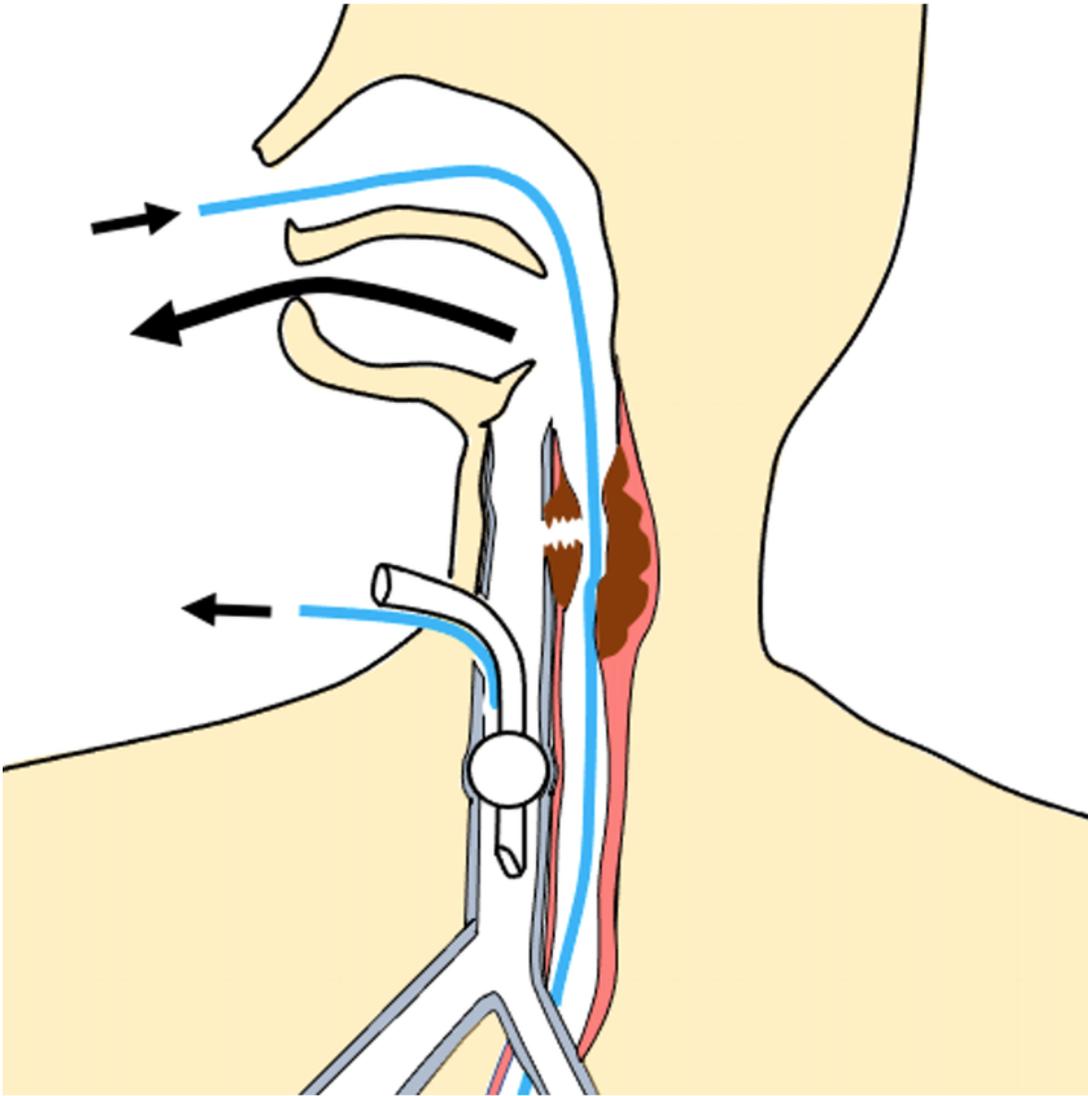


Figure 5

Schematic illustration of the management in the present case

To prevent saliva and digestive fluid from entering the trachea, continuous suctioning over the cuff of the tracheal cannula and continuous saliva suctioning in the oral cavity were performed. Enteral nutrition

using a nasogastric tube prevented the backflow of digestive fluid into the fistula and allowed strict preoperative nutritional management.