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A case of hypopharyngeal cancer with stenosis, perforation, and pyogenic spondylitis development after chemoradiotherapy



Mioko Matsuo^{a,*}, Fumihide Rikimaru^b, Yuichiro Higaki^b, Muneyuki Masuda^b

^a Department of Head and Neck Surgery, Japan Community Health Care Organization Kyushu Hospital, Kitakyushu City, Japan

^b Department of Head and Neck Surgery, National Hospital Organization Kyushu Cancer Center, Fukuoka City, Japan

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ABSTRACT

INTRODUCTION: Chemoradiotherapy plays an important role in preserving function and morphology in head and neck cancer. However, in a few cases, chemoradiotherapy has been shown to result in late complications, such as hypopharyngeal perforation, which is very rare.

PRESENTATION OF CASE: A 65-year-old man, who had undergone chemoradiotherapy for hypopharyngeal cancer 30 months previously, presented with high fever and neck pain. He subsequently developed hypopharyngeal stenosis, hypopharyngeal perforation, and a retropharyngeal abscess followed by pyogenic spondylitis. He underwent surgical treatment (resection with reconstruction) and was administered an antibacterial agent and steroids for an extended period. This treatment regimen was successful, and the patient has survived disease-free without symptoms.

DISCUSSION: Chemoradiotherapy-induced hypopharyngeal perforation is an extremely rare condition. In the present case, the perforation was large (2 cm), and the hypopharyngeal cavity was originally constricted. Pharyngeal reconstruction with a jejunal autograft was therefore necessary. Through the present case, we reconfirmed that although the primary purpose of chemoradiotherapy is organ preservation, it can also lead to organ destruction and fatal complications. It is important that physicians be aware of the possibility of hypopharyngeal perforation so as to avoid delayed diagnosis and treatment of similar rare cases.

CONCLUSION: Hypopharyngeal perforation can sometimes be fatal because it can lead to pyogenic spondylitis. Suitable surgical techniques and appropriate doses of antibacterial agents for long-term use were appropriate treatments for the patient in this case.

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1. Introduction

Chemoradiotherapy (CRT), an established treatment for head and neck cancers, helps preserve head and neck function and morphology. However, CRT can cause various adverse effects. Hypopharyngeal perforation, although rare, is one such example. Here, we report an extremely rare case of hypopharyngeal perforation after CRT along with a review of the literature.

2. Presentation of case

The work has been reported in line with the CARE criteria [1].

Abbreviations: CRT, chemoradiotherapy; PEG, percutaneous endoscopic gastrostomy; MRI, magnetic resonance imaging.

* Corresponding author at: Division of Head and Neck Surgery, Japan Community Health Care Organization Kyushu Hospital, 1-8-1 Kishinoura, Yahatanishiku, Kitakyushu City, Fukuoka 806-8501, Japan. Fax: + 81 93 642 1868.

E-mail addresses: miolovemio@hotmail.co.jp (M. Matsuo), fumiriki@nk-cc.go.jp (F. Rikimaru), yhigaki@nk-cc.go.jp (Y. Higaki), masuda.m@nk-cc.go.jp (M. Masuda).

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A 65-year-old man presented at our hospital in July 2014 with aphagia, neck pain, and fever. He had been previously diagnosed with hypopharyngeal cancer (posterior wall, T2N0M0; Fig. 1) in November 2011 at a different hospital, for which he had received CRT (66 Gy, 2 Gy × 33 fractions; cisplatin, 120 mg/body). In May 2014, he was referred to another hospital because of swallowing difficulty, where he was diagnosed with recurrent hypopharyngeal cancer, deemed inoperable. Palliative treatment was selected, and the patient underwent percutaneous endoscopic gastrostomy. Subsequently, he developed neck pain and fever (38 °C) that persisted for >1 month. In July 2014, he was referred to our department.

2.1. physical examination

Subjective symptoms at admission consisted of 38 °C fever persisting for 1 month, neck pain, inability to retroflex the neck, and hypoesthesia of the fingers. Computed tomography demonstrated low-density areas with air in the retropharyngeal and pre-vertebral spaces of cervical vertebrae [3–5]. Suspected fistula formation with the hypopharynx was also observed (Fig. 2a, b). Magnetic resonance

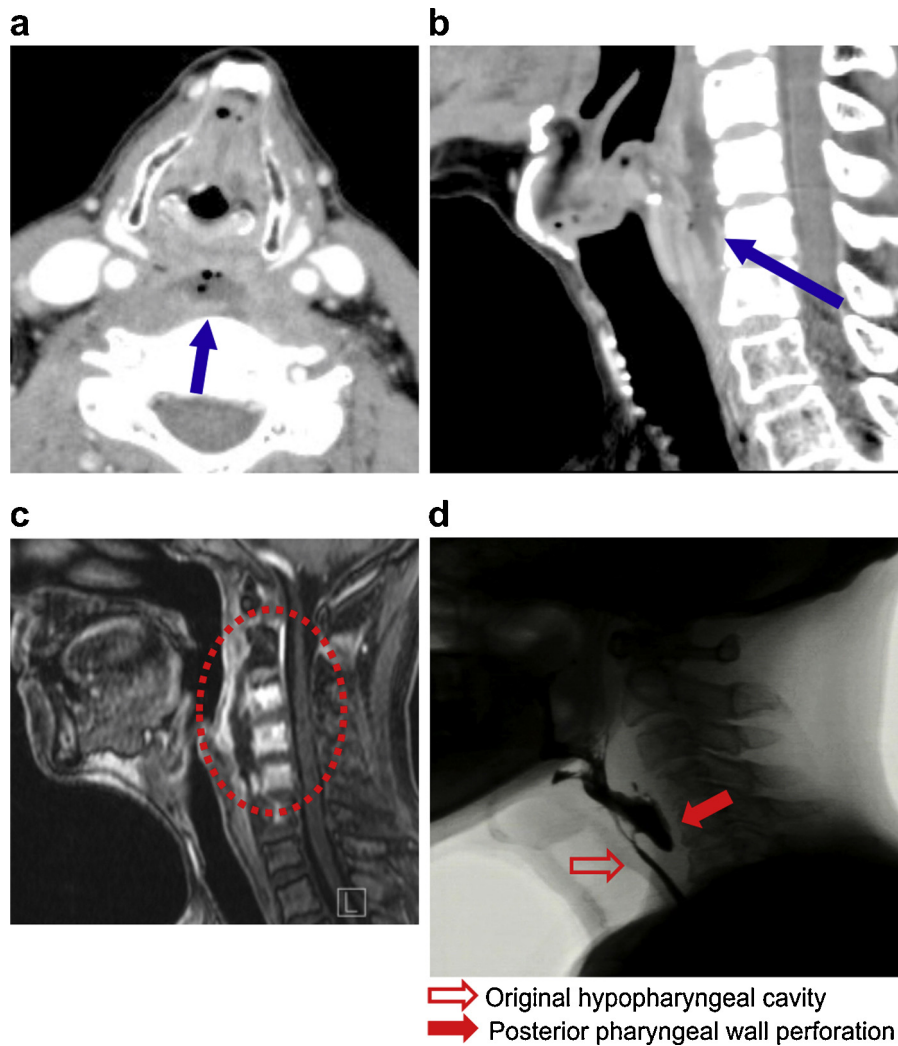


Fig. 2. ((a) and (b)) Computed tomography, (c) magnetic resonance imaging, and (d) transillumination findings.

imaging (MRI) revealed the disappearance of the pre-vertebral muscles in the same site and pyogenic spondylitis (Fig. 2c). On videofluorography, the contrast medium flowed into the retropharyngeal space from an approximately 2-cm perfusion site in the posterior pharyngeal wall and accumulated in the cecum; in addition, the hypopharyngeal cavity was observed to have originally been narrow (Fig. 2d).

2.2. Treatments

Hypopharyngeal stenosis and perforation due to CRT or recurrent cancer was considered to have resulted in a retropharyngeal abscess, which subsequently led to pyogenic spondylitis. The patient received an antibacterial agent (cefepime, 2 g/day) and steroids (prednisolone, tapered from 60 mg), after which he underwent observation with a curved laryngoscope. Expansion of the hypopharynx revealed a large perforation in the posterior hypopharyngeal wall and pervasion of the necrotized pre-vertebral muscles in the base of the perfusion site and the vertebra itself (Fig. 3a). The left half of the pyriform sinus showed adhesions. Histopathological analysis of the tissues from the blind biopsy of the mucosa surrounding the perforation as well as of the necrotic tissue revealed inflammatory granulation.

At 3 weeks post-admission, the patient was scheduled for total pharyngo-laryngo-esophagectomy, neck dissection, necrotized pre-vertebral muscle debridement, pharyngeal reconstruction with a free jejunal autograft, and coverage of the anterior aspect of the vertebra with a pectoralis major muscle flap. During surgery, the following were observed: advanced adhesion between the hypopharynx and the surrounding tissue; complete pre-vertebral muscle necrosis at the third and fourth cervical vertebrae; and pervasion of infected granulation tissue in the anterior aspect of the vertebrae. When the unhealthy granulation was completely

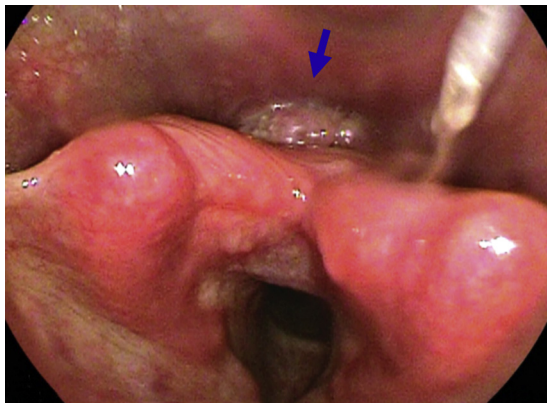


Fig. 1. Fiberscopy findings on initial examination for hypopharyngeal cancer at another hospital.

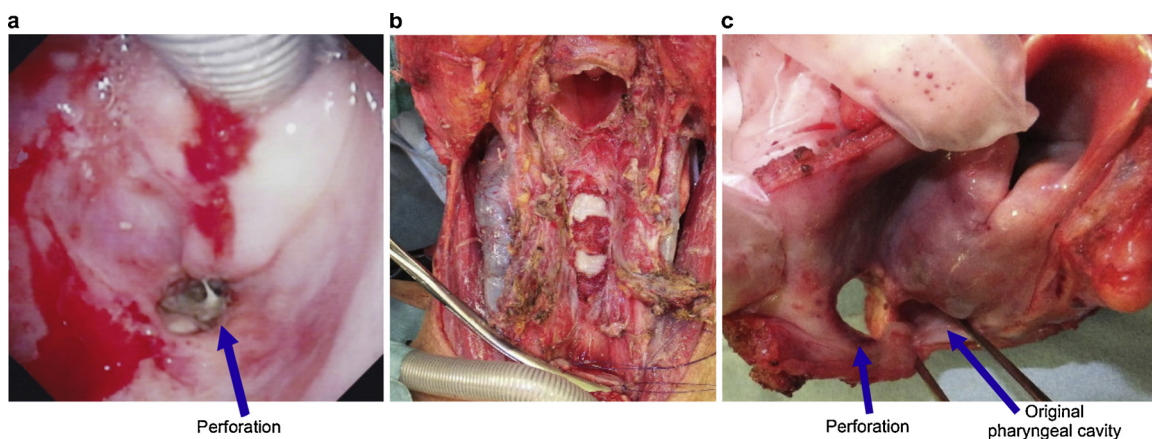


Fig. 3. (a) Curved laryngoscope findings, (b) post-resection cervical findings, and (c) resected specimen.

removed, normal vertebrae were observed; therefore, debridement was terminated (Fig. 3b). The range for the disappearance of normal pre-vertebral muscles was narrower; the anterior aspect of the vertebrae was covered with tissue from the thyroid rather than the pectoralis major muscle. The resected specimen demonstrated a large, 25-mm perforation in the posterior pharyngeal wall and stenosis in the original pharyngeal cavity (Fig. 3c). Pathological examination revealed the recurrence of squamous cell carcinoma in a tiny part of the mucosal surface; however, there was no invasion towards the muscle layer. Most tissues were necrotized, and there was only infected granulation tissue in the anterior aspect of the vertebrae. The patient was diagnosed with recurrent hypopharyngeal cancer (rTisNOMO), CRT-induced hypopharyngeal stenosis and perforation, and perforation-induced pyogenic spondylitis. Oral feeding was initiated 1 week post-operation; the percutaneous endoscopic gastrostomy tube was removed in week 3. Administration of an antibacterial agent alone (minocin, 50 mg/day) was continued, while steroids were discontinued.

2.3. Clinical course

One month post-surgery, the patient experienced a relapse of the fever (38 °C) and exacerbation of the lightheadedness, neck pain, and finger numbness. MRI demonstrated retropharyngeal abscess re-formation, epidural abscess, and exacerbation of pyogenic spondylitis compared to that observed pre-operation (Fig. 4a). An orthopedic surgeon was consulted, but there was concern about the risk of death owing to sepsis and spinal paralysis; therefore, surgical therapy was deemed dangerous and unsuitable steroid (dexamethasone, 8 mg) and antibacterial agent (cefepime, 2 g/day) administration was resumed, after which his symptoms improved again. Dexamethasone was tapered from 8 mg to 1 mg over the course of 4 months and ceased thereafter. Additionally, 100 mg minocin was continuously administered as an antibacterial agent for 4 months. The retropharyngeal abscess and epidural abscess then disappeared, while spondylitis also demonstrated incremental improvement (Fig. 4b). Nine months following surgery, the patient is disease-free without symptoms.

3. Discussion

CRT is superior to other head and neck treatment options in terms of preservation of function. However, post-CRT late effects can become serious and may drastically reduce the quality of life. One such late effect is perforation. The frequency of esophageal CRT-induced perforation is reported to be about 1% [2]; thus, it is known as an adverse event that occurs at a fixed proba-

bility. We assume that CRT-induced hypopharyngeal perforation is an extremely rare condition owing to the lack of literature. There are few reports of hypopharyngeal perforation due to other causes (Table 1) [3–5]. Regarding head and neck cancers, perforation caused by dilation for stenosis has been reported [3–5]. A number of reports have recently emerged regarding perforation as a complication of transoral robotic surgery and endoscopic laryngo-pharyngeal surgery [6,7]. We presumed the reason for the perforation was CRT-induced tissue fragility. After CRT, tissues become fibrotic and do not expand. In fact, remarkable stenosis of the original cavity caused by fibrosis was recognized in the present case. Moreover, CRT causes narrowing of the vessels, which results in delayed wound healing and increased risk of infection. Thus, we believe that a small wound in the pharynx after CRT led to the massive perforation.

Treatment for hypopharyngeal perforation includes conservative therapy (fasting, gavage, antibiotics, and hyperbaric oxygen therapy) and surgical treatment (simple suturing, resection, and resection with reconstruction). Surgical treatment is considered necessary for patients with perforations >10 mm in size and patients resistant to conservative therapy [3,5–7]. Here, the perforation was larger than 2 cm, and the hypopharyngeal cavity was originally constricted; therefore, total pharyngo-laryngoesophagectomy and pharyngeal reconstruction with a jejunal autograft was necessary. We used thyroid tissue alone to cover the anterior aspect of the vertebrae, and not the pectoralis major muscle tissue, which is typically the preferred approach. One could argue that the subsequent, temporary exacerbation of spondylitis may not have occurred if the major pectoralis muscle tissue had been used; however, based on the patient's tendency toward healing, the thyroid tissue may ultimately have been appropriate coverage material.

Pyogenic spondylitis causes symptoms such as fever and pain, sensory abnormality, paralysis, and spine deformation with loss of support [8–10]. The principles of treatment are to administer appropriate antibiotics and for the patient to rest completely from an early stage [8,11]. However, spondylitis requires surgical treatment in some cases. The primary surgical treatment for cases of epidural abscess-induced acute paralysis is laminectomy (a palliative operation for achieving decompression and drainage). For patients resistant to conservative therapy and with advanced vertebral body destruction, the primary surgical treatment is anterior decompression and fusion (a radical operation for curettage of the nidus) [8].

Spondylitis resolution requires a long period of time. Even when conservative therapy appears to improve inflammation, discontinuation of antibacterial agents may lead to relapse; thus, long-term

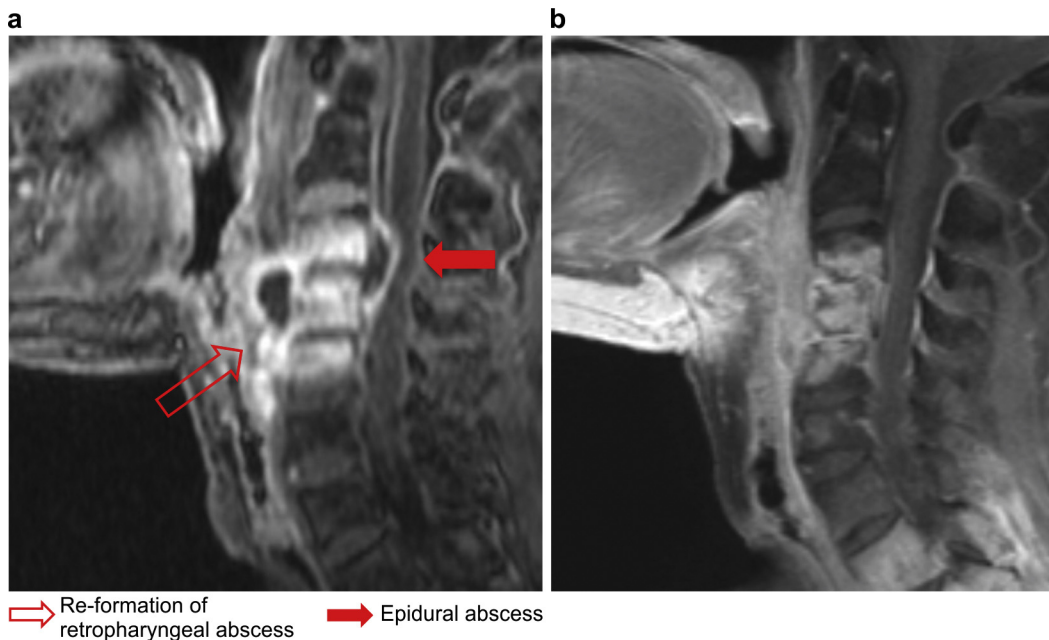


Fig. 4. Magnetic resonance image obtained (a) at the time of cervical spondylosis, and (b) upon improvement of the recurrent cervical spondylosis.

Table 1

Prior reports of all-cause hypopharyngeal perforation.

Author	Mao et al. [3]	Stojakov et al. [4]	Hinojar et al. [5]
Case	Dilation for stenosis in 8 cases of head and neck cancer	15 cases of hypopharyngeal perforation	7 cases of hypopharyngeal perforation
Treatment	Conservative therapy in 6 cases Surgical treatment in 2 cases	Conservative therapy in 3 cases Surgical treatment in 12 cases	Conservative therapy in 3 cases Surgical treatment in 4 cases
Prognosis	–	13.3% mortality	–

administration (of at least several months) of antibacterial agents is recommended [8,11,12]. However, no clear guidelines have been established [11]; decisions are made on a case-by-case basis. In a case where osteoradionecrosis of the spine following CRT for hypopharyngeal cancer resulted in pyogenic spondylitis and epidural abscess, Kuba et al. reported that antibacterial agents were administered for 10 months post-laminectomy [13].

In the present case, although spondylitis-induced symptoms tended to improve following surgery, the spondylitis was exacerbated, with an epidural abscess developing at 1 month post-surgery. We believe this was a result of insufficient dose of the antibacterial agent. The findings of this case indicate that the treatment for spondylitis requires a sufficient dose of antibacterial agents that is administered over a long term (more than approximately 4 months), as well as an surgical treatment (decompression and drainage, or curettage of the nidus).

4. Conclusion

We report the case of a large perforation of the hypopharynx following CRT and pyogenic spondylitis. Despite an extensive review, we found no previous reports of similar cases, leading us to believe that the present case is extremely rare.

Conflicts of interest

None.

Funding

None.

Ethical approval

Informed consent was obtained from the patient. Because this is a case report, ethical approval was not required.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review from the Editor-in-Chief of this journal on request.

Authors' contribution

Mioko Matsuo is the first author of this report and surgeon for that surgery. She also analyzed the data and wrote the manuscript. Fumihide Rikimaru, Yuichiro Higaki, and Muneyuki Masuda assisted with the operation.

Guarantor

The corresponding author Mioko Matsuo is the guarantor of this work.

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