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CASE REPORT

Successful hyperbaric oxygen therapy for laryngeal radionecrosis after chemoradiotherapy for mesopharyngeal cancer: case report and literature review

Madoka Abe · Yoshiyuki Shioyama · Kotaro Terashima · Mioko Matsuo · Iwao Hara · Satoru Uehara

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Abstract Laryngeal radionecrosis is one of the most troublesome late complications of radiotherapy, because it is frequently resistant to treatment and laryngectomy is required in the worst case. Here, we report a case of laryngeal radionecrosis, successfully treated by use of hyperbaric oxygen (HBO) therapy, in which laryngectomy was avoided. A 67-year-old male received radical chemoradiotherapy (CRT) for mesopharyngeal cancer, which included radiotherapy with a total dose of 71.4 Gy/38 Fr and chemotherapy with CDDP + S-1. He developed dyspnea and throat pain 9 months after completion of CRT. Laryngoscopy revealed vocal cord impairment because of severe laryngeal edema. He was diagnosed as having laryngeal radionecrosis and initially received conservative therapy combined with antibiotics, steroids, and prostaglandins. Because his dyspnea was persistent despite this treatment, HBO therapy was administered 20 times, and resulted in complete remission of the dyspnea. HBO therapy, therefore, is regarded as an effective conservative therapeutic option for laryngeal radionecrosis.

M. Abe (✉) · K. Terashima · S. Uehara
Department of Radiology, National Hospital Organization Kyushu Cancer Center, 3-1-1 Notame, Minami-ku, Fukuoka 811-1395, Japan
e-mail: abe.m@nk-cc.go.jp

Y. Shioyama
Department of Heavy Particle Therapy and Radiation Oncology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

M. Matsuo
Department of Head neck Surgery, National Hospital Organization Kyushu Cancer Center, Fukuoka, Japan

I. Hara
Section of Dentistry and Oral Surgery, Keikoukai Hara Hospital, Fukuoka, Japan

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Introduction

Chemoradiotherapy (CRT) is an important treatment modality for head and neck cancer with regard to preservation of organ structure and function. It is used widely as the primary treatment for early-stage cancers. Acute adverse effects, for example mucositis, dermatitis, and guttural edema, develop, to different extents, in almost all cases of CRT; usually, however, these are resolved within a few months after the treatment. On the other hand, serious late adverse effects, for example mucosal ulceration of the gingiva, neck fistula, and osteo/chondroradionecrosis, are observed in rare cases. Despite the rarity of these late adverse effects, because of severe and persistent symptoms that are often resistant to treatment patients' quality of life tends to be substantially impaired. Laryngeal radionecrosis is one of the most troublesome late adverse effects, because laryngectomy is sometimes inevitable in severe cases. Hyperbaric oxygen (HBO) therapy is a standard adjuvant treatment modality for mandibular osteoradionecrosis (ORN) [1]. However, reports of its use to treat laryngeal radionecrosis are limited and a treatment procedure has not yet been established [2]. Here, we report a case of laryngeal radionecrosis successfully treated with HBO therapy.

Case report

A 67-year-old male received CRT for mesopharyngeal cancer (left lateral wall, cT2N2bM0) as initial treatment at our department from May to June 2010. Radiotherapy with

a total dose of 71.4 Gy/38 Fr using 4 MV X-ray was performed in combination with chemotherapy using cisplatin and S-1. Of the 71.4 Gy the patient received, 41.4 Gy was irradiated in 23 fractions on the initial field including the whole neck and supraclavicular region. 30 Gy was then boosted in 15 fractions on a field fitted to the primary tumor and metastatic lymph nodes. The estimated dose to the larynx was 95–100% of the prescribed dose and no hot spot was detected in the larynx (Fig. 1). During the first 5 days of radiotherapy, 20 mg/m^2 CDDP was administered to the patient as the first *kur* (total amount 160 mg). However, this chemotherapy regimen had to be changed to 80 mg/day of S-1 because of renal failure, and S-1 was administered for 14 days instead of the second *kur* of CDDP (total amount of 1120 mg). The initial responses of the primary site and cervical lymph node metastases were complete response and partial response, respectively. Therefore, left radical neck dissection was performed 1 month after completion of CRT. The patient complained of throat pain and hoarseness, and laryngoscopy revealed marked mucositis on the treatment site and laryngeal edema at the time of CRT completion. However, all of these symptoms resolved within 1 month, with laryngoscopy confirming the resolution of mucositis. Laryngeal edema, on the other hand, was still observed 6 months later.

Nine months after CRT, he revisited our hospital, complaining of dyspnea and throat pain. He presented stridor with the oxygen saturation (SpO_2) of 97–98% at room air. Laryngoscopy revealed severe mucositis of the larynx and meso-hypopharynx. In addition, the glottis could not be seen clearly, because of marked laryngeal edema, and the right and left vocal cords appeared to be fixed and impaired, respectively (Fig. 2). Therefore, he was diagnosed with grade III laryngeal radionecrosis based on Chandler's classification (Table 1) [3] and was admitted to the hospital as an emergency. Medical interview revealed no history of alcohol consumption, smoking, use of steroids, or tooth extraction during or after CRT, all of which can trigger radionecrosis. Computerized tomography (CT) scan on the same day revealed an obvious low-density area indicative of severe edema in meso-hypopharynx and larynx. In addition, the thyroid cartilage and the arytenoids cartilages were found to be fragmented and collapsed (Fig. 2). Conservative therapy, initiated immediately upon admission, included antibiotics, steroids, and prostaglandins, combined with other supportive care, for example steam inhalation and nutrition support. The amount of administered steroids was reduced from 200 mg predonine to 10 mg in 3 weeks, and antibiotics and prostaglandins were administered intravenously for the initial 2 weeks, and then orally. Although this treatment resolved the stridor and throat pain, dyspnea persisted even after 3 weeks of this therapy. Laryngoscopy found some improvement of laryngeal edema but the right vocal cord was found still fixed. Therefore, the patient was transferred to another hospital to receive HBO therapy. HBO therapy was

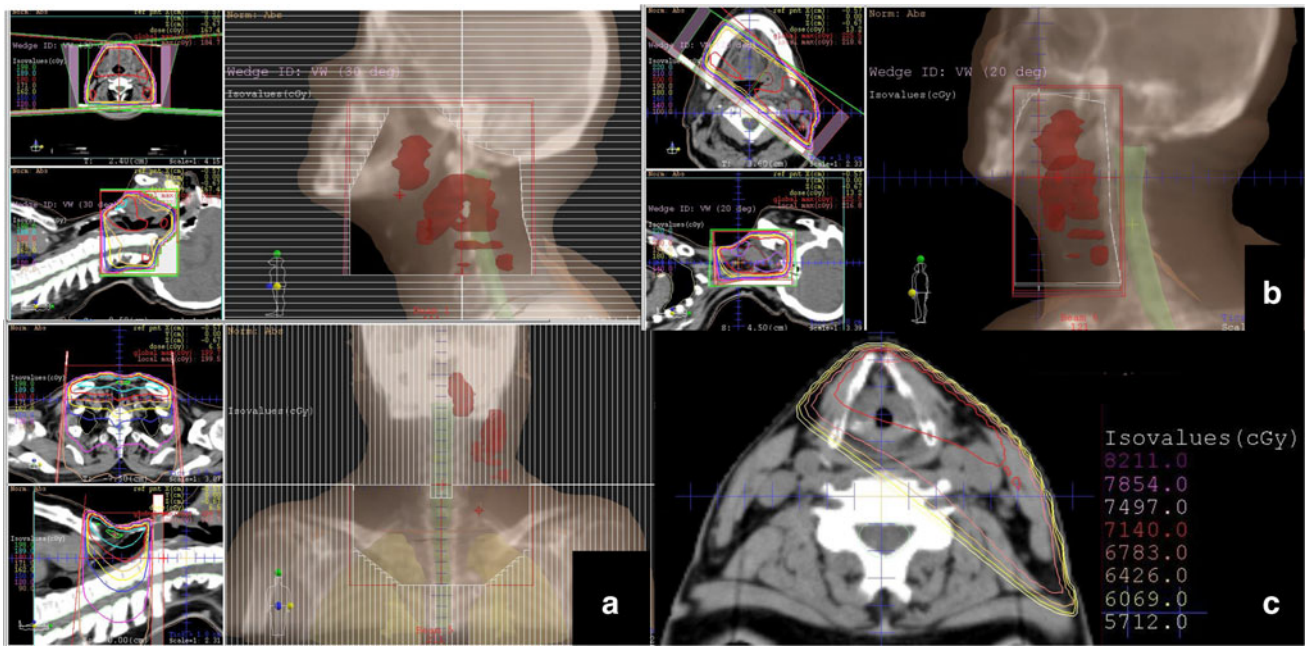

Fig. 1 **a** Initial planning of radiotherapy: bilateral neck and supraclavicular region were irradiated, using the half-beam method. **b** Boost planning of radiotherapy: oblique opposed beams were set to boost a field which fitted the primary tumor and lymph node metastases. **c** Section of the larynx at CT planning: the larynx was covered by the 95% line (*orange line*) of the prescribed dose. No hot spot was observed in the larynx

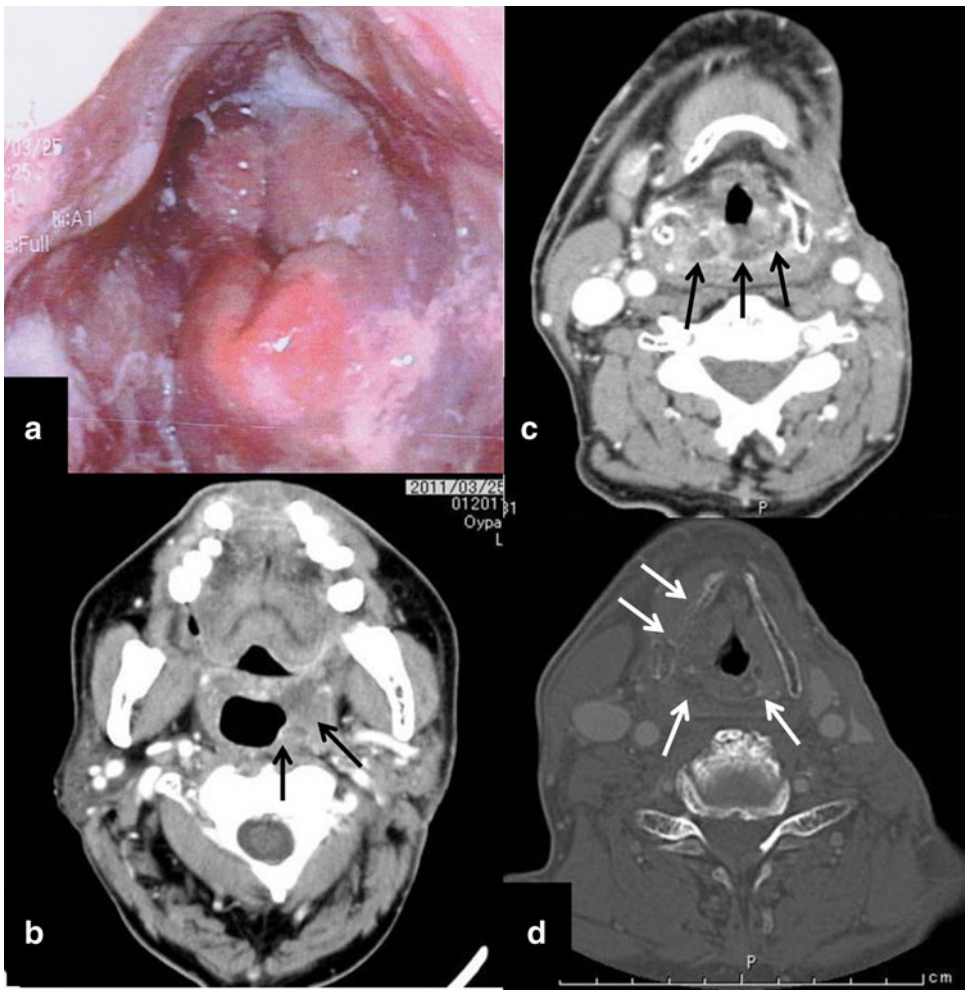

Fig. 2 **a** Laryngoscopy 6 months after completion of chemoradiotherapy: marked mucositis of the larynx is revealed. The glottis is hardly visible because of severe edema. **b–d** CT scan on the same day as laryngoscopic examination: the low-density area indicative of severe edema has expanded into the meso-hypopharynx and larynx (*black arrows*). The shapes of the thyroid cartilage and the arytenoids cartilages are obscure and fragmented (*white arrows*), implying chondronecrosis

Table 1 Chandler's classification for laryngeal necrosis (from Ref. [3])

Grade	Symptoms	Signs
I	Slight hoarseness Slight mucosal dryness	Slight edema, telangiectasia
II	Moderate hoarseness Moderate mucosal edema	Slight impairment of cord motility, moderate edema and erythema
III	Severe hoarseness with dyspnea Moderate odynophagia and dysphagia	Severe impairment of cord motility or fixation of one vocal cord Marked edema, skin changes
IV	Respiratory distress, severe pain Severe odynophagia, weight loss Dehydration	Fistula, fetor oris Fixation of skin to larynx Laryngeal obstruction and edema occluding airway, fever

performed daily at 2 atmospheres absolute (ATA) with 100% oxygen for 1 h each. After 20 sessions of HBO therapy, his dyspnea completely resolved, and movement of the vocal cords was confirmed by laryngoscopy, recovering to normal. The CT scan also revealed marked shrinkage of the low-density area with the shapes of the cartilages obviously becoming well defined, implying improvement of the radionecrosis (Fig. 3). Furthermore, laryngoscopy performed at subsequent monthly check-ups revealed gradual improvement of laryngeal edema and no recurrence of cancer.

Discussion

Chandler classified radiation-induced laryngeal injury into four stages according to clinical findings and symptoms (Table 1) [3]. This system is very useful and widely used for establishing guidelines for therapy. Chandler's grade III and IV are regarded as "radionecrosis" by clinical consensus, although pathological evidence is lacking. The reported incidence of laryngeal radionecrosis after radical radiotherapy has been less than 1% since the 1990s. Although typical occurrence of laryngeal necrosis is

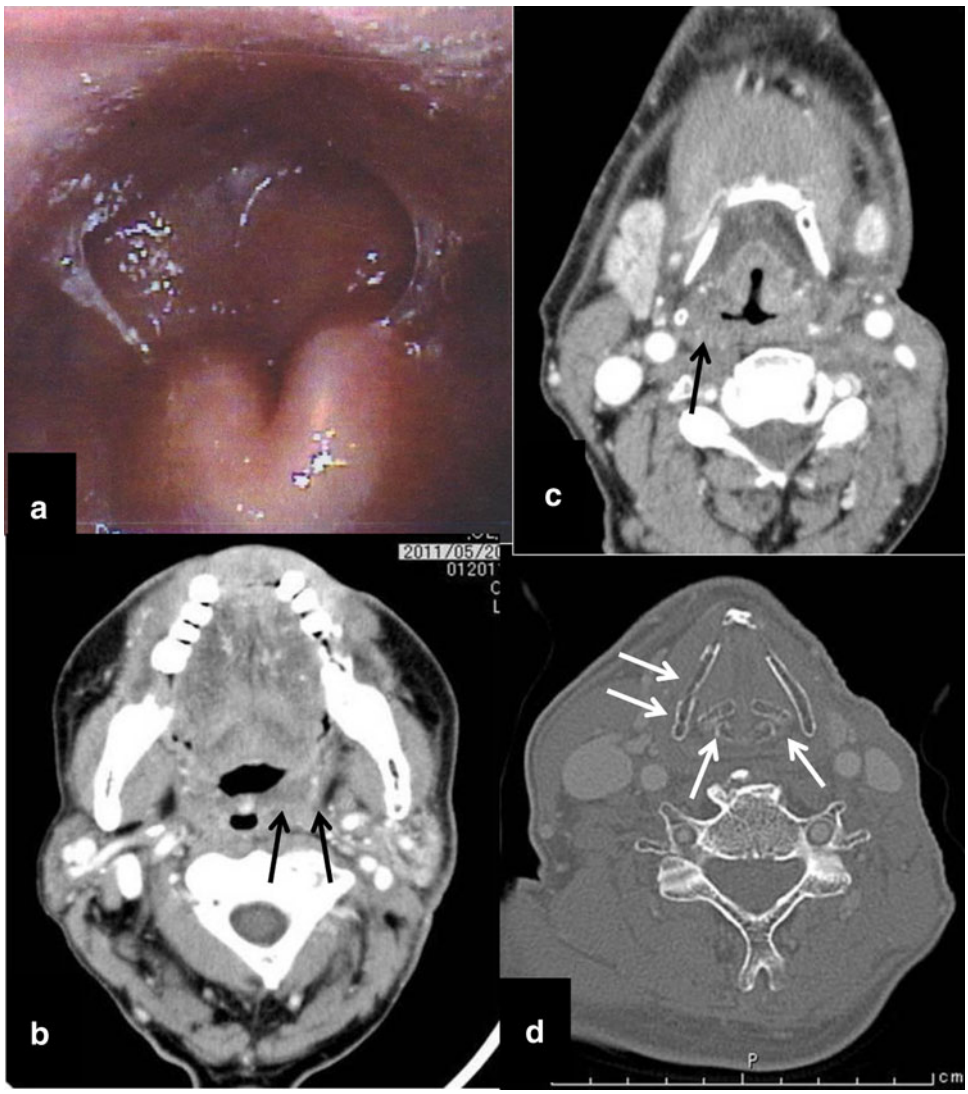

Fig. 3 **a** Laryngoscopy after 20 sessions of HBO therapy: mucositis is obviously resolved and edema is slightly improved. **b–d** CT scan after 20 sessions of HBO therapy: the low-density area has become almost negligible (*black arrows*). The shapes of cartilages are more defined and fragmentation is not observed (*white arrows*)

accompanied by predisposing factors, for example continuous smoking and alcohol consumption, diabetes, steroid use, infection, and local tumor recurrence after radiotherapy [2], the patient in our case had no such history. Because neck dissection can induce hypoxic conditions in the larynx, this could have been the trigger of radionecrosis in our case. However, this remains speculative, because no complication was observed after neck dissection and a definitive causal relationship cannot be drawn.

Initial standard treatment for laryngeal radionecrosis is conservative therapy including steam inhalation, nutrition support, antibiotics, steroids, and, in recent times, prostaglandins. When a patient does not respond well to these treatments, HBO therapy and surgical intervention are considered as the next step. Hypoxia, hypocellularity, and hypovascularity due to irradiation have been thought of as the main causes of radionecrosis, although its mechanism of pathogenesis has not been fully elucidated [1]. HBO therapy is regarded as an effective means of rescuing such conditions, because it stimulates angiogenesis, fibroblast and osteoblast proliferation, and collagen formation in irradiated tissues. HBO therapy has been used for management of ORN, particularly mandibular ORN, since the 1960s [4]. Marx established the procedure for HBO therapy combined with surgery for ORN in 1983 [1]; this has become the standard adjuvant treatment for ORN. On the other hand, reports of HBO therapy for laryngeal radionecrosis are limited and a treatment procedure has not yet been established. In 2000 Filntisis et al. [2] reported 18 cases treated with HBO therapy and conducted a literature review of 25 cases. However, few reports have been published since then [5–9]. The cases reported previously were all of Chandler's grade III/IV laryngeal radionecrosis and received radiotherapy of 45–86 Gy. HBO regimens varied from 2.0 to 2.5 ATA for 60–120 min with the number of treatment sessions ranging from 6 to 80 (Table 2). In such

Table 2 Summary of the published literature on HBO therapy for laryngeal radionecrosis (from Refs. [2, 5–9])

Authors	Number of patients	Chandler's classification	Chemoradiotherapy	HBO therapy (ATA × min × numbers)	Outcome
Hart et al. [2]	5	IV	RTx; N/A CTx; N/A	2 × 120 × 60	4 improved, 1 failed
Farmer et al. [2]	1	IV	RTx; N/A CTx; N/A	2 × 120 × 40	Improved
Davis et al. [2]	1	IV	RTx; N/A CTx; N/A	2.4 × 90 × 60	Improved
Strauss [2]	1	IV	RTx; N/A CTx; N/A	N/A × N/A × 20	Failed
Ferguson et al. [2]	8	III/IV	RTx; 60–70 Gy CTx; N/A	2 × 120 × 39–76 (49)	7 improved, 1 failed
Feldmeier et al. [2]	9	III/IV	RTx; 45–70 Gy CTx; N/A	2.4 × 90 × 8–41 (28)	All improved
Filntisis et al. [2]	18	III/IV	RTx; 50–75.45 Gy CTx; N/A	2 × 120 × 6–80 (43)	13 improved, 5 failed
Hsu et al. [5]	1	IV	RTx; 60 Gy CTx; −	2 × 60 × 40	Improved
Nishida et al. [8]	1	IV	RTx; 64.8 Gy CTx; +	2 × 120 × 20	Improved
Matsushita et al. [9]	2	IV	RTx; 79.3–80 Gy CTx; +	2.5 × 60 × N/A	All improved
Narozny et al. [6]	6	III/IV	RTx; 60–86 Gy CTx; N/A	2.5 × 60 × 8–20 (16)	All improved
Scott et al. [7]	5	III/IV	RTx; 66.6–70 Gy CTx; N/A	2.5 × 90 × 15–25	4 improved, 1 N/A

RTx radiotherapy, *CTx* chemotherapy, *N/A* not available

reports, the therapy regimen largely depended on each hospital's guideline and the number of treatments was usually determined by clinicians, on the basis of the patient's clinical symptoms. The effectiveness of HBO therapy was estimated to be 86% overall, with all of the successful cases avoiding laryngectomies. Interestingly, all of Chandler's grade III cases responded well to the treatment, indicating the importance of early HBO intervention.

Regarding the adverse effects of HBO therapy, the previous studies reported several cases in which myopia and otalgia developed as manifestations of barotraumas, necessitating myringotomies. However, these symptoms resolved quickly, and no severe HBO complications, for example pulmonary injury and seizure activity, were reported [2, 7–9]. In addition to adverse effects, recurrent tumor acceleration induced by HBO therapy may be another concern. However, there has been no convincing evidence that HBO therapy stimulates tumor growth; previous literature and our case revealed no definite cancer growth enhancement as a result of HBO therapy [2, 5–9].

In conclusion, HBO therapy is an effective treatment option and should be considered, in combination with other conservative therapy, for laryngeal radionecrosis, especially in the situation of increased availability of HBO facilities in recent years.

References

1. Marx RE. A new concept in the treatment of osteoradionecrosis. J Oral Maxillofac Surg. 1983;41:351–7.
2. Filntisis GA, Moon RE, Kraft KL, Farmer JC, Scher RL, Piantadosi CP. Laryngeal radionecrosis and hyperbaric oxygen therapy: report of 18 cases and review of the literature. Ann Otol Rhinol Laryngol. 2000;109:554–62.
3. Chandler JR. Radiation fibrosis and necrosis of the larynx. Ann Otol Rhinol Laryngol. 1979;88:509–14.
4. Pasquier D, Holesher T, Schmutz J, Dische S, Mathieu D, Baumann M, et al. Hyperbaric oxygen therapy in the treatment of radio-induced lesions in normal tissues: a literature review. Radiother Oncol. 2004;72:1–13.
5. Hsu YC, Lee KW, Ho KY, Tsai KB, Kuo WR, Wang LF, et al. Treatment of laryngeal radionecrosis with hyperbaric oxygen therapy: a case report. Kaohsiung J Med Sci. 2005;21:88–92.
6. Narozny W, Sicko Z, Kot J, Stankiewicz C, Przewozny T, Kuczkowski J. Hyperbaric oxygen therapy in the treatment of complications of irradiation in head and neck area. UHM. 2005;32:103–10.
7. London SD, Park SS, Gampper TJ, Hoard MA. Hyperbaric oxygen for the management of radionecrosis of bone and cartilage. Laryngoscope. 1998;108:1291–6.
8. Nishida A, Honda N, Kitani Y, Tsujimura M, Adachi T, Fujiki N, et al. Treatment of laryngeal radionecrosis with hyperbaric oxygen therapy: a case report. Jibirinshou. 2007;100:1021–6.
9. Matsushita H, Nemoto K, Ogawa Y, Ariga H, Takeda K, Sakayauchi T, et al. Effects of hyperbaric oxygen therapy (HBO) on radiation-induced late sequelae. J Jpn Soc Ther Radiol Oncol. 2007;19:147–55.