

TREATMENT OF LARYNGEAL RADIONECROSIS WITH HYPERBARIC OXYGEN THERAPY: A CASE REPORT

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An 81-year-old male with early-stage laryngeal carcinoma had been treated with 60 Gy curative radiotherapy. He complained of a sore throat, foul odor in the mouth, progressive dyspnea, and fever 2 months after the completion of radiotherapy. Direct laryngoscopy revealed narrowing of the glottis with diffuse ulcerative necrotic tissue. Biopsies at multiple sites and pathology revealed intense coagulation necrosis with complete denudation of covering epithelium without any malignancy. Since laryngeal radionecrosis was suspected, the patient received hyperbaric oxygen (HBO) therapy 40 times for 1 hour of 100% O₂ at 2 atm absolute pressure. His clinical symptoms gradually improved and repeated endolaryngeal biopsies were undertaken near the end of HBO therapy and again 6 months later. The patient's larynx healed completely with diffuse fibrosis and no malignant cells were found on pathology. Radionecrosis must be differentiated from cancer recurrence following curative radiotherapy for early laryngeal cancer. HBO therapy could be a useful treatment adjunct for laryngeal radionecrosis.

Key Words: radionecrosis, hyperbaric oxygen therapy, laryngeal cancer, complication
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Radiotherapy is often the primary treatment modality for early laryngeal carcinoma because it preserves voice quality. Salvage surgery can be used whenever residual or recurrent disease occurs. The main complications of radiation in laryngeal cancer are laryngeal edema, radiation changes to the skin, perichondritis, and cartilage necrosis. In severe complications that lead to laryngeal radionecrosis, patients may suffer from hoarseness, pain in the neck and throat, airway obstruction or respiratory distress, aspiration, neck fistula, or dysphagia [1]. Hence, it is important to make a differential diagnosis between radionecrosis and residual or recurrent cancer of the larynx. Hyperbaric oxygen (HBO) therapy has been an effective adjuvant modality in the management of laryngeal radionecrosis. We report a case

of laryngeal radionecrosis treated successfully with HBO therapy.

CASE PRESENTATION

An 81-year-old male received radiotherapy of 60 Gy (30 fractions of 2 Gy/fraction) for early-stage laryngeal carcinoma (T₁N₀M₀) from December 2001 to February 2002 at another medical institution. He developed a cough with yellowish sputum, fever, chills, fetor oris, tenacious sputum, aspiration of food, and dyspnea 2 months after the completion of radiotherapy. Direct laryngoscopy at the previous hospital showed only glottic narrowing. Biopsies of the larynx showed no malignancy. He was transferred to our institution for care because his symptoms were not improving. Under direct laryngoscopy following emergency tracheotomy, marked foul odor and band-like necrotic tissue with dislodged necrotic pieces of cartilage in the posterior glottic area were found (Figure 1). The subglottis seemed to be clear. Biopsies at multiple sites of the glottic area showed

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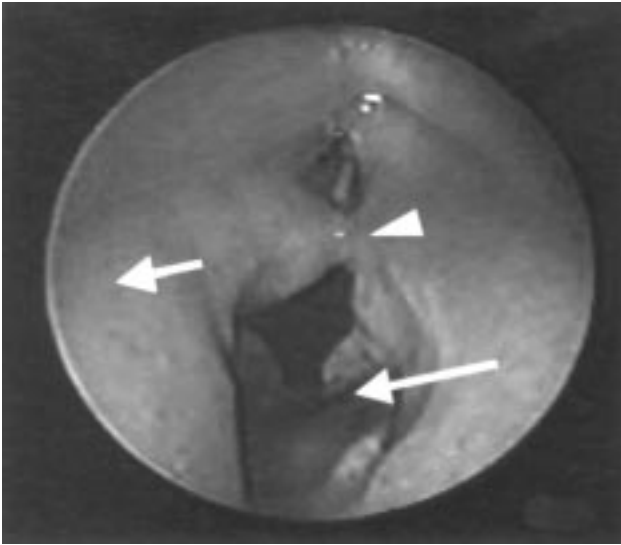


Figure 1. Direct laryngoscopy shows irregular swelling and partial synechia of the false cord (arrowhead). Some whitish debris is evident over the surface of the true cords without visible tumor on the day of arrival. Glottic chink narrowing is seen due to synechia of the anterior two-thirds of the vocal folds. The subglottis is unaffected. Foul-odor necrotic tissue and cartilage at the posterior glottis are present (long arrow) and the arytenoids (short arrow) are swollen.

intense coagulation necrosis with complete denudation of the covering epithelium, degeneration and thrombosis of blood vessels, and the presence of fibrinoid exudates (Figure 2). The underlying stroma revealed inflammation and focal foreign-body reaction, and several degenerated atypical cells and fibrosis were also noted.

Radionecrosis of the larynx was suspected so the patient

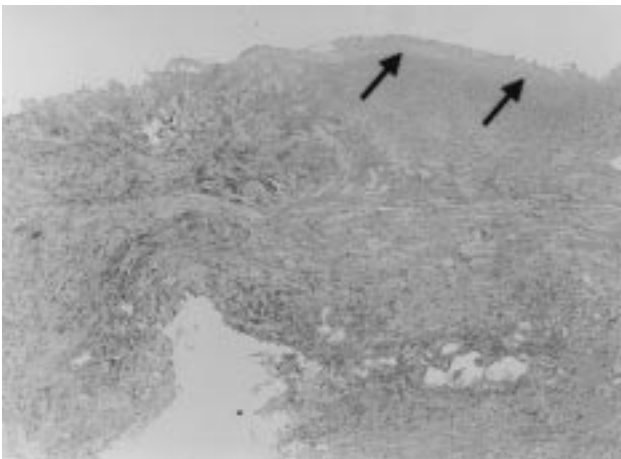


Figure 2. Microscopic features at first biopsy. Intensive coagulation necrosis with complete denudation of covering epithelium is visible (arrows). There are abundant fibrinoid deposits without conspicuous inflammation. (Hematoxylin & eosin; original magnification $\times 8$.)

received supportive treatment and HBO therapy at 2 atmospheres absolute (ATA) with 100% O₂ for 1 hour per session. After 20 HBO treatments, his symptoms improved significantly. The amount of tenacious sputum decreased considerably and the fetor oris also improved. Direct laryngoscopy and biopsies were performed twice, once toward the end of treatment and again 6 months after the completion of HBO therapy (Figure 3). The larynx healed completely with marked fibrosis and only minor granulation, and no malignant cells were found by pathology. Although the patient improved clinically, the sequelae of marked endolaryngeal destruction and fibrosis leading to glottal stenosis required a long-term tracheotomy. He has had no recurrence of cancer after 3 years of follow-up.

DISCUSSION

The reported incidence of severe radiation reactions following 50–60 Gy to the larynx ranged from 5% to 12% in the 1970s but was less than 1% in the 1990s [2]. Most patients with laryngeal radionecrosis develop the condition within 1 year of radiation therapy. The longest latent period for laryngeal radionecrosis was more than 50 years [3], compared to only 2 months in our case.

Symptoms of laryngeal radionecrosis include pain, hoarseness, respiratory stridor, laryngeal edema or ulceration, vocal cord paralysis, aspiration, and neck fistula. Our case could be classified as grade IV using the Chandler grading system, and tracheotomy to maintain the airway and prevent aspiration is necessary in this group (Table) [1].

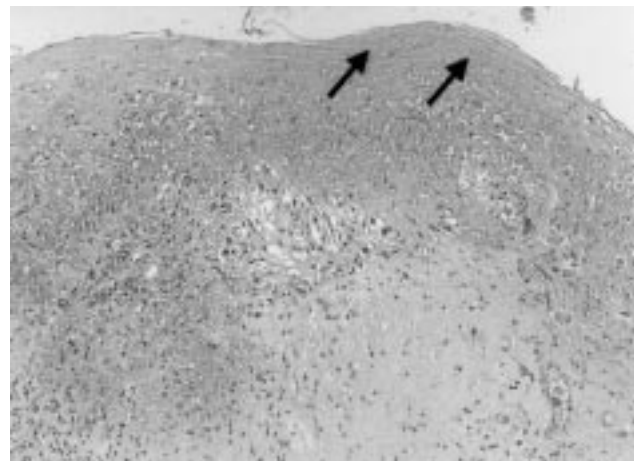


Figure 3. Regenerated squamous epithelium noted 6 months after hyperbaric oxygen therapy (arrows). (Hematoxylin & eosin; original magnification $\times 20$.)

Table. Grading system for radiation necrosis of the larynx [1]

Grade	Symptoms	Signs	Treatment
I	Slight hoarseness, slight dryness	Slight edema, telangiectasis	None
II	Moderate hoarseness, moderate dryness	Slight impairment of cord mobility, moderate edema and erythema	None
III	Severe hoarseness with dyspnea, moderate odynophagia and dysphagia	Severe impairment or fixation of at least one vocal cord, marked edema, skin changes	Steam, antibiotics
IV	Respiratory distress, severe pain, severe odynophagia, weight loss, dehydration, fever	Fistula, fetor oris, fixation of skin to the larynx, laryngeal obstruction, edema occluding the airway, toxicity	Tracheotomy and/or laryngectomy

Adapted with permission from Reference 1.

The clinical findings showed diffuse sloughing and a markedly foul odor, necrotic soft tissues at the posterior glottis, and arytenoids without lesions at the membranous vocal fold, which are uncommon in laryngeal malignancy. These unusual findings could be clues to radionecrosis or laryngeal reflux disease. Although computerized tomography imaging frequently provides nonspecific results, the diagnosis of laryngeal radionecrosis can be strongly suggested in patients with sloughing of arytenoid cartilage, fragmentation and collapse of the thyroid cartilage, and/or the presence of gas bubbles around the cartilage [4].

The mechanism of radionecrosis is small-vessel arteritis and thrombosis due to the effects of radiation, which reduces the blood supply to the hyaline cartilage and results in necrosis. Predisposing factors include alcohol, smoking, diabetes, hypertension, steroid use, and infiltration of cartilage with tumor before treatment [5]. Pathologic examinations showed intense coagulation necrosis with features of radiation effect, but no malignant disease was found after multiple biopsies at the completion of, and 6 months after, HBO therapy. Clinicians should rule out the presence of residual or recurrent malignancy before making the diagnosis of laryngeal radionecrosis. Positron emission tomography with 18F-2fluoro-2deoxyglucose has been used widely to diagnose radionecrosis in brain tumors, and it is also reportedly useful in distinguishing benign from malignant changes in the larynx after radiation treatment [6]. This non-invasive technique may be an adjunct to biopsies, which can potentially traumatize the radiation-damaged tissue and precipitate necrosis.

Our patient, classified as having grade IV laryngeal radionecrosis, showed a positive response to HBO therapy. The clinical symptom of foul odor in the mouth quickly improved after about 20 HBO treatments. The sequelae of radionecrosis were bilateral vocal cord fixation in the median

position and glottal stenosis, resulting in the need for a long-term tracheostomy. We believe that the synechia of anterior vocal cords and fibrosis, cartilage sloughing of cricoarytenoid joints leading to fibrosis, might explain the irreversibility of vocal paralysis. The treatment of radiation necrosis with HBO therapy was first reported by Hart and Mainous [7]. Only 43 reported cases of laryngeal radionecrosis have been treated with HBO therapy [5]. The reported HBO regimens are 2 ATA for 120 minutes or 2.4 ATA for 90 minutes, with the number of treatments ranging from 20 to a maximum of 80. An estimated failure rate of 22.2% has been reported [5]. Eight of the 43 reviewed cases who did not improve were in Chandler grade IV. Our patient had been treated with 2 ATA/60 minutes 40 times and showed significant clinical improvement.

The presence of residual or recurrent malignancy within the radiation necrosis lesion is not an absolute contraindication for HBO therapy [8], although HBO therapy may accelerate tumor growth in head and neck cancer [9]. Total laryngectomy may be needed in patients with a nonfunctioning larynx, who fail to improve over a 6-week period of intensive medical treatment, or in those with documented residual or recurrent malignant disease [2].

Laryngeal radionecrosis may be a life-threatening situation if left unrecognized. Early airway intervention, antibiotic treatment, and nutrition supply are important supportive treatments. Since the availability of HBO therapy has increased in hospitals in recent years, it could be a useful treatment for radionecrosis of the larynx.

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以高壓氧治療喉部放射線性壞死 — 病例報告

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一位 81 歲早期喉癌男性曾經接受 60 格雷劑量的治療性放射線療法。放射線治療結束後 2 個月，病患主訴咽喉痛，口臭，呼吸困難與發燒。以直達式喉鏡發現聲門狹窄與廣泛性潰瘍壞死組織。經多處切片病理顯示凝固性壞死與上皮完全剝落，並無發現惡性細胞。由於考慮喉部放射性壞死，病患接受了共 40 次的高壓氧治療。臨床症狀逐漸改善，並且於接近高壓氧治療結束與結束後 6 個月再一次接受切片檢查。患者喉部完全癒合但有廣泛纖維化，但病理檢驗無惡性發現。早期喉癌在接受治癒性放射線治療後，放射線性壞死必須要與癌症復發做鑑別診斷。高壓氧對於喉部放射性壞死可做為一個有用的輔助性治療。

關鍵詞：放射線性壞死，高壓氧治療，喉癌，併發症

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