Hyperbaric oxygen as an adjunctive treatment for severe laryngeal necrosis: a report of nine consecutive cases

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Feldmeier JJ, Heimbach RD, Davolt DA, Brakora MJ. Hyperbaric oxygen as an adjunctive treatment for severe laryngeal necrosis: a report of nine consecutive cases. Undersea & Hyperbaric Med 1993; 20(4):329-335.—Laryngeal necrosis is a rare complication of therapeutic radiation, but when it does occur there is no established, definitive treatment and laryngectomy is frequently required. This report is a retrospective review of all patients referred for hyperbaric oxygen (HBO) therapy to a single hyperbaric medicine unit for treatment of their laryngeal necrosis between 1980 and 1985. Nine patients were in this series. One patient had had a vertical hemilaryngectomy and another a supraglottic laryngectomy before referral. Eight of the nine patients had a Chandler grade IV necrosis and the ninth had a Chandler grade III necrosis. All nine patients were able to maintain their voice until death or last follow up. Seven of the nine patients maintained good voice quality while two exhibited some hoarseness. All patients with tracheostomies were able to be decannulated, and all patients with fistulae had these closed. No untoward reactions to HBO occurred. Based on this review, HBO is recommended as a therapeutic option whenever laryngeal necrosis occurs and there is a chance to save the larynx.

chondroradiation necrosis, hyperbaric oxygen, laryngeal preservation

Radiation therapy is the treatment of choice for early stage laryngeal cancer where the goals of treatment are both cure and voice preservation (1-4) The larynx is often included incidentally in radiation portals for head and neck tumors involving other anatomic sites. Almost all patients experience some discomfort during and just after radiation therapy for head and neck cancers. In most cases, acute mucositis and laryngeal edema resolve within a few weeks after the completion of irradiation. After treatment, an occasional patient will have persistent laryngeal edema lasting as long as 6 mo. If no mucosal lesion is visible, it becomes a diagnostic dilemma to differentiate recurrent or persistent tumor vs. necrosis secondary to radiation (5). Both tumor and necrosis may cause pain, airway compromise, foul smelling breath, edema,
hoarseness, and exposed cartilage. Both usually occur within the first 2 yr after treatment (6, 7).

To differentiate between radiation necrosis and laryngeal tumor, deep biopsy may be required (8). Biopsy can itself worsen the necrosis and even promote fistula formation (9). The incidence of pure radiation necrosis of the larynx has been reported to occur at rates from less than 1 to 7% of cases (10–14). The higher levels of incidence are associated with larger radiation treatment portals, higher doses per radiation treatment fraction, and the failure to compensate for the variable thickness of the larynx when using lateral opposed portals. Neutron radiation therapy has also been associated with more frequent occurrences of necrosis (15). Deeply ulcerated cancers of the larynx or those that invade cartilage are more likely to develop necrosis when irradiated (16).

Initial treatment for presumed laryngeal necrosis is symptomatic. Recommendations include humidification of the inspired air along with antibiotics, steroids, and analgesics as necessary. Tracheostomy may be required if the airway is compromised. If response to these conservative measures is inadequate, laryngectomy often follows (5–9). Since the likelihood of an occult tumor with secondary necrosis is more likely than with radiation necrosis alone, many head and neck oncologists recommend laryngectomy when edema and other symptoms persist for more than 6 mo. after the completion of irradiation. Flood and Brightwell (17) reported a series of laryngectomies done under these circumstances, and tumor was found in five of seven laryngeal specimens obtained.

Chandler (17) has published a grading system for quantifying the severity of laryngeal radiation necrosis. This system is very useful for establishing guidelines of therapy and is summarized in Table 1. Grade I and II laryngeal necrosis patients generally respond favorably to conservative management, whereas grade III and IV patients are at significant risk of progressing to require laryngectomy.

The pathophysiology of laryngeal radiation necrosis is characterized by fibrosis, endarteritis, tissue ischemia, and hypoxia (18, 19). Hyperbaric oxygen therapy (HBO) has been demonstrated to induce neovascularization in irradiated tissues, especially in the case of mandibular radiation necrosis (20–22). HBO has had excellent success

<table>
<thead>
<tr>
<th>Grade</th>
<th>Symptoms</th>
<th>Signs</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>Slight hoarseness; slight mucosal dryness</td>
<td>Slight edema; telangectasia</td>
</tr>
<tr>
<td>II</td>
<td>Moderate hoarseness; moderate mucosal dryness</td>
<td>Slight impairment of cord motility; moderate edema and erythema</td>
</tr>
<tr>
<td>III</td>
<td>Severe hoarseness with dyspnea; moderate odynophagia and dysphagia</td>
<td>Severe impairment of cord motility or fixation of one vocal cord; marked edema; skin changes</td>
</tr>
<tr>
<td>IV</td>
<td>Respiratory distress; severe pain, severe odynophagia; weight loss; dehydration</td>
<td>Fistula; fetor oris; fixation of skin to larynx; laryngeal obstruction and edema occluding airway; fever</td>
</tr>
</tbody>
</table>
as an adjunct to surgery in resection and reconstruction of severely affected cases of mandibular radiation necrosis (23).

A previous report by Ferguson et al. (24) described eight cases of laryngeal necrosis treated with HBO. Four of these patients had Chandler’s grade III and the other four had Chandler’s grade IV laryngeal necrosis. All eight patients improved with HBO, although one of the grade IV patients ultimately required laryngectomy and a latissimus dorsi mycutaneous flap to close the resultant surgical defect.

MATERIALS AND METHODS

This report is a retrospective review of all patients referred for HBO and treated for laryngeal necrosis at the hyperbaric medicine facility at Southwest Methodist Hospital in San Antonio, Texas, between 1980 and 1985. The review was limited to this group of patients to ensure an adequate period of follow up. Also, the review was limited to those patients who had not had a total laryngectomy before referral. One patient had had a vertical hemilaryngectomy and another had had a supraglottic laryngectomy before HBO.

Nine patients met these criteria. Pertinent patient characteristics are delineated in Table 2. Eight of the nine patients were Chandler grade IV necrosis whereas the ninth patient was a Chandler’s grade III necrosis.

Hyperbaric oxygen was administered in a multiplace hyperbaric chamber compressed with air to a pressure of 2.4 atm abs. Patients breathed 100% oxygen through a hood or head tent which sealed around the neck. High flow rates through the supply side of the hood were maintained. Excess oxygen and exhaled CO₂ were allowed to exhaust outside the chamber to prevent CO₂ accumulation within the hood and to prevent oxygen buildup within the chamber itself. Inspired oxygen was humidified to prevent drying of respiratory mucosa and to reduce the risk of sparks due to static electricity. Oxygen levels within the chamber were monitored and regulated by flow rates of compressed air in and out of the chamber. For safety purposes, the chamber environment was controlled to keep oxygen levels at or below 25%.

Patients were accompanied by medical attendants during the HBO treatments. The treatment profile typically consisted of a 5- to 10-min compression phase. During the compression phase, compressed air was pumped into the chamber to raise pressure to 2.4 atm abs. This phase was followed by the treatment proper consisting of three 30-min, 100% oxygen periods separated by 10-min air breaks. Air breaks were interjected to prevent or minimize oxygen toxicity. The final phase of the HBO treatment was the decompression phase typically lasting from 10 to 15 min. During decompression, the compressed air was allowed to exhaust under its own force out of the chamber. Treatments were delivered to each patient once per day, 6 days/ wk.

RESULTS

None of the nine patients required a laryngectomy due to progression of their necrosis. The three patients who had had tracheostomies for airway compromise were able to have their tracheostomies decannulated, and they closed spontaneously. Two of the four patients with fistulae had these closed without surgery, and the other
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age at Referral</th>
<th>Sex</th>
<th>Original Tumor Site/Stage</th>
<th>Radiation Dose (X)</th>
<th>Time From Radiation to Necrosis</th>
<th>Presentation</th>
<th>Chandler Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>69</td>
<td>M</td>
<td>supraglottic larynx, stage unknown</td>
<td>4,500</td>
<td>3 mo.</td>
<td>necrosis with fistula</td>
<td>IV (fistula)</td>
</tr>
<tr>
<td>2</td>
<td>60</td>
<td>M</td>
<td>T1N0MO larynx</td>
<td>6,600</td>
<td>9 mo.</td>
<td>airway compromise; coughing up pieces of cartilage</td>
<td>IV (emergent tracheostomy)</td>
</tr>
<tr>
<td>3</td>
<td>60</td>
<td>M</td>
<td>T1N0MO larynx</td>
<td>6,500</td>
<td>2 yr</td>
<td>supraglottic laryngectomy prior to HBO; necrosis with fistula</td>
<td>IV (fistula)</td>
</tr>
<tr>
<td>4</td>
<td>56</td>
<td>M</td>
<td>T1N0MO supraglottic larynx</td>
<td>5,000</td>
<td>8 mo.</td>
<td>airway compromise with necrosis</td>
<td>IV (emergent tracheostomy)</td>
</tr>
<tr>
<td>5</td>
<td>82</td>
<td>M</td>
<td>T1N0MO larynx</td>
<td>6,600</td>
<td>3 mo.</td>
<td>airway compromise with necrosis</td>
<td>IV (fistostomy)</td>
</tr>
<tr>
<td>6</td>
<td>64</td>
<td>M</td>
<td>TXN2aMO unknown primary</td>
<td>6,300</td>
<td>18 mo.</td>
<td>extensive soft tissue necrosis neck and larynx with fistula</td>
<td>IV (fistula)</td>
</tr>
<tr>
<td>7</td>
<td>65</td>
<td>M</td>
<td>T1N0MO larynx</td>
<td>7,000</td>
<td>7 mo.</td>
<td>necrosis with severe pain</td>
<td>IV (severe pain)</td>
</tr>
<tr>
<td>8</td>
<td>71</td>
<td>M</td>
<td>T1N0MO</td>
<td>6,600</td>
<td>5 mo.</td>
<td>persistent cough, necrosis with fistula</td>
<td>IV (fistula)</td>
</tr>
<tr>
<td>9</td>
<td>56</td>
<td>M</td>
<td>T2N2aMO</td>
<td>6,800</td>
<td>7 mo.</td>
<td>moderate pain, hoarseness and odynophagia; hemilaryngectomy prior to HBO</td>
<td>III (pain)</td>
</tr>
</tbody>
</table>
HBO FOR SEVERE LARYNGEAL NECROSIS

Two had surgery (perichondrial repair in one and myocutaneous flap in the other) to close their fistulae. All patients had functional voices until death or last follow up. After treatment, seven of the nine had voice quality which would be characterized as good, and the two remaining patients had slight hoarseness. One of these patients with hoarseness is the one who had the hemilaryngectomy before HBO.

Five of the nine patients are alive and well. Four of the patients have died. Two of these died due to complications of second malignancies (colon and lung). Two died of causes not directly related to their malignancy or laryngeal necrosis. One of these died secondary to ethanol abuse, and the other had a respiratory arrest. One of the survivors has been successfully treated with surgery for a neck recurrence 1 yr post-HBO and for a base of tongue malignancy 5 yr post-HBO. This same patient had curative irradiation for a lung tumor 2 yr post-HBO. Table 3 shows individual summaries of therapeutic outcome. None of the patients had any lasting complications due to HBO, although several experienced a temporary change in visual acuity with a tendency toward myopia.

DISCUSSION

Laryngeal necrosis is a very rare complication of therapeutic radiation. When radiation is well designed and delivered, necrosis results in 1% or less of patients.

Table 3: Details and Results of Treatment

<table>
<thead>
<tr>
<th>Patient*</th>
<th>Number of HBO Treatments</th>
<th>Results and Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>28</td>
<td>Had resolution of fistula without surgery; talked with good quality voice until death due to lung cancer 4 yr posttreatment</td>
</tr>
<tr>
<td>2</td>
<td>45</td>
<td>Alive and well with 10-yr follow up; good voice quality</td>
</tr>
<tr>
<td>3</td>
<td>15</td>
<td>Fistula closed without surgery; died secondary to ethanol abuse 4 yr post-HBO; voice quality good until death</td>
</tr>
<tr>
<td>4</td>
<td>29</td>
<td>Rapid resolution of airway compromise. Died 3 yr post-HBO due to colon cancer; voice quality good until death</td>
</tr>
<tr>
<td>5</td>
<td>27</td>
<td>Alive and well 8 yr post-HBO; voice quality good</td>
</tr>
<tr>
<td>6</td>
<td>34</td>
<td>Died of respiratory arrest 2 yr post-HBO; had base of tongue and neck recurrence but controlled with surgery; good voice quality until death; fistula closed with flap</td>
</tr>
<tr>
<td>7</td>
<td>28</td>
<td>Voice quality slightly hoarse; alive and well 7 yr post-treatment; required neck dissection for salvage 1 yr after HBO; also had successful surgical resection of BOT primary and successful radiation for lung primary</td>
</tr>
<tr>
<td>8</td>
<td>8</td>
<td>Had surgical perichondrial repair; fistula closed; alive and well with slight hoarseness 7 yr post-HBO (hemilaryngectomy before HBO)</td>
</tr>
<tr>
<td>9</td>
<td>41</td>
<td>Alive and well 6 yr post-treatment; resolution of pain and odynophagia; voice quality good</td>
</tr>
</tbody>
</table>

*Patient order is the same as Table 2.
However, the loss of a larynx due to a complication of treatment is no less devastating than a loss due to radical resection for malignancy.

All patients in our study were able to maintain their larynx, and voice quality was good except in the two who demonstrated slight hoarseness.

Three of the nine patients developed recurrent or second primary tumors. One of these patients is alive and well after curative resection of neck and base of tongue recurrences and after curative irradiation for a lung primary. This incidence of subsequent or recurrent malignancies is not unexpected. Approximately 25% of patients cured of head and neck primary malignancies are expected to demonstrate subsequent second primary malignancies (25). In some series the incidence of second primary tumors has been as high as 40% (26).

Chondroradiation necrosis of the larynx, like osteoradionecrosis, is considered a late effect of radiation therapy. As a late effect, there is typically a latent period between radiation and the onset of the necrosis. The onset of mandibular osteoradionecrosis is rare earlier than 6 mo. after radiation, and the primary time of occurrence is from 6 to 18 mo. after radiation (27).

In this group of patients, the onset of laryngeal radiation necrosis was considerably earlier than the previously reported onset of mandibular osteonecrosis. Three patients had onset of necrosis at or before 5 mo. after irradiation. Seven of these nine patients had onset of chondronecrosis at or before 9 mo. after radiation therapy.

Seven of the nine patients had doses of irradiation varying from 6,300 to 7,000 cGy. These are fairly typical curative doses for primary laryngeal cancers or cancers of other anatomic locations of the head and neck. However, one patient developed laryngeal necrosis at a dose of 4,500 cGy and another at 5,000 cGy. Both of these doses are considerably lower than the updated TD 5/5 for laryngeal cartilage (tolerance dose at a 5% incidence of complications within 5 yr) reported by Emami et al. (28).

The patient who had only 4,500 cGy had significant arteriosclerotic disease evidenced by a myocardial infarction 4 yr before HBO, with resultant cardiac aneurysm and supraventricular arrhythmias. Arteriosclerotic changes due to diabetes or manifested by hypertension have been reported previously as risk factors for laryngeal necrosis (19).

None of the patients demonstrated any permanent untoward reactions to the HBO therapy. Based on this review of nine patients with high Chandler's grade radiation necrosis of the larynx and the previous report by Ferguson et al. (24), HBO therapy is recommended as a component of aggressive intervention in cases of severe laryngeal necrosis to prevent laryngectomy and maintain voice quality.

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REFERENCES

HBO FOR SEVERE LARYNGEAL NECROSIS


