

Laryngeal Cartilage Necrosis after Laser surgery and Radiotherapy

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Abstract

Introduction

Advanced techniques of radiotherapy have decreased the late complication rate to < 1% at the larynx. Cartilage necrosis is one of rare toxicities associated with radiotherapy.

Case presentation

We present the case of post-irradiation thyroid cartilage necrosis in an adult patient with glottic cancer. The radiotherapy was performed 3 weeks after primary surgery using CO₂ laser (hemi-laryngectomy, neck dissection). The cancer region and bilateral lymph nodes were exposed to a daily fraction of 1.8 Gy up to a total dose of 59.4 Gy in IMRT technique. 5.5 months after radiotherapy the patient suffered from serious dyspnoea and dysphonia. Laryngeal edema and an unknown mass in the anterior larynx commissure were seen during the ENT examination. During the direct endoscopy a “foreign body” was removed and edematous tissue was visualized in the surrounding region. Histological examination showed necrotical cartilage without evidence of cancer recurrence. After postoperative anti-edematous, mycolytic and antibiotic therapy the patient was discharged free of complaints.

Conclusion

This case report details the clinical difficulties in determining the differences between laryngeal chondronecrosis, laryngeal foreign body and cancer recurrence and emphasizes the importance of this late radiotherapy toxicity for the management of emergencies in ENT practice

Keywords: Laryngeal necrosis; Laser surgery; Radiotherapy

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Introduction

Late toxicities of radiotherapy are defined as symptoms which occur three months or later after the end of irradiation. Well known laryngeal problems secondary to radiotherapy include secondary interstitial edema of the soft tissue, inflammation of the perichondrial tissue, atrophy or fibrosis of the skin, as well

as a fibrosis of the mucosa or soft tissue [1-3]. Typically, the laryngeal region will be included in the irradiation fields of patients with cancer of the larynx, hypopharynx or upper esophagus. We know some predisposing factors for higher rates of late complications, such as combined treatment modalities, higher irradiation doses >60 Gy, local infections, pre-existing cartilage infiltration by the tumor or a poor patient immune system [4-5]. In 1979 [6] described approximately 12% serious reactions after radiotherapy of the larynx. Cartilage necrosis was included [6]. 15 years later [1] observed decreased complication rates nearly 1%. They stressed new radio-techniques as the base for this positive development. Another development of this period is the launching of new multimodal therapy approaches, which has improved the rates of organ preservatio as well as new forms of acute and late toxicities.

One of the most serious late complication of laryngeal radiotherapy include laryngeal cartilage necrosis post treatment. Mostly it develops within the first year after cancer treatment [2]. There are also reports about very late cartilage necrosis 25 and 44 years after radiotherapy [2, 4]. In 1979 Chandler developed a classification of laryngeal irradiation reactions (4 stages), which has been widely accepted until now (Table 1) [6]. The used symptoms of irradiation reactions are not specific and can be similar to those of cancer recurrence or acute viral or bacterial infection of the region. Some of the symptoms need emergency therapy [7, 8]. Subjective dyspnoea remains the leading point and is the land mark for any clinical decision.

Table 1.Chandler's classification for irradiation reaction in the larynx [6]

Grade	Symptoms	Sign	Treatment
0	None	None	None
I	slight hoarseness, slight dryness	slight edema, teleangiectasis	none
II	moderate hoarseness, moderate dryness	impairment of vocal cord mobility, moderate edema and erythema	none
III	severe hoarseness, dyspnea, moderate odynophagia, and dysphagia	fixation of vocal cord, marked edema and skin changes	steam, antibiotics
IV	respiratory distress, severe pain, weight loss, dehydration, fever	fistula, fetor oris, fixation of skin to larynx, airway obstruction	tracheostomy and/or laryngectomy

In this article we present the case of laryngeal cartilage necrosis following combination treatment with laser surgery and irradiation therapy of glottic squamous cell carcinoma. It demonstrates the clinical difficulties and the relevance of this complication for the management of emergency cases in ENT practice.

Case history

In November 2011 a 73-year-male patient was treated for pT3 pN0 (0/3) cM0 R0 GI squamous cell carcinoma of the right glottis. The surgical treatment consist a laser-assisted hemi-laryngectomy and functional neck dissection (level II and III) of the right lymph node region. We used a CO2 laser in CW mode (10 W/m²). The right false cords as well as the vocal cord were resected. The arytenoid cartilage remained in the larynx. The adjunctive Intensity-Modulated Irradiation Therapy (IMRT,

RapidArc / COMART) was performed 3 weeks after surgery. It had included the total dose of 50.4 Gy in daily fractions of 1.8 Gy, which were applied 5 times per week to the cancer region and bilateral neck lymph nodes (level II-IV). Additionally, the irradiation boost was administered for former glottic cancer region with daily fractions of 1.8 Gy until a total dose of 59.4 Gy. The radiotherapy regimen was well tolerated, and had caused grade 1 xerostomia as well as mucositis (RTOG Toxicity Criteria) during the treatment. Both side effects regressed quickly after the end of the therapy.

Follow-up staging investigations, e.g. ultrasound, nasopharyngeal endoscopy and CT scans of thorax and neck have not shown any signs of local recurrence of the cancer. The patient was controlled by flexible nasopharyngeal endoscopy at our out-door department every four weeks.

After 5.5 months the patient entered the emergency department of our hospital because of serious stridor with dyspnoea and dysphonia, which had started in a time window of 48 hours. The primary endoscopy revealed edema of the supraglottic region and unknown masses in anterior commissure of the larynx. The patient was stable enough that tracheostomy was not required and signs of dyspnea could be managed by medical management. We had started drug administration including dexamethason 48mg IV, sodium selenite 1.000 µg IV and inhalative epinephrine immediately. No improvement of dyspnea was seen after 48 hours. Because of the lack of improvement the decision was made to perform direct endoscopy under general anesthesia to determine the cause for ongoing problems and to remove and investigate the laryngeal masses. The retraction of hard masses by grasping forceps led us to the clinical diagnosis of a possible nutritional foreign body (bone or cartilage?) in the upper airways. Furthermore we have resected the surrounding edematous tissue from the ary-cartilage as well as from the anterior part of supraglottic region in order to secure free breathing for the patient and to get an overview about the interesting area of the anterior laryngeal commissure. Figure 1 is showing the primary endoscopic picture before the retraction of “foreign body”, including the obstruction of the

glottis Figure 2 demonstrates the enlarged airway following removal of the necrotic cartilage at the end of the endoscopic procedures. Both views are from the endoscope that is placed at the beginning introitus of the larynx.

Figure: 1

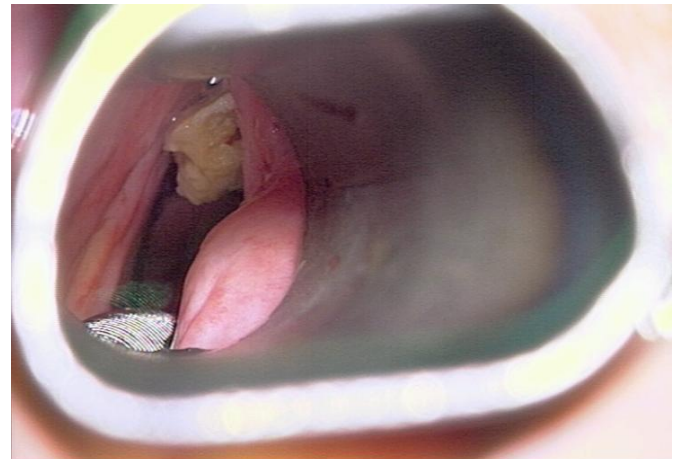


Figure 1 Pre-operative situation of the larynx

Figure: 2

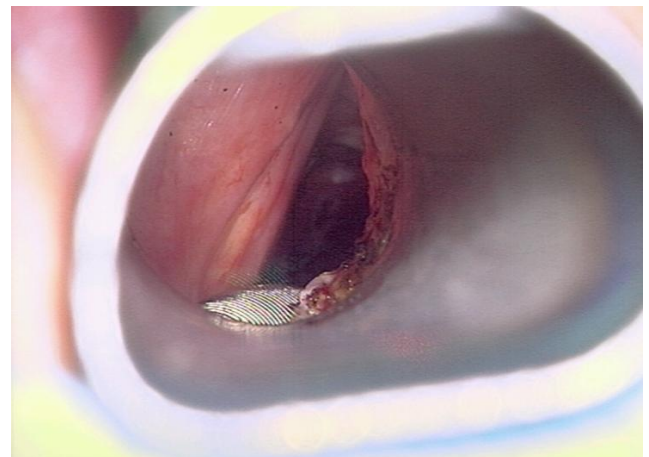


Figure 2 Post-operative situation of the larynx

The removed material was submitted for histopathology. The histopathologic diagnosis was necrotic cartilage without evidence of active neoplasia (Figure 3)

Figure: 3

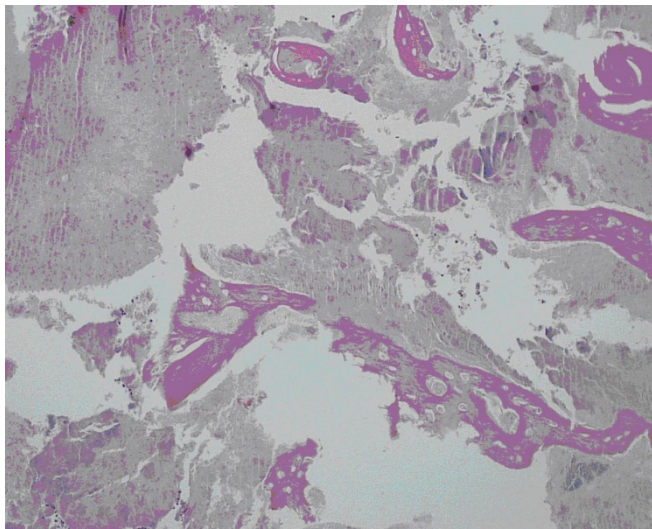


Figure 3 Histological finding of removed material (HE)

The medical treatment (cortisone, selenium) was continued 48 hours after surgery. The patient was discharged free of dyspnea and stridor 5 days after endoscopic procedures. The last tumor control was performed in June 2014. The laryngeal airways were open and free breathing was possible. No dyspnea and dysphonia were observed.

Discussion

The technique and schedule of radiotherapy is mainly responsible for the majority of late toxicities which we will see in surviving head and neck cancer patients [17]. There was the hope that modern radiotherapy techniques (3d planning, intensity modulating radiotherapy) and improved schedules would be able to be similar effective regarding the cancer but less aggressive for surrounding tissues [7]. The rate of serious complications has decreased dramatically as we described above. This case demonstrates the development of a rare laryngeal complication despite modern surgery, modern radiotherapy and established schedule of combination.

Today we know that late complication rate of radiotherapy depends on the irradiation dose. The common total dose of 60-70 Gy is described as the maximum tolerated with conventional fractionation to get the low rates and levels of side effects [9,

10]. Nothing is known about the relation between Intensity Modulating Radio Therapy (IMRT) and the late toxicities in the laryngeal area. This modern technique was introduced to head and neck irradiation between 1995 and 2000 [18], and we are earning the first late complications now days. Our patient received 59.4 Gy in IMRT technique. Normally we await laryngeal edema of the interstitial tissue during the first year. A necrosis of cartilage is unusual at this dose, but the time of occurrence is typical. But our patient has had a further critical point in his history. We have performed CO₂ laser surgery which is producing additional thermal tissue damage.

Probably we have observed a combined late toxicity following the combination of thermal tissue reaction during the laser surgery and the adjunctive irradiation. This is the only way to explain the lower total irradiation doses which were necessary to produce the seen necrosis. Of course, the clinical picture was complex, and edema and cartilage necrosis had developed simultaneously.

It was observed previously that other combined therapy modality such as chemo-radiotherapy or the combination between surgery and following irradiation increases the complication rate, including chondronecrosis [7]. Many pathological studies showed particular changes of laryngeal cartilage during and after radiotherapy such as obstruction of lymphatic channels, increased vascular permeability, degeneration of perichondrium [11-13]. Those reactions decrease the cartilage resistance potential to factors, which endanger the integrity of the cartilage such as tumor invasion, infection, and surgical intervention. In our case, the combination of organ-preserving surgery and small field irradiation therapy could have reasonable contributions to necrosis of laryngeal cartilage [7, 9].

According to previous data, radiotherapy causes most frequently necrosis of the arytenoid cartilage [14]. The damage of thyroid cartilage in our case could be explained by the particular overlapping location of surgical intervention and the additional

irradiation dose to the tumor region that was focused on the anterior commissure.

Symptoms of radiotherapy complications such as dysphonia, dyspnoea, hoarseness, pain are not specific and need differential diagnostic, in first line because of tumor recurrence possibility [4, 5, 15]. In our case, it was difficult to distinguish clinically between cancer recurrence, foreign body and necrosis during the first endoscopy. Of course it may be criticized that the primary physician has not performed a CT scan of the larynx. Lastly, the examination of larynx in general anesthesia and histological examination were necessary to obtain material and to remove the obstructing masses from upper airway. Only histologist was able to confirm the tumor free situation and to declare necrosis as reason for the clinical picture. It is extremely important to distinguish the different diagnoses because of the possible masking of the recurrent tumor under inflammatory reactions, edema or necrosis [14].

The idea of foreign body was denied by the patient during the anamnesis but could not be excluded because of the serious post-irradiation edema of the larynx that could have consequences for swallowing and/or aspiration. This secondary edema is often seen and endoscopy is limiting the endoscopic and clinical control. In accordance with the previous observations, the treatment of laryngeal chondronecrosis needs a combined therapy including usually antibiotics, steroid and surgical procedures [1, 7]. There was also a report about positive experience with hyperbaric oxygen therapy [16]. Literature emphasizes surgical procedures as tracheostomy, laryngectomy or the submucosal resection of destroyed cartilage [5]. We have chosen a combined endosurgical performance, because it offers both, the best cosmetic result and immediately free airways for the patient. So we were able to avoid more aggressive surgical and intensive care management. Frequently controls are necessary to observe the longtime effects of our therapy, and the patient has to be very compliant for this way of treatment.

Is there any way to prevent the development of such cartilage necrosis? Probably the surgeon should administer antibiotics during and after the laser surgical resection. It is also possible to prolong the time between tumor resection, wound healing and the start of irradiation. This time window is limited by a possible repopulation of tumor cells. At our department, we have introduced a regular peri-operative antibiotic prophylaxis if cartilage is involved in the tumor resection.

Conclusion

Our case report shows the difficulties in distinguishing between laryngeal cartilage necrosis, foreign body and cancer recurrence. Although modern surgical and radiological techniques should decrease acute and late complications, multimodal treatment schedules produce specific new forms of toxicity, for example laryngeal chondronecrosis as the consequence of laser surgery plus irradiation.

Learning points

1. The necrosis of laryngeal cartilage is a rare late complication of combined treatment modalities. It is caused by radiotherapy as well as laser surgery. This complication has importance for the daily work of ENT clinicians because it occurs as potential emergency situation (aspiration).
2. It is important to exclude a recurrent or residual tumor after radiotherapy.
3. Cartilage damage has to be treated by a complex surgical and medical strategy in the hand of experienced oncologists.

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