

Rare Case of Cystic Adenoid Carcinoma of the Larynx Treated by Post-Operative Radiation Therapy

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Abstract

Adenoid cystic carcinoma (C.A.K.) is a malignant tumor most commonly developing in the main or accessory salivary glands. The most frequent sites of C.A.K are located in the salivary glands of the oral cavity, in particular in the hard palate and with less frequency in the nasal cavity, paranasal sinuses and pharynx. The laryngeal localization of C.A.K is extremely rare. The cervical scanner is the imaging of choice for the early diagnosis of CAK of the larynx. Diagnosis is made by pathology examination of the biopsy specimen supplemented by immunohistochemistry. We report the case of a 26-years-old patient, who presented for 18 months, progressive dysphagia to solids, and then laryngeal dyspnea requiring emergency tracheotomy. Surgery followed by postoperative radiotherapy was used for treatment.

Keywords: Cystic Adenoid carcinoma; Larynx; Radiation therapy

Introduction

Adenoid cystic carcinoma (ACC) is a malignant tumor most commonly developing in the major or accessory salivary glands, with a frequency of 10%-20%, accounting for only 2%-4% of all malignant tumors of the head and neck [1,2].

The most frequent sites of ACC are in the salivary glands of the oral cavity, particularly in the hard palate, and with less frequency in the nasal cavity, paranasal sinuses, pharynx, and larynx [3].

Laryngeal localization of ACC is extremely rare (<1% of all cancers

of the larynx) [4]. Its diagnosis is generally made at an advanced stage due to its propagation in the submucosa; its optimal treatment consists of surgery combined with postoperative radiotherapy if indicated.

Case Observation

Twenty-six years old male, presents in his past medical history, a tobacco consumption of half pack/year for 07 years, weaned; there is no alcohol consumption.

He has presented for 18 months, progressive dysphagia to solids. Laryngeal dyspnea suddenly set in, leading to emergency tracheostomy and worsening.

His physical otorhino-laryngological examination revealed a tumor of the larynx without cervical lymphadenopathy.

Direct laryngoscopy showed a tumor process of the left piriform sinus which invades the aryepiglottic fold and the left arytenoids; overflowing on the anterior commissure.

The initial cervical CT revealed a tumor process involving the 3 floors of the larynx with lysis of the cricoid cartilage and arytenoid cartilages (**Figure 1**).

A tumor biopsy was performed. The immunohistochemistry tests found anti AE1/AE3 antibodies positive (+); positive anti CK7 antibody (+); Anti P63 antibody negative (-), anti Ck17 antibody positive (+); anti AML positive (+) antibodies. Thus, the morphological appearance and the immune-histochemical profile of the biopsy specimen are in favor of the diagnosis of adenoid cystic carcinoma of the larynx.

Given the diagnosis and the loco-regional involvement of the tumor, surgery by total laryngectomy and bilateral functional lymph node dissection was chosen for this patient.

Histological analysis of the operative specimen confirms the diagnosis of ACC with a massive 35% contingent, infiltrating all areas above the glottis, glottis, and subglottis, of which 4.5 cm in the subglottis comes into contact with the anterior commissure. There is a presence of numerous perinervous sheaths as well as an intratracheal tumor nodule. The limits of the right lateral excision are 5 mm; left lateral to 2 mm; the left and right posterior limits less than 1 mm; the closest tracheal border is on the right, located less than 2 mm from the tumor.

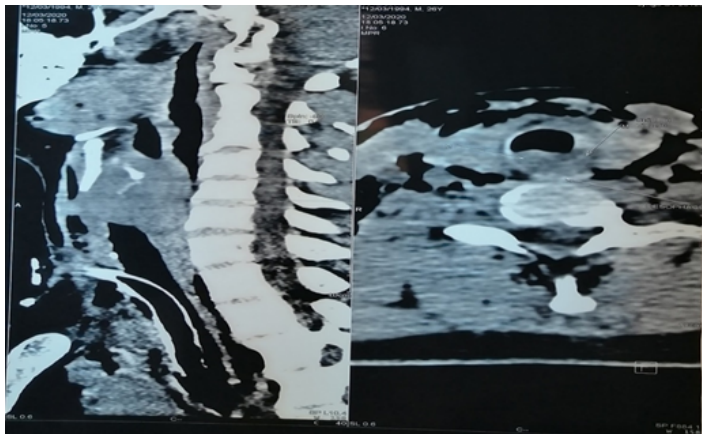


Figure 1 tumor process of the 3 stages with effacement of the vocal cords arriving in intimate contact with the esophagus.

The right cervical lymph node exploration found in 22 lymph nodes examined, lymph node metastasis from the IV area with capsular rupture and the presence of a tumor focus of 1 mm; while the left cervical lymph node exploration found lymph node metastasis in area II with capsular rupture in 24 lymph nodes examined.

According to our results, adjuvant radiotherapy on the operating bed and lymph node areas was decided in this patient. We proceeded to treatment by volumetric arc therapy.

The data was acquired using a dedicated scanner with 3 mm sections, extending widely over the base of the skull at the top and reaching the hull at the bottom using a 5-point thermoformed mask fixing the head, neck, and shoulders:

The data was transferred to data processing software (TPS). The target volumes were defined while respecting 3 dose levels: High risk; intermediate-risk and low risk (**Figure 2**).

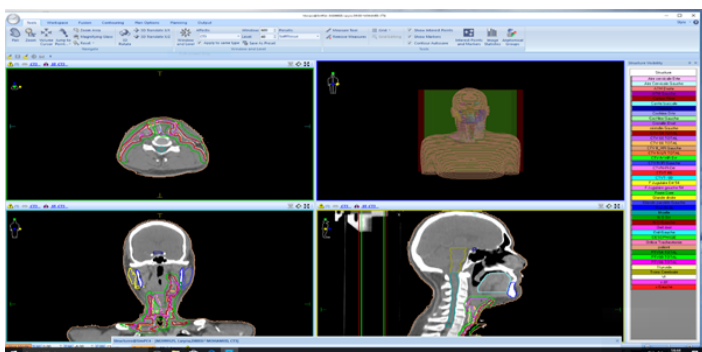


Figure 2 Delineation of target volumes

The planning target volume at high risk (PTV1) covered the following volumes: the tumor bed, cervical lymph node areas with microscopic tumor involvement (IV on the right and II on the left); the whole increased by a margin of 5 mm.

The estimated planning target volume at intermediate risk (PTV2), covered in addition to (PTV1), the tracheostomy opening, area VI, the cervical lymph node areas above and underlying the areas with microscopic involvement: either the left IB and III areas, adjacent to the left area II; as well as areas III and V a, b on the right, adjacent to area IV on the right; the whole increased by a margin of 5 mm.

Finally, the planning target volume at low risk (PTV3) which covered in addition to PTV 2, the rest of the drainage areas of the larynx, areas IVa on the left and II on the right as well as the path of the X nerve bilaterally up to at the base of the skull; the whole increased by a margin of 5 mm.

We performed a placement under the treatment device consisting of a linear accelerator with arc therapy radiotherapy (VMAT) technique (**Figure 3**).

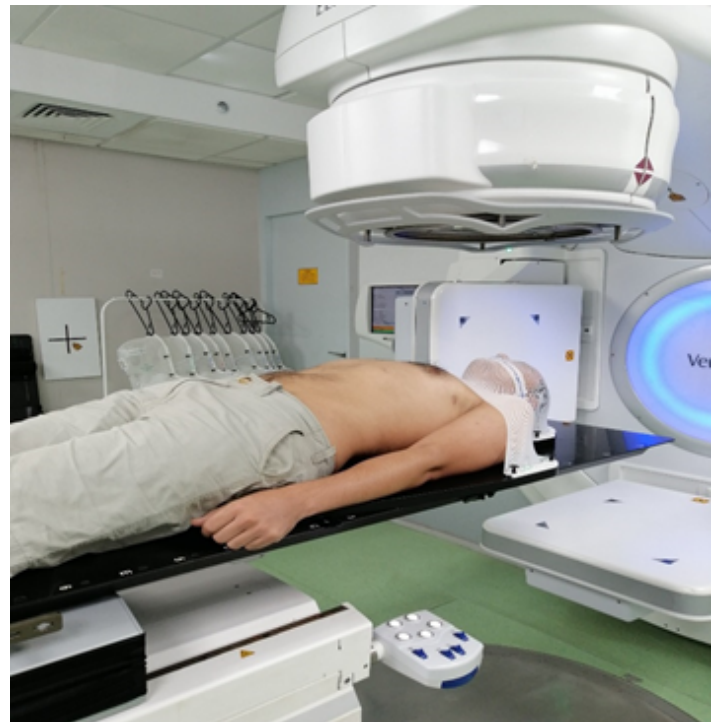


Figure 3 Placement under the treatment device

Thus, the treatment was administered on PTV1 at a total dose of 66 Gy in 2 Gy/daily fraction; on PTV2 at a total dose of 60 Gy in 02 Gy/daily fraction and PTV3 at a total dose of 50 Gy in 02 Gy/daily fraction. The overall treatment time of radiation therapy was 55 days.

We did not administer concomitant chemotherapy. With 06-month follow-up, we did not notice any side effects of grade 3 or grade 4 toxicities. However, we had a grade 2 radiation mucositis requiring symptomatic treatment.

Discussion

ACC is a malignant tumor of the exocrine glands. As such, it can involve locations as varied as the skin, esophagus, and uterine cervix, main or accessory salivary glands [5]. In contrast, ACC of the larynx is very rare <1%, due to the scarcity of accessory salivary glands in the larynx [6]. Indeed, there is a very low density of accessory salivary glands in the larynx (23-47 glands/cm²) compared to the oral cavity for example (600-1000 glands/cm²) [4]. ACCs of the larynx occurs on average by the age of fifty [7,8].

The main site of predilection of the laryngeal CAK is the subglottic region (58.2%), followed by the supraglottic region (32.1%), and the glottic region (9.7%) [9]. The symptoms of ACC of the larynx are closely related to the anatomical location of the tumor. Indeed, dyspnea is often associated with subglottic ACCs, dysphagia with supraglottic ACCs, and dysphonia with glottic ACCs. In our case, the location of the ACC concerned the 03 floors of the larynx. However, some patients with ACC may be asymptomatic and present to the hospital at an advanced stage [10,11]. Indeed, it is a very slowly proliferating cancer, which occurs on a normal laryngeal mucosa [10]. ACCs of the larynx are distinguished from other histological types of laryngeal tumors by 04 main characteristics: A high risk of damage, neurologic, [12] invasive local growth in nerves, bones, muscles, lymphatic and blood vessels, a high rate of recurrence and a lower rate of cervical lymph node metastasis [13,14].

The cervical CT scan is the imaging of choice for the early diagnosis of ACC of the larynx [15]. It can visualize the local and lymph node extension of the tumor. It is preferable to MRI, which has a longer image acquisition time and causes movement artifacts [16]. We used a cervical CT in our case.

ACC appears macroscopically as a poorly demarcated tumor, the encapsulation of which is imperfect [17]. It is also common to observe from the first excision an invasion of the nerve sheaths [5]. Histologically, ACC is a basal cell-type malignant tumor that is composed of epithelial and myoepithelial cells. The histopathological classification of this carcinoma can be divided into 3 types: tubular, cribriform, and solid. The most common type is the solid type with poor prognosis [18,19,20], cribriform, which is the most common, and tubular form, which has the best prognosis [3]. Histological analysis of the biopsy specimen is essential for the diagnosis of ACC as the symptoms do not differ greatly from squamous cell carcinoma [3]. It must be supplemented by the immune-histo-chemical study which makes it possible to make the differential diagnosis between ACC and other tumors of the same type. Indeed, ACC exhibits morphological features similar to tumors such as basal cell adenocarcinoma, basaloid squamous cell carcinoma, undifferentiated nasal sinus carcinoma, and central neurocytoma [21].

Treatment of ACC should take into account the location of the tumor, the stage at diagnosis, and the histologic grade [22]. The

initial standard of treatment for potentially resectable ACCs consists of tumor surgery associated with lymph node dissection to ensure healthy margins [18]. However, this goal is difficult to achieve because ACC has a high propensity to infiltrate adjacent tissues, especially by perineural invasion [18]. Many authors recommend the combination of radiotherapy with surgery in the treatment of ACCs because it gives better results in terms of overall survival than surgery alone or radiotherapy alone [14,18]. Also, this combination surgery radiotherapy gives good results in terms of local control and survival without recurrence. Indeed, Avery et al. Reported a retrospective study of 15 cases of ACC of the head and neck, treated by surgery and followed by radiotherapy. The recurrence-free survival rate was 100% at 5 years and 86% at 10 years. There was no loco-regional recurrence [23]. This result has been confirmed in numerous studies conducted at MD Anderson Cancer where excellent loco-regional control has been observed thanks to the addition of postoperative radiotherapy to surgery [24,25].

The volume of radiotherapy should include the original tumor bed as well as the regional lymph nodes only if they are affected or considered to be at high risk of invasion [26,25]. The recommended radiation dose for patients with ACC of the larynx is 60-66 Gy in standard fractionation of 2 Gy. [27,28]. Salgado et al [28] reported a retrospective study of 98 cases of ACC of the head and neck, treated with surgery followed by radiotherapy. The median radiation dose was 63 Gy (60-70 Gy). The 5-year local control rate was 87.9% and the 5-year loco-regional control rate was 83%. There were no grade 4 or 5 toxicities; only 20% of acute grade 3 toxicity and 6% of late grade 3 toxicities. If there is a risk of involvement of a branch of a nerve at the base of the skull in the ACC, the path of this nerve should be included in treatment [16]. In our case, the path of the X nerve was included bilaterally.

The radiotherapy technique for accessory salivary gland carcinomas of a given location is comparable to that of squamous cell carcinoma of the same location [16]. In the event of perineural invasion, IMRT can reduce the target volume to irradiation compared to conventional techniques by bilateral opposing fields [16]. We used volumetric arc therapy radiotherapy for our patient. Chemotherapy (alone or concomitantly with radiotherapy) has no place in the treatment of ACC of the locally advanced larynx because not only of its limited effectiveness; but also systemic effects and toxicities associated with its use [29,30]. In our case, the treatment was done by surgery followed by postoperative radiotherapy. There was no use of concomitant chemotherapy (Figure 4).

ACC of the larynx can progress to early hematogenous or neurologic metastatic spread [12,13,29,30]. This tumor can also progress to the occurrence of late metastases after several years of treatment of the primary tumor [31]. In our case, the 06-month follow-up did not view any loco-regional recurrence or distant metastasis.

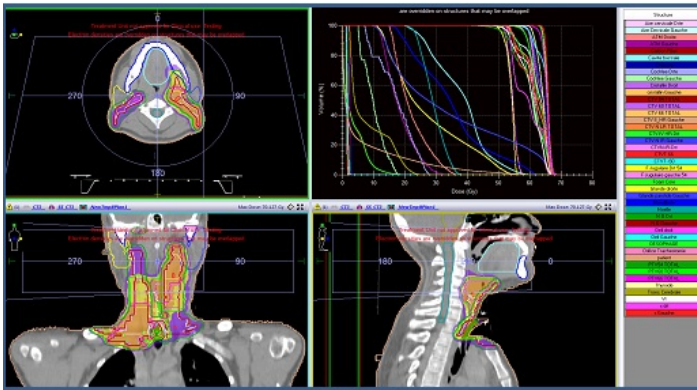


Figure 4 Dosimetry parameters of radiotherapy by arc therapy

Conclusion

ACCs of the larynx are rare. Surgery is the cornerstone of treatment. However, postoperative radiotherapy retains an important place in the adjuvant treatment of locally advanced non-metastatic ACCs to obtain good local and loco-regional control.

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