

Adenoid Cystic Carcinoma (ACC) of the Tracheo-Bronchial Tree Treated with Laser Therapy and Irradiation: Report of Two Cases

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Abstract: Adenoid cystic carcinoma (ACC) of the tracheo-bronchial tree is an uncommon tumor. ACC is generally diagnosed as a lesion involving the trachea; endobronchial involvement is extremely rare.

At present, surgical resection and reconstruction followed or not by post-operative irradiation is considered as the therapy of choice for definitive cure. Endoscopic treatment of these tumors is uncommonly reported in the literature.

We report two cases of ACC of the tracheo-bronchial tree successfully treated by laser and post-operative irradiation.

Keywords: Adenoid cystic carcinoma, Tracheo-bronchial tree, Radiotherapy, Nd-YAG-laser.

INTRODUCTION

Unusual tracheo-bronchial tumors represent 4% to 6% of all lung tumors (benign and malignant) [1]. Adenoid cystic carcinoma (ACC) accounts for less than 0.2% of all lung tumors [2]. Patients suffering from ACC and mucoepidermoid carcinoma have a better prognosis than those with other histological subtypes [3].

ACC is a malignant neoplasm originating in the salivary glands, most commonly in those of the head and neck area [4]. Primary ACC diagnosed in the trachea or in the bronchial tree, likely originating from submucosal seromucinous glands, is very uncommon [5].

ACC developing in the lung is regarded as a slow growing, low-grade malignancy. It is diagnosed in patients younger than those with squamous cell carcinoma, the most common lung cancer, and is usually not associated with a smoking history. The natural history and response to therapy differ from that of other malignant tracheo-bronchial tumors. In spite of the relatively benign evolution, this disease has a high risk of incomplete resection because its extension is commonly beyond the visible gross tumor. Even though unresected cases can be controlled successfully for many years, ACC is considered relatively resistant to treatment, and can metastasize late in the course of disease [6].

Surgical resection is considered the treatment of choice, followed by adjuvant irradiation in cases of incomplete resection. Laser therapy is an endoluminal treatment proposed for patients suffering from malignant airway obstruction: with a bronchoscopic procedure it can re-establish airway patency and eradicate macroscopic lesions but its use has been rarely reported for ACC.

The purpose of the present report is to discuss our experience in the conservative management of two cases of ACC of the tracheo-bronchial tree treated with laser and post-operative irradiation.

CASE REPORTS

Case 1

A nonsmoker 31-year-old male was referred to the Pneumology Department of our Hospital. He had a past history of asthma at young age with recurrent crises during the last 5 years. In the last 2 years, dry cough and slowly increasing obstructive symptoms (nonproductive cough, wheezing, and shortness of breath) were reported.

Owing to the lack of specific symptoms of tracheal disease, these signs had been initially attributed to other factors with a consequent delayed diagnosis after their onset.

Bronchoscopic examination revealed a polypoid mass 3 cm in diameter located in the middle of the trachea, starting 3 cm below the vocal cords and resulting in a marked obstruction of the lumen. A biopsy was performed with a diagnosis of ACC. The MRI of the thorax revealed an endotracheal, exophytic mass of 2.5 cm located in the middle of the trachea without hilar or mediastinal pathologic lymph nodes.

The patient refused invasive radical surgery. Primary management included the macroscopical total removal of the obstructing tumor with Neodymium-Yttrium-Aluminium Garnett (Nd-YAG) laser. Photoresection *via* rigid bronchoscopy under local anaesthesia was performed requiring the placement of a silicone prosthesis.

Laser treatment restored the lumen to normal caliber and a total body CT scan performed after the ablation resulted negative for macroscopic residual lesions, regional and/or distant metastases.

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Irradiation of the treated site with the photon beams of a 6 MV linear accelerator was started two months later. The clinical target volume (CTV) was considered the site of the resected tumors with a margin of 2.5 cms and the planning target volume (PTV) was obtained adding a further 0.5 cm margin. A total dose of 60 Gy in 30 daily fractions (2 Gy per fraction, five fractions a week) was delivered using four oblique wedged fields. The dose was delivered as specified according to the ICRU 50 report. Radiotherapy (XRT) was well tolerated with mild acute side effects (grade 2, following the RTOG-EORTC recommendations [7]) cough and dysphagia. The silicone prosthesis was later removed without problems. The patient remains well, without evidence of recurrence, 63 months after the treatment.

Case 2

A 47 year-old female, smoker up to 31 years of age, with a past history of recurrent rhinitis, suffered of slowly progressive cough (only recently effective), dyspnoea on exertion, hoarseness, and chest pain in the last six months. Primary treatment with corticosteroids and bronchodilators had obtained only a minor clinical relief. At the time of admission to our Hospital, physical examination revealed no abnormality and a chest X-ray was negative.

Thoracic CT scan showed a solitary mass, about 2.5 cm in diameter, at the boundary of the lower third of the trachea extending along the right main bronchus across the orifice of the right upper lobe. Bronchofiberscopy depicted the tumor as a white/yellow lobulated mass occupying more than two thirds of the lumen with a pathological diagnosis of ACC. The patient was considered not suitable for surgery for medical reasons.

The patient underwent a photo resection with Nd-YAG laser *via* rigid bronchoscope: the macroscopic complete

resection of the tumor was obtained and a silicon prosthesis was inserted. A bronchoscopy, repeated after one month, showed a complete patency of the trachea and no macroscopic signs of tumor. A course of adjuvant radiotherapy (total dose 60 Gy; 2 Gy per fraction, five times a week) using 6 MeV photons with a 4-fields box technique was delivered with target volumes (CTV, PTV) defined as above. The treatment caused a RTOG-EORTC Grade 1 oesophagitis and a non-pathological fracture of the 6th right rib due to paroxysmal cough. The follow-up was negative up to 64 months when multiple pleuro-pulmonary metastases were observed. The patient started supportive care and is still alive with disease 76 months after the initial diagnosis.

DISCUSSION

Adenoid cystic carcinoma, also called cylindroma, is a distinctive malignant tumor that can arise from sub mucosal glands of the respiratory tract [2]. The most common involved site in the lung is the trachea [8], being bronchial lesions very uncommon.

The biological behaviour of ACC of this slow growing, low-grade malignancy differs from other tracheo-bronchial neoplasms for its indolent evolution and often delayed diagnosis. Chances of local-regional control are high even though local or metastatic recurrences can lately occur.

The best clinical outcome is provided by complete surgical resection and reconstruction [9,10]. The risk of incomplete resection is however high because of its unique histological invasion characteristics exhibiting an infiltrative growth pattern with a propensity for perineural invasion [5].

Metastases to lymph nodes are rare and mediastinal dissection can be safely omitted [11].

Table 1. Reported Survival in Most Relevant Recent Series of ACC of the Tracheo-Bronchial Tree

Author	Year	Cases	Therapy (If Any)	5-Years Surv.	10-Years Surv.	Notes
Maziak <i>et al.</i> [19]	1996	32	surgery+XRT	79%	51%	
Regnard <i>et al.</i> [16]	1996	67	surgery	73%	57%	Better results in pts. undergoing complete vs incomplete surgery
Perelman <i>et al.</i> [17]	1996	66	surgery	35.9%	27.1%	
Prommegger and Salzer [6]	1998	16	surgery	79%	57%	55% distant metastases
Kanematsu <i>et al.</i> [12]	2002	16	surgery	Res. 90% Unres. 40%	Res. 76% Unres. 0%	
Bhattacharyya [13]	2004	19	surgery	78.3%		Mean survival 115 months
Gaissert <i>et al.</i> [14]	2004	135	surgery+XRT	Res. 52.4% Unres. 33.3%	Res. 29% Unres. 10%	
Clough <i>et al.</i> [15]	2006	13	surgery	38.5%	-	Better mean survival in resected pts. (66 months) vs unresectable pts. (36 months)
Webb <i>et al.</i> [18]	2006	19	surgery±XRT	42%	26%	
Molina <i>et al.</i> [10]	2007	39	surgery±XRT	Surgical pts. 57%, non surgical pts. 53%	Surgical pts. 45%, non surgical pts. 31%	40.5% distant metastases

XRT: radiotherapy, Res.: resectable, Unres.: unresectable; vs: versus, pts.: patients.

A clear difference in survival is reported between resected and unresected patients. A summary of the recent literature on series of ACC of the tracheo-bronchial tree with at least 10 cases treated is reported in Table 1.

The role of XRT in the primary management of this tumor is still controversial and derived from retrospective analyses, small series or case reports. Primary radiation is generally reserved for patients with advanced disease at presentation, for recurrences or for patients suffering of significant symptoms [20,21].

Post-operative XRT is used primarily because of positive or close surgical margins and considering the propensity of these tumors to spread submucosally and perineurally [18]. The recommended dose to be delivered is between 54 and 60 Gy [14,22], but there are no prospective studies examining dose-response relations and/or fields width variation.

Grillo and Mathisen [20] recommend to avoid extensive resection and to use post-operative XRT to improve cure rate.

Adjuvant radiotherapy after incomplete resection is mandatory to control residual lesions and can provide long-term survival [23].

The use of laser therapy in endobronchial/tracheal tumors has demonstrated its activity in the past two decades primarily as a palliative measure or as a treatment performed after failure of other treatment modalities: most attention has focused on the use of the Nd-YAG laser [24].

This technique may allow a prolonged survival when combined with other therapies [25,26]. Debulking can be achieved with good precision using the laser; however it does not provide confirmation of resection margins and can leave tumor behind.

Okahara *et al.* [27] in 1996 presented the first case of ACC of the trachea successfully treated under endoscopy with a Nd-YAG Laser followed by 70 Gy of conventional XRT. Similar positive experiences with this combined approach were reported by Aggarwal *et al.* [28] and Albers *et al.* [29].

Although the primary care of ACC is surgical resection, laser therapy, in combination with XRT, can be successfully applied with good prognosis in cases where a conservative approach alternative to surgery could be preferred. This is foreseeable in patients refusing or not felt to be candidates to surgery or when laser therapy is used as initial disostructive measure showing the ability to completely clean the lumen. Moreover, this option can be considered either when the tumor is unresectable or the patient has distant metastases considering the possible prolonged survival also when residual tumor is left behind [9] and the minimally associated morbidity.

Our experience supports the utility of laser resection followed by local XRT in terms of local control. At five years of follow-up, our cases are locally controlled (but one with distant metastases). Even though it is to consider that in view of the slow-growing nature of ACC this period of time could be not long enough, we emphasize the good result in terms of local control obtainable with this conservative approach.

CONCLUSIONS

Despite their generally slow and indolent growth in other locations, ACC of the tracheo-bronchial tree may be aggressive tumors.

Surgical resection (segmental, tracheal or bronchial resection) is considered the best therapeutic choice.

Endoscopic laser photo resection could be a valid conservative alternative, when surgery is not feasible or is refused, offering a significant relief of symptoms allowing for better ventilation of the airway and achieving an optimal debulking with good precision.

Post-operative XRT is essential after laser therapy to eradicate possible microscopic or macroscopic residual disease allowing a good prognosis in terms of local control.

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