



Clear-Cell Carcinoma of the Larynx: A Report of an Unusual Case

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Clear-cell carcinoma (CCC) of the larynx is an extremely rare neoplasm with high malignancy potential and poor outcome. We herein report the 11th case of CCC of the larynx in a 42-year-old female who was managed with definitive radiochemotherapy. Due to a paucity of this entity, treatment option is not clearly defined, however, considering its grave nature, surgery should be offered primarily along with adjuvant radiotherapy with or without chemotherapy.

Key words: Clear-cell carcinoma, larynx, radiotherapy

INTRODUCTION

Clear-cell carcinoma (CCC) of the larynx is an unusual diagnosis, with only ten previously reported cases in literature. Although it is much more common in the kidneys, ovaries, uterus, and lungs, this neoplasm typically presents in the head and neck as a salivary tumor (1% of salivary neoplasms).¹ CCC typically consists of clusters of large cells with clear cytoplasm, with high mitotic activity. It has been described as a variant of either mucoepidermoid or adenocarcinoma, or of squamous cell origin. In the larynx, CCC has been shown to have a predilection for the supraglottis and typically presents as a large, exophytic mass with cartilage erosion. It is an aggressive neoplasm, with a high recurrence rate and poor long-term survival. In previous reports, four laryngeal CCC were classified as adenocarcinoma variant, and six were a variant of squamous cell carcinoma. We present the seventh case of CCC of the larynx of squamous origin.

CASE REPORT

An otherwise healthy, 42-year-old female, a known hypertensive on medications for 2 years with a history of tobacco smoking for 25 years presented with cough for 4 months. General and systemic examination was unremarkable. Contrast-enhanced computed tomography scan of the

face and neck showed diffuse asymmetric thickening with homogeneous enhancement of the epiglottis extending to pre- and para-epiglottic space and involving the aryepiglottic folds. Multiple subcentimetric to enlarged cervical lymph nodes are observed with the largest node measuring 16 mm × 7.8 mm in level II on the right side [Figure 1]. Direct laryngoscopy revealed an ulceroproliferative growth over the laryngeal surface of the epiglottis without vocal cord involvement [Figure 2]. Biopsy from the growth showed tumor cells with clear cytoplasm lying in the solid nest and surrounded by hyalinizing fibrocollagenous stroma; focal areas in the tumor show squamous differentiation, suggesting clear-cell variant of squamous cell carcinoma of the larynx [Figure 3]. The chest radiograph was normal. Hence, she was staged as cT3 N2c M0 as per the American Joint Committee on Cancer staging manual, eighth edition. She was treated with definitive radiochemotherapy with external beam radiation dose of 66 Gy in conventional fractionation to the primary site and bilateral necks and weekly cisplatin 40 mg/m² concurrently. She was planned by two-dimensional radiotherapy with source-to-surface distance technique on telecobalt. Although the option of total laryngectomy with bilateral neck dissection was offered to the patient for which she denied. She tolerated treatment well and was evaluated after 6 weeks of treatment completion with direct laryngoscopy

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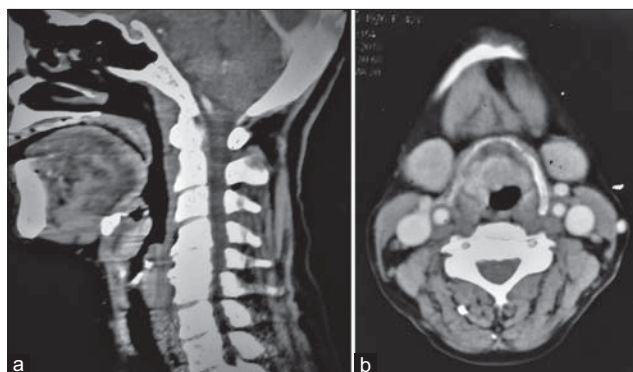


Figure 1: Contrast-enhanced computed tomography showing diffuse asymmetrical thickening with homogeneous enhancement in the epiglottis and aryepiglottic folds (a) sagittal view, (b) axial view



Figure 2: Direct laryngoscopy showing an ulceroproliferative growth over the laryngeal surface of the epiglottis

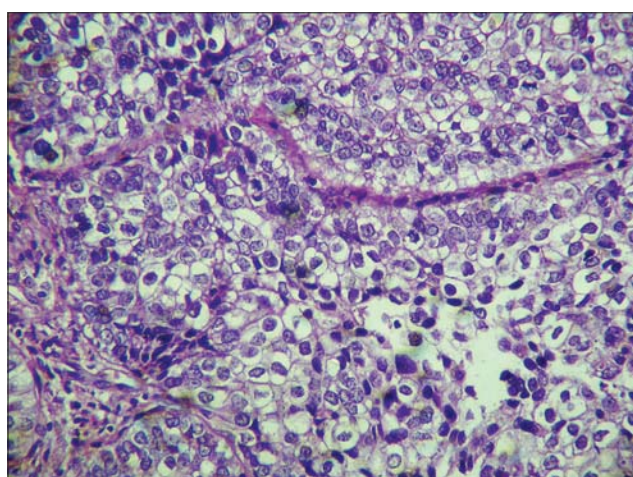


Figure 3: Histopathological examination showing tumor cells with clear cytoplasm lying in a solid nest and surrounded by hyalinizing fibrocollagenous stroma, and focal areas in the tumor show squamous differentiation, suggesting clear-cell variant of squamous cell carcinoma of the larynx

which showed complete remission. She is disease-free after 6 months follow-up till date.

DISCUSSION

CCC frequently arises in the kidney or lung and has also been reported in the ovary and uterus.^{2,3} CCC of the larynx is a rare entity, with only ten previously reported cases. We report the seventh case of squamous type. These tumors are characterized by large cells with abundant clear cytoplasm and frequent mitoses. Based on histological staining, these can be divided into squamous type or adenocarcinoma type, both of which are considered poorly differentiated. Squamous type will stain positive for cytokeratin, p63, periodic acid-Schiff (PAS), and carcinoembryonic antigen but negative for mucin and show squamous differentiation, glycogen deposition, and cytoplasmic lipid absence.¹ Adenocarcinoma will stain negative for PAS and show no squamous differentiation, whereas clear-cell variant of mucoepidermoid will stain PAS and mucin positive. CCC of the larynx has a predilection for the supraglottis (50%) and tends to present in elderly males (80%), with a median age of 65 years [Table 1]. Similarly, in our index case also, there was massive supraglottic involvement, but contradicting literature presented case was a middle-aged female. Like other laryngeal neoplasms, smoking and alcohol are the major risk factors, and dysphonia and dysphagia are the most common complaints. The tumor typically presents at an advanced stage with laryngeal cartilage erosion (80%) and positive neck lymphadenopathy (70%), as was also found in our case. Because of the small number of cases and uncertain histogenetic classification of this tumor, the biological behavior of the neoplasm is not well understood. However, CCC of the larynx is considered a highly aggressive neoplasm with a high locoregional recurrence rate (87.5%) and a mean survival time of 12 months (range 3–24 months). Distant metastases also arose in the two patients treated with postoperative radiotherapy, further indicating aggressiveness of this tumor. Surgical resection has been the treatment of choice for this neoplasm. Given the aggressive nature of CCC of the larynx, total laryngectomy with bilateral neck dissections, with consideration for postoperative chemotherapy and radiation therapy should be offered.⁴ Frequent follow-up is necessary to detect recurrences, as a similar morphology in the salivary glands has a high recurrence rate.⁵ However, our index case received definitive chemoradiation in keeping with her wish to preserve the larynx.

CONCLUSION

CCC of the larynx is a rare but aggressive neoplasm. We report the seventh case of CCC of the larynx of squamous

Table 1: Characteristics of clear-cell carcinoma of the larynx, as described in the literature

Author	Age (years)	Gender	Site	Stage	Type	Treatment	Recurrence	Mortality
Hoff <i>et al.</i> ¹	65	Male	Supraglottic	T4N2c	Squamous	TL + BND, CCRT	NR	NR
Testa <i>et al.</i> ²	71	Male	Supraglottic	T2N0	Squamous	SGL + BND	NR	NR
Sahraoui <i>et al.</i> ⁴	58	Male	Glottic	T4N2b	Squamous	TL + BND, CCRT	5 months	18 months
Nayak <i>et al.</i> ⁵	15	Male	Glottic	T2N0	Squamous	FLL	NR	NR
Pesavento <i>et al.</i> ⁶	41	Male	Supraglottic	T3N2c	Adeno	TL + BND	14 months	18 months
Pesavento <i>et al.</i> ⁶	61	Male	Supraglottic	T4N2c	Adeno	SGL + BND	2 months	3 months
Pesavento <i>et al.</i> ⁶	62	Male	Supraglottic	T4N2c	Adeno	TL + BND	5 months	6 months
Seo <i>et al.</i> ⁷	76	Female	Subglottic	T1N0	Adeno	XRT, TL	6 months	7 months
Dalla Palma and Blandamura ⁸	76	Female	Glottic	T3N2b	Squamous	TL + ND, CCRT	Mets at 1 month	10 months
Soranzo and Perissinotto ⁹	76	Male	Glottic	T4N2b	Squamous	TL + ND	Mets at 6 months	10 months
	42	Female*	Supraglottic	T3N2c	Squamous	CCRT	NR	NR

*Present case. FLL=Frontolateral laryngectomy; TL=Total laryngectomy; BND=Bilateral neck dissection; CCRT=Concurrent chemoradiation; SGL=Supraglottic laryngectomy; ND=Neck dissection; NR=Not reported; XRT=External Beam Radiation Therapy

origin. Although natural history of these rare tumors is not well understood because of the paucity of cases encountered, this malignant lesion seems to be associated with a poor prognosis, hence to be treated aggressively.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understand that her name and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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