

## Case Report

# Lymphoepithelial cell carcinoma of larynx masquerading as squamous cell carcinoma

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## ABSTRACT

Lymphoepithelial carcinoma is one of the common neoplasms seen to occur in nasopharyngeal subsite. Lymphoepithelial carcinoma (LEC) of the larynx is an uncommon entity; with 34 such cases reported in literature. Lymphoepithelial carcinoma (LEC) seems to behave in a fashion similar to nasopharyngeal carcinoma, except that most cases have not been associated with Epstein barr virus (EBV). We describe this patient with lymphoepithelial carcinoma (LEC) of supraglottic larynx who was treated with total laryngectomy and adjuvant radiotherapy and is on regular follow-up showed no evidence of local or distant metastasis.

**Keywords:** Lymphoepithelial carcinoma, Supraglottic larynx, Radiotherapy, Total laryngectomy, Epstein barr virus

## INTRODUCTION

Lymphoepithelial carcinoma (LEC) is a common neoplasm mostly located in the nasopharynx where it represents 40% of all neoplasms.<sup>1,2</sup> Although there is worldwide distribution, it has an endemic geographic distribution, particularly in Southeast Asia and Eskimos.<sup>3</sup> The most common sites of LEC other than nasopharynx includes Sino nasal tract, oral cavity, salivary glands, nasolacrimal duct, oropharynx, thymus, hypopharynx, esophagus, stomach, trachea, lung, and others.<sup>1-4</sup> There have been many terms used for non-nasopharyngeal Lymphoepithelial carcinoma (LEC) like undifferentiated carcinoma of nasopharyngeal type, undifferentiated carcinoma with lymphoid stroma, lymphoepithelioma, lymphoepithelial like carcinoma and lymphoepithelial carcinoma. However, the latter has been approved by the World Health Organization.<sup>5</sup>

Though the Non- nasopharyngeal and nasopharyngeal LEC share the same microscopic appearance, their relationship with Epstein Barr Virus is different. In fact,

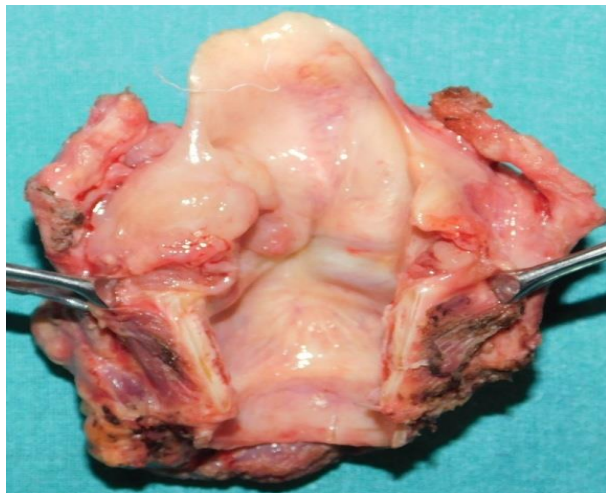
the former is less likely associated to EBV.<sup>2,3</sup> LEC is extremely rare in the larynx.<sup>4</sup>

We present herein one new laryngeal presentation and, through this case, we discuss the clinical and histopathologic findings, the diagnostic problems and therapeutic aspects of this rare neoplasm.

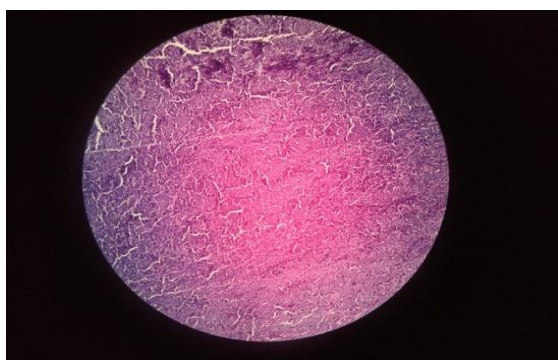
## CASE REPORT

A 55-year-old, known smoker for 40 years, presented with a 1 year history of dysphonia, dyspnoea and occasional dysphagia. Laryngoscopy showed a mass occupying supraglottic level of the larynx with glottic extension. The preoperative laryngeal biopsy showed atypical malignant cells composed of squamous histology in the background admixed with lymphocytes. Repeated biopsies revealed similar findings before the final biopsy suggested well differentiated squamous cell carcinoma. Cross sectional computed tomography scan demonstrated a laryngeal wall thickening especially at the glottic and supraglottic levels with early involvement of thyroid

cartilage with left cervical lymphadenopathy without any other distant metastasis. Patient underwent total laryngectomy with left Modified radical neck dissection preserving Spinal accessory nerve. On grossing, there was a lesion occupying the left supraglottic region of the larynx with extension to glottis (Figure 1).



**Figure 1: Gross specimen after total laryngectomy.**



**Figure 2: Histological examination of the supraglottic primary growth.**

Post-operative period was uneventful and HPE revealed nests of nonkeratinized round to oval, poorly differentiated tumour cells with large round vesicular nuclei and prominent nucleoli (Figure 2). The cytoplasm was poorly limited admixed within the background of lymphoid cells. Surface epithelium also exhibits some alterations like hyperplasia and keratosis, without any dysplasia. IHC revealed cytokeratin 5/6 intense positivity. Patient underwent adjuvant radiotherapy. Patient is on strict follow up and is having disease free survival until now.

## DISCUSSION

First described independently in 1921 by Regaud and schmincke, lymphoepithelial carcinoma has been a distinctive tumour known for its association with Epstein Barr virus. Regaud and Schmincke each described the

pathology of lymphoepithelioma separately.<sup>7</sup> LEC of the larynx is an extremely rare and aggressive tumor which accounts for 0.2% of all laryngeal cancers.<sup>2</sup> In the larynx the most common subsite, would be the supraglottic component.<sup>2</sup> It is common amongst the older age group (mean 62 years) with male predominance (male/female ratio=3:1).<sup>7</sup> The main symptom is dysphagia or hoarseness.<sup>8</sup>

Toker and Peterson postulated that the site of origin of these lesions may be active basal epithelium of the larynx, which is similar to epithelium of tonsillar crypts. In general, lymphocytes are believed to be general and are believed to be a nonneoplastic component of a lymphoepithelioma. When metastasis occur, only the epithelial component of the tumor is found at the distant site.<sup>9</sup>

Micheau et al have described three LEC of the larynx that arose in laryngoceles associated with abundant lymphoid tissue they suggested that this lymphoid-lined structure could be considered a true "tonsil," similar to Waldeyer's ring of the nasopharynx, and speculated that LEC of the larynx probably originate from this site.<sup>4</sup> But further studies are lacking to confirm the same.<sup>10</sup>

Macroscopically, the tumor forms a mass that may or may not be ulcerated. Diagnosis can be challenging because the tumor may arise from hidden, submucosal sites. Microscopically, laryngeal LEC is similar to the nasopharyngeal one.<sup>5</sup> It comprises solid sheets or irregular islands of malignant epithelial cells intimately intermingled with prominent component of lymphocytes and plasma cells.<sup>2-4</sup> Tumor cells are large, with indistinct cell borders, round to oval vesicular nuclei, and a single large central nucleoli.<sup>3</sup> There has been an infrequent association with squamous cell carcinomas or squamous cell carcinoma in situ in around half of the patients.

On Immunostaining with keratin and epithelial membrane antigen there is a strong positivity in lymphoepithelial carcinoma.<sup>2</sup> The presence of IHC stains for cytokeratin constituted a proof of epithelial differentiation. The distinction from large cell lymphoma and melanoma is prognostically important immunohistochemistry is essential in differential diagnosis by demonstrating expression of cytokeratin in LEC. Immunostaining with melanocyte differentiation markers (HMB45 or Melan-A) and lymphoid markers is useful to eliminate melanoma and lymphoma respectively. Nasopharyngeal carcinoma with laryngeal metastasis must also be eliminated.<sup>5,6,8,9</sup>

The relationship between EBV and LEC of the larynx remains controversial. Laryngeal LEC is less likely associated with EBV than its nasopharyngeal counterpart.<sup>2</sup>

Relationship between LEC and smoking is different in laryngeal and nasopharyngeal location. In the former, smoking may play a role while in the latter, it is not

considered to be a risk factor.<sup>1,4</sup> In our case, the patient had a smoking practise for over 30 years.

The adequate therapy for LEC of the larynx is unknown. Although most patients have been treated with either partial or total laryngectomy with neck dissection, Stanley et al describe four patients that were treated initially with radiation. Of these four, three subsequently died of extensive distant metastases, while the other survived 8 years without a recurrence.

This suggests, like its counterpart in the nasopharynx, that LEC of the larynx is radio-responsive and that either surgery, radiation, or both are useful in the management of local and regional disease. The challenge, therefore, lies in early diagnosis and prevention and treatment of metastases with adjuvant chemotherapy.<sup>1</sup> The initial stage is the primary determinant of prognosis. Death from disease occurs in about one third of patients.

This case report highlights the importance of a clinical pathologist and his role in histopathological characterisation of the lymphoepithelial carcinoma and distinction from its close counterpart squamous cell carcinoma of larynx which is in record the most common histology amongst smokers.

Because correct diagnosis aids in institution of proper primary modality of treatment, the value of a histopathologist remains crucial. Radiosensitive feature of this tumour adds to increased chance of laryngeal preservation amongst early stage tumours that would otherwise need surgical management for residue after radiotherapy. Further studies on a larger scale are required to establish the advantages of chemotherapy for prolonged 5-year and overall survival.

## CONCLUSION

LEC of the larynx is an extremely rare and an aggressive tumor. It has the same microscopic features as its nasopharyngeal counterpart. Radiotherapy is advisable as the unique therapy for local tumor. In the early stages of lymphoepithelioma, radiotherapy is the method of choice. In advanced cases of lymphoepithelioma, radiotherapy supplements surgical treatment. A correct diagnosis and a close collaboration between the pathologist and clinicians are mandatory for an optimal treatment strategy.

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