

Lymphoepithelial carcinoma of the larynx

Kouadir Asmaa, El Mazghi Abderrahmane, Hassouni Khalid

ABSTRACT

Introduction: Lymphoepithelial carcinoma of the larynx accounts only for 0.2% of all laryngeal cancers. These tumors are exceedingly rare and aggressive neoplasm. The relationship between Epstein–Barr virus (EBV) and laryngeal lymphoepithelial carcinoma remains controversial. **Case Report:** Herein, we describe a case of 81-year-old male, with a chronic smoking history, presented with complaint of dysphonia over one year period. The evolution was marked by the occurrence of dysphagia and severe dyspnea requiring emergency tracheostomy. Computed tomography scan of the neck showed a mass involving the entire larynx associated to cervical adenopathies. Endoscopic examination confirmed the findings of an ulcerated lesion affecting the three parts of the larynx and extending to the base of the tongue as well as to the postericoid region. A biopsy of the lesion has been performed. **Histological**

examination and immunohistochemistry revealed lymphoepithelial carcinoma of the larynx. Screening for Epstein–Barr virus (EBV) by immunohistochemical examination was negative. As the tumor was considered inoperable, the patient was treated solely with radiation therapy. Conclusion: Although rarely found in the larynx, it is essential to distinguish the lymphoepithelial carcinoma from squamous cell carcinoma. Immunohistochemistry must be the basis of the positive diagnosis. Epstein–Barr virus associated lymphoepithelial carcinoma has been exceptionally reported. This tumor is radiosensitive and radiotherapy should be considered as the main treatment.

Keywords: Epstein–Barr virus, Larynx, Lymphoepithelial carcinoma

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INTRODUCTION

Lymphoepithelial carcinoma (squamous cell carcinoma with associated lymphoid stroma) commonly occurs in nasopharynx. It rarely occurs at other sites like the nasal cavity, thymus, base of tongue, and parapharyngeal area. Lymphoepithelial carcinoma (LEC) arising in the larynx is unusual. It accounts only for 0.2% of all laryngeal cancers [1]. The relationship between

Epstein–Barr virus (EBV) and laryngeal lymphoepithelial carcinoma remains controversial [1, 2]. We report a case of locally advanced lymphoepithelial carcinoma of the larynx which was treated solely with radiation therapy.

CASE REPORT

An 81-year-old male, with a chronic smoking history, presented with complaint of dysphonia over one year period. The evolution was marked by the occurrence of dysphagia and severe dyspnea requiring emergency tracheostomy. Neck clinical examination revealed multiple hard, fixed cervical lymph nodes ranged from 1.5–3 cm in diameter.

Computed tomography (CT) scan of the neck (Figure 1) showed a mass involving the entire larynx associated to left jugulo-carotid lymphadenopathies measuring 30 mm in the long axis diameter for the largest. Endoscopic examination confirmed the findings of an ulcerated lesion affecting the three parts of the larynx and extending to the base of the tongue as well as to the postcricoid region. A biopsy of the lesion has been performed and fragmented tissue biopsies were histologically investigated.

Histopathological examination revealed laryngeal mucosal lined by a non-keratinizing malpighian epithelium. The chorion was the site of tumor proliferation arranged in syncytial clusters made up of large cells with vesicular nuclei and a prominent nucleolus. The cytoplasm was clear and abundant with blurred cytoplasmic boundaries. There was an associated tumor necrosis. This tumor was surrounded by a lymphoid stroma (Figure 2). Tumor cells expressed cytokeratin CK5/6 on immunohistochemistry (Figure 3). Screening for EBV by immunohistochemistry using anti-LMP 1 antibody (latent membrane protein 1) was negative. The diagnosis of lymphoepithelial carcinoma (LEC) of the larynx was established. The results from

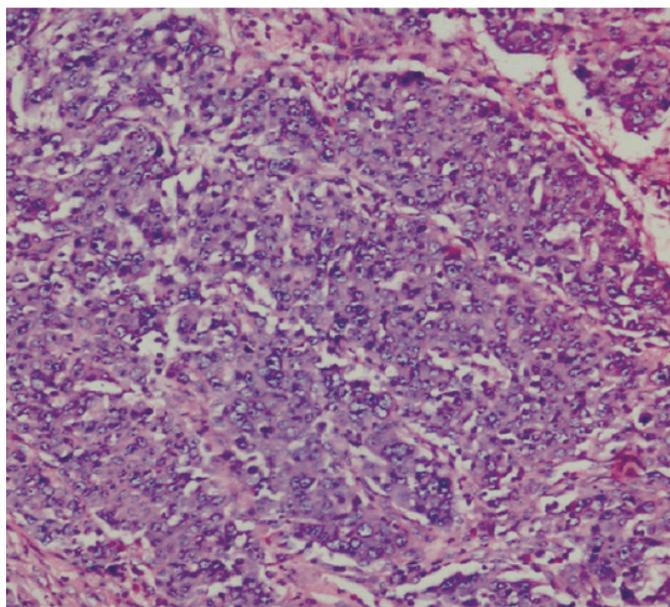


Figure 2: Histopathologic examination revealing sheets of undifferentiated cells with large nuclei and poorly defined cytoplasmic borders (H&E stain, ×200).

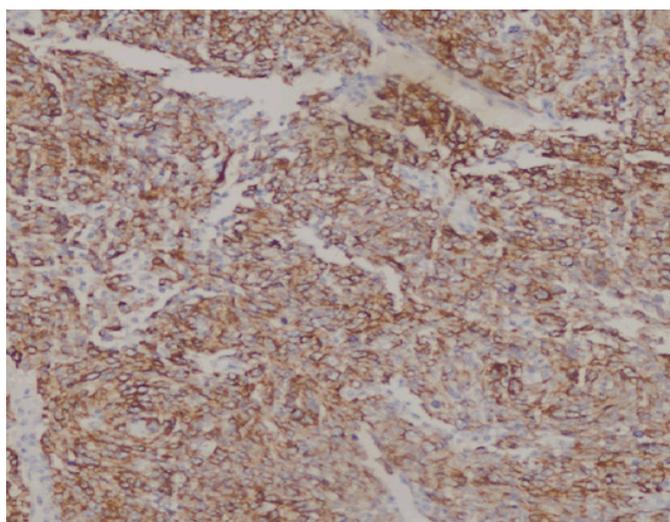


Figure 3: Immunohistochemistry analysis showing strong cytoplasmic staining with cytokeratin characterizing lymphoepithelial carcinoma (CK, ×200).

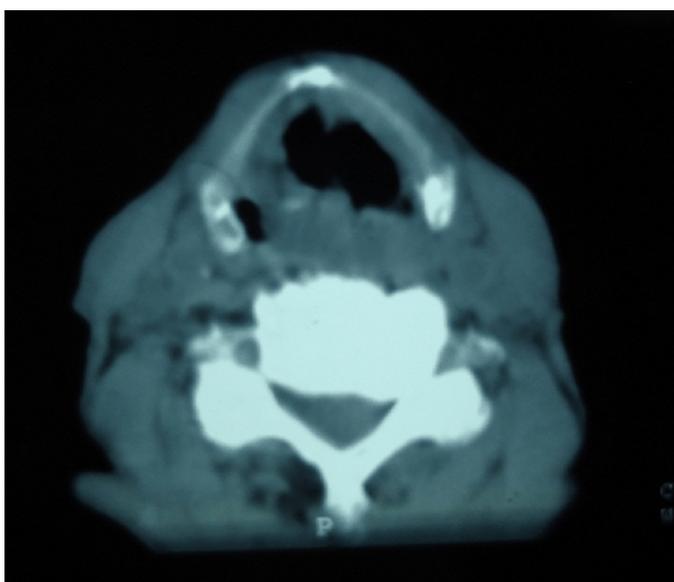


Figure 1: Computed tomography showing laryngeal tumor mass.

metastatic workup, including chest X-ray, abdominal ultrasound and bone scan were negative. The tumor was classified as T4N2bM0 and the case was discussed at multidisciplinary consultation meeting (RCP). As the tumor was considered inoperable the RCP decision was to treat the patient by exclusive radiotherapy.

Actually, the patient underwent three-dimensional conformal radiation therapy with 6 MV photons to a total dose of 70 Gy in 35 fractions to the primary tumor. The lymphadenopathies received a total dose of 66 Gy in 33 fractions and the draining regional cervical lymphatics received a prophylactic dose of 50 Gy in 25 fractions which were delivered over a similar period of time. The

patient tolerated therapy with modest mucositis and altered taste. The patient died nine months later because of lung metastases discovered six months after the end of the treatment.

DISCUSSION

Lymphoepithelial carcinoma of the larynx is an exceedingly rare and aggressive neoplasm with a propensity for early cervical lymph node and distant metastasis. Actually, only about thirty cases of LEC of the larynx have been reported in literature. At the time of diagnosis, lymph node invasion has been reported in 75% of cases whereas systemic metastases have been reported in 29% of cases [1, 2]. This tumor usually occurs in men between the ages of 50 and 70 years [1, 3]. There is a tendency for this tumor to occur in the supraglottic larynx [1]. Risk factors for the development of this carcinoma include excessive use of tobacco and alcohol [4]. Clinical symptoms are dominated by hoarseness and dysphagia [1].

The histology of laryngeal lymphoepithelial carcinoma is similar to its more common nasopharyngeal counterpart. In fact, this neoplasm is composed of large, poorly differentiated, non-keratinized cells with large, round, vesicular nuclei, each containing a single large usually centrally located, basophilic to deep red prominent nucleolus [2].

Regarding immunohistochemical analysis, it has been noted that the lesional cells express cytokeratin. So as major differential diagnosis of LEC of the larynx includes non-Hodgkin's lymphoma and squamous cell carcinoma, a correct diagnosis should include cytokeratin-positive immunohistochemistry to identify the poorly differentiated squamoid component [1, 2, 5].

Compared to nasopharyngeal lymphoepithelial carcinoma which is consistently associated with EBV, the relationship between EBV and LEC of the larynx remains controversial [1]. Actually, MacMillan et al. reported that the tumor is only rarely associated with the EBV in individuals of non-Asian descent [2, 3]. Marioni et al. reported that EBV plays a limited role in the etiology of LEC of the larynx. Of the 34 cases of laryngeal LEC considered in his report, only 16 were evaluated for the presence of EBV, and EBV screening was positive in only four patients [1, 2]. However, there is no major prognostic significance related to the presence of EBV in lymphoepithelial carcinoma [3, 5]. In our case, screening for EBV by immunohistochemistry was negative.

In terms of treatment, lymphoepithelial carcinoma is a highly radiosensitive tumor, and such radiosensitivity allows conservative first line treatment [1, 6]. Stanley et al. used primary radiation therapy in four patients with LEC of the larynx with good local control [7]. Ferlito also reported a case of LEC of the larynx treated solely

with radiation therapy in which his patient died in less than one year as a result of distant metastases [8]. Surgery is indicated for locally advanced tumors [6]. Chemotherapy may be recommended in patients with early regional lymphadenopathies in order to decrease the distant metastasis rate [1, 3]. In our case, surgery and chemotherapy have been declined during the discussion of the case at the multidisciplinary consultation meeting because of the aging of patient.

CONCLUSION

Although rarely found in the larynx, it is essential to distinguish the lymphoepithelial carcinoma from squamous cell carcinoma. Immunohistochemical examination demonstrating cytokeratin expression must be the basis of positive diagnosis by identifying the poorly differentiated epithelial component. As few cases of laryngeal lymphoepithelial carcinoma were published, the role of Epstein–Barr virus in the pathogenesis of this tumor is difficult to be clearly determined. Radiation therapy is recommended as the sole treatment modality for local disease. Chemotherapy may also play a role in patients with advanced disease as well as in those with lymph node invasion.

Author Contributions

Kouadir Asmaa – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

EL Mazghi Abderrahmane – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Hassouni Khalid – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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