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Case Report

Typical laryngeal carcinoid tumor with recurrence and lymph node metastasis: a case report and review of the literature

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Abstract: Typical carcinoid tumor of the larynx is an extremely rare lesion which arises from neuroendocrine cells scanning in the laryngeal mucosa or submucosal glands. Conventionally, it is a well-differentiated neuroendocrine carcinoma, conservative surgery represents the treatment of choice, and the patient usually has a good prognosis with rarely recurrence and metastasis. In this report, we present a case of typical laryngeal carcinoid tumor with recurrence and lymph node metastasis. The patient was a 58-year-old man, complaints of intermittent burning pain in his both ears for 2 years, and for the recent one month the pain turn to continuous accompanied with a mild discomfort in the throat, he had neither hoarseness, dysphagia, nor any otorrhea and hearing loss. The patient was scheduled to undergo a tracheotomy and then a biopsy under supporting laryngoscopy. During the operation, the frozen section diagnosis from the first and the second time both indicated that the biopsy specimens originated from musculo-epithelia, it couldn't be differed from malignant to benign. So the mass was simply removed under supporting laryngoscopy. The histopathology from paraffin sections revealed typical carcinoid of the larynx and the second procedure consisted of supraglottic laryngectomy with clear margins, the otalgia resolved and the patient had no difficulty with phonation or swallowing. After 1 year follow-up, the patient was found a mass on his right neck with symptom free, B-ultrasonography indicated several enlargement lymph nodes with some merged on both sides of the neck, the patient was scheduled to undergo a "total-laryngectomy with radical neck dissection on the left side and an elective neck dissection on the right side". The specimens were positive for cytokeratin, chromogranin A and synaptophysin, a final diagnosis of typical carcinoid was made for the recurrence lesion and the metastasis of the lymph nodes. Though the post-operative recovery was uneventful, the prognosis was not good, the patient died six months later. Here, we review the pertinent references on this subject, and discuss the main managements for typical carcinoid tumor of the larynx.

Keywords: Typical carcinoid, larynx, recurrence, metastasis

Introduction

Typical carcinoid tumor of the larynx is an extremely rare lesion which arises from neuroendocrine cells scanning in the laryngeal mucosa or submucosal glands. Being absence of characteristic manifestation in early stage, it is often confused with other laryngeal carcinomas [1]. Typical carcinoid tumor is a well-differentiated neuroendocrine carcinoma (NEC), conventionally, local excision is thought to be enough for such a neoplasm, and the patient usually has a good prognosis with rare recurrence and metastasis [2-5]. In our hospital in July 2003, a patient of laryngeal typical carcinoid tumor was admitted. He had been given operation of "supraglottic laryngectomy" with clear margins, but after 1 year follow-up, the patient was found recurrence and lymph node metastasis. He had to be given a further operation, and the prognosis was not good. Here we report the case and discuss the pertinent problem on this subject.

Case report

A 58-year-old man was admitted to our hospital with complaints of intermittent burning pain in his both ears for 2 years, and for the recent one month the pain turn to continuous accompa-

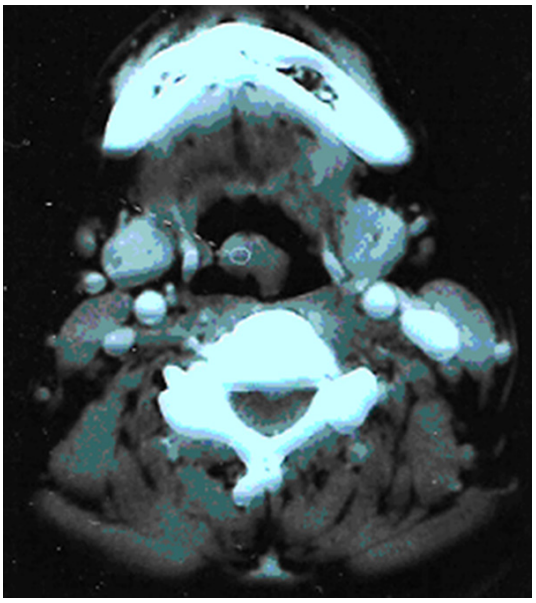

Figure 1. CT scan of the larynx with a mass on epiglottis.

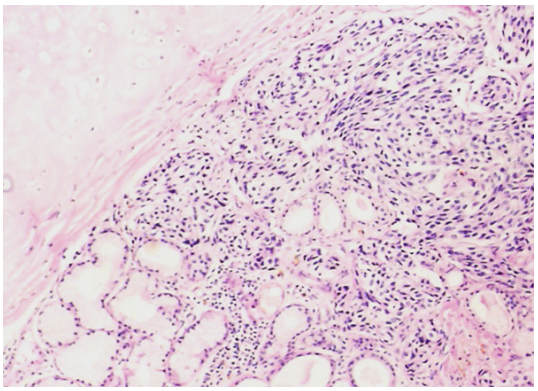

Figure 2. Uniform tumor cells in nests arrangement without evident infiltration to laryngeal cartilage and glands (HE × 100).

nied with a mild discomfort in the throat, he had neither hoarseness, dysphagia, nor any otorrhea and hearing loss. On physical examination, the general condition was good, the auricles, external auditory canals and the tympanic membrane were clear, the oral cavity and the oropharynx were clear too. Indirect laryngoscopy revealed the presence of a deep red lump on laryngeal aspect of the epiglottis, measuring 1.5 × 2.0 cm with smooth mucosa covering the surface. The lingual aspect of the epiglottis and the epiglottic vallecula were normal, but the epiglottis seemed fixed, and the vocal cord could not be visualized, no lymph node

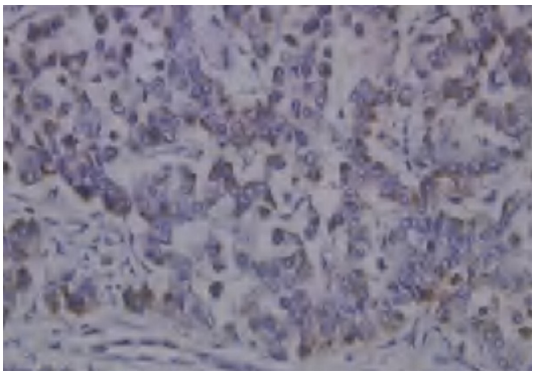

Figure 3. Strongly positive staining for chromograniA in tumor cells (Envision™ × 200).

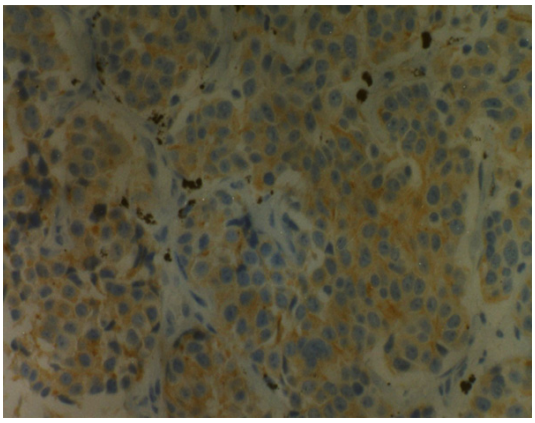

Figure 4. Positive staining for synaptophysin in tumor cells (Envision™ × 200).

was palpated on both sides of the neck. A computed tomography (CT) scan with three-dimensions rebuilding demonstrated that the mass was on the epiglottis and infiltrated the left aryepiglottic fold, CT value increased remarkabaly from 49.2 Hu to 79.2 Hu after enrichment (**Figure 1**). According to the result of the indirect laryngoscopy and the CT scan, we firstly considered the mass as “epiglottic haemangioma”.

The patient was scheduled to undergo a tracheotomy and then a biopsy under supporting laryngoscopy. During the operation, the frozen section diagnosis from the first and the second time both indicated that the biopsy specimens originated from musculo-epithelia, it couldn’t be differed from malignant to benign. So the mass was simply removed under supporting laryngoscopy. After operation, the histopathology from paraffin sections were described (**Figure 2**) as: the tissue was covered with squa-

Table 1. Classification of neuroendocrine carcinoma (NEC) of the larynx and their characteristics

Tumor	Prevalence	Predominance	Metastasis	Treatment	prognosis
Epithelial origin					
Typical carcinoid (well-differentiated NEC)	+	Male	Rare	Local excision	Good
Atypical carcinoid (moderately differentiated NEC)	++++	Male	Common (45%)	Excision with neck dissection	Moderate
Small-cell NEC (poorly differentiated)	+++	Male	Common (50%)	Chemo- and radiotherapy	Very poor
Neural origin					
Paraganglioma	++	Female	Very rare	Local excision	Excellent

mous-epithelial cells, containing sheets and nests of uniform round cells. These cells had amounts of eosinophilic cytoplasm and round nuclei, without nuclear pleomorphism, hemorrhage and necrosis. The immunohistochemical (IHC) study showed: cytokeratin (CK)+, chromogranin A (CgA)+ (**Figure 3**), synaptophysin (Syn)+ (**Figure 4**), S-100 protein+, vimentin (VM)+, CD31-, CD34-, smooth muscle actin (SMA)-, desmin (Des)-, leucocyte common antigen (LCA)-, the finally diagnosis was: typical carcinoid of the larynx. The second procedure consisted of supraglottic laryngectomy with clear margins, the otalgia resolved and the patient had no difficulty with phonation or swallowing.

After 1 year follow-up, the patient was found a mass on his right neck with symptom free. Indirect larynscopy revealed some enlargement of the right arytenoids cartilage, the local mucosa seemed oedema and deep red. B-ultrasonography indicated several enlargement lymph nodes with some merged on both sides of the neck. The larger ones were about 2.8 cm × 2.1 cm on the right and 3.0 cm × 1.7 cm on the left. The patient was scheduled to undergo a "total- laryngectomy with radical neck dissection on the left side and an elective neck dissection on the right side". The specimens were positive for cytokeratin, chromogranin A and synaptophysin, a final diagnosis of typical carcinoid was made for the recurrence lesion and the metastasis of the lymph nodes. Though the post-operative recovery was uneventful, the prognosis was not good, the patient died six months later.

Discussion

Typical carcinoid tumor belongs to the groups of neuroendocrine tumors of the epithelial origin. This neoplasm usually occurs in gastrointestinal track or bronchial system but rarely in the larynx [6-8]. The total number of known and documented cases is likely no more than 13 up to 2002 [9]. Their predominant location is the supraglottis with the arytenoids and the aryepiglottic fold being the most frequent sites [10]. The diagnosis is primarily based on light microscopy. Histologically, they are characterized by organoid architecture, uniform cellular features and lack of pleomorphism, necrosis and mitosis [2, 10]. But sometime it may appear to be undifferentiated by light microscopy [6]. In our case, during surgery, the first and second outcome of frozen sections couldn't distinguish it from malignant to benign, and distorted it as musculo-epithelial origin. Theoretically, neuroendocrine tumors have neuroendocrine production, but the carcinoid syndrome was found to occur only at the rate of 7.7% of overall 11057 cases reported from 1953 to 2002 [8]. So only according to the history of the patient, image examination and light microscopic finding, they may be confused with other laryngeal tumors. The correct diagnosis should be confirmed by immunohistochemical study and electron microscopic investigation [2, 6, 7]. As to our case, the positive staining of Syn, CgA, S-100 and CK indicated it from neuroendocrine system; while the negative of SMA, Des, VM denied it from musculo-epithelia; similar, and the negative of the CD31, CD34, LCA denied it from leucocythemia and lymphoma. Depending on the above information combined with microscopic feature that it had uniform tumor cells without mitosis and necrosis, we demonstrated it as "typical carcinoid tumor of the larynx".

The World Health Organization (WHO) developed a classification system for neuroendocrine noeplasms in larynx, categorizing them as typical carcinoids, atypical carcinoids, small-cell neuroendocrine carcinomas and paragangliomas (**Table 1**) [11]. Different types have different biological behavior, their specific pathologic identification has significant bearing in the treatment and prognosis, so it is para-

mount importance that otolaryngologist and pathologists should be able to correctly identify the specific type in order to optimized patient treatment and survival [12]. Clinically, atypical carcinoids are the most common of the neuroendocrine tumors of the larynx with over 300 cases reported in the literature [2-4]. They are considered to be much more aggressive and have a propensity to metastasize. The mainstay of treatment is surgery, elective neck dissection should be performed because of the high likelihood of cervical lymph node infiltration. But to typical carcinoid tumor, usually it is treated preferably by conservative surgery, elective neck dissection is often beyond our consideration because of the lack of lymph node metastasis at diagnosis, prognosis is commonly excellent following excision with clear margins [2-5]. But in our case, the patient suffered a relapse and lymph node metastasis only after one year. In the current report, Ferlito et al. said laryngeal carcinoid tumors had a capacity for metastasis, and so were more aggressive than their light microscopic features [13]. Metastasis in carcinoid tumor of the kidney had also been reported [14]. The above information indicated that though typical carcinoid is a well-differentiated tumor, it still has the potential for aggressive behavior. Generally, conservative surgery represents the treatment of choice, and the prognosis is relatively optimistic. But the fact that our patient had a poor prognosis of relapse, metastasis and death emphasized the need of a radical resection, the need of a thoroughly cervical lymph node examination before surgery and close follow-up after surgery, elective even radical neck dissection should be performed when necessary.

Disclosure of conflict of interest

None.

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