Case Report / Olgu Sunumu

Well-differentiated neuroendocrine tumor: a rare tumor of the larynx

İyi diferansiye nöroendokrin tümör: Larenksin nadir görülen bir tümörü

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Neuroendocrine tumors of the larynx are rarely seen neoplasms. Atypical carcinoid tumor is the most common type of the neuroendocrine tumors of the larynx, whereas the typical carcinoid tumor is the most infrequent type. Preferable treatment in typical carcinoid tumor is particularly conservative surgery without neck dissection. Radio-chemotherapy is ineffective. In this report, we present a 61-year-old female case of typical carcinoid tumor of the larynx with histological findings and applied treatment modality.

Key Words: Larynx; neuroendocrine carcinoma; typical carcinoid tumor.

Larenksin nöroendokrin tümörleri, nadir görülen neoplazmlardır. Atipik karsinoid tümör, larenkste en sık görülen nöroendokrin tümör iken, tipik karsinoid tümör en nadir görülen tiptir. Tipik karsinoid tümörün tedavisinde boyun diseksiyonu olmaksızın yapılan konservatif cerrahi tercih edilmektedir. Radyo-kemoterapi etkisizdir. Bu yazıda, larenkste tipik karsinoid tümörü olan 61 yaşında bir kadın olgu, histopatolojik bulguları ve uygulan tedavi yöntemi ile birlikte sunuldu.

Anahtar Sözcükler: Larenks; nöroendokrin karsinom; tipik karsinoid tümör.

The larynx is the most common site of cancer in the head and neck region, whereas laryngeal cancers are listed as rare diseases by the "Office of Rare Diseases of the National Institutes of Health." Laryngeal cancers account for nearly 2-5% of new malignancies worldwide each year. Approximately 85-90% of these cancers are of the squamous cell type. Of the non-squamous cell types, neuroendocrine neoplasms are the most common, although they are an uncommon (less than 1% of all laryngeal tumors) variant and morphologically heterogeneous group of tumors of the larynx.[1,2]

Based on tissue origin, neuroendocrine tumors of the larynx are separated into two categories epithelial and neural. The epithelial tumors are divided into three subtypes based on degree of differentiation: typical carcinoid (well differentiated neuroendocrine carcinoma, grade 1), atypical carcinoid (moderately differentiated neuroendocrine carcinoma, grade 2 or large cell neuroendocrine carcinoma) and small cell neuroendocrine carcinoma (poorly differentiated neuroendocrine carcinoma, grade 3). Atypical carcinoid tumor is the most common of the neuroendocrine tumors of the larynx, followed by small cell neuroendocrine carcinoma, paraganglioma and the typical carcinoid.[1] While paraganglioma is the most unique subtype of neural type tumor,[1,3,4] the typical carcinoid tumor

Available online at
www.kbbihtisas.org
doi: 10.5606/kbbihtisas.2013.36097
QR (Quick Response) Code

Received / *Geliş tarihi:* April 18, 2012 Accepted / *Kabul tarihi:* July 19, 2012

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is the most rare subtype of neuroendocrine tumor in the larynx and carries the best prognosis.[3,5,6] In this report we present a case of typical carcinoid tumor presenting as a giant mass in the larynx of a woman.

CASE REPORT

A 61-year-old female was referred to our clinic with respiratory distress lasting for two weeks. The patient did not use tobacco or alcohol, and has no other systemic disease in her medical history. On flexible fiberoptic laryngoscopic examination a giant hemorrhagic-appearing supraglottic mass, that originated from the right aryepiglottic fold extending to the right ventricle was seen. The mass was covering the vocal cords and moved briskly with respiration, so that vocal cord mobilities were not well evaluated (Figure 1a and 1b). Palpable lymph nodes were noted in the second and third neck regions. There were no other abnormalities in the remainder of the otorhinolaryngologic or pulmonary examinations. On general physical examination systemic hypertension was determined, and treatment was begun immediately before the surgery by an internal specialist.

The results of the laboratory tests were normal, including complete blood count, sedimentation rate, glucose level and electrolytes. Direct suspension laryngoscopy was performed under general anesthesia. Before surgery, the probability of tracheotomy, if intubation could not be performed, was explained to the patient and her husband and consent was obtained. The intubation was performed seamlessly. On direct laryngoscopy, an approximately 1.5x2 cm large hemorrhagic-appearing mass with a smooth surface originating from the right aryepiglottic fold with a large pedicle and extending to the right ventricle was removed with its pedicle from the right aryepiglottic fold. Histopathological examination was performed.

Histopathological examination

Grossly, the specimen was a fairly circumscribed polypoid tissue fragment measuring 2x1.5x1 cm. The cut surface was solid, grey white in color and fish flesh appearance. Microscopic examination showed a subepithelial tumoral proliferation with trabecular and "ribbon-like" nests of uniform small round cells which has fine granular chromatin pattern and scant eosinophylic cytoplasm (Figure 2a and 2b). There was no tumor necrosis. Mitotic activity was low which is 2 per 10 high-power field (HPF). On immunohistochemistry, tumor cells showed diffuse and strong positivity for CD56, chromogranin A and neuron-specific enolase (NSE), and occasional positivity for S-100 and carcinoembryonic antigen (CEA) (p) (Figure 2c and 2d). A final diagnosis of typical carcinoid/low-grade neuroendocrine carcinoma was rendered. The surgical margins were reported as positive.

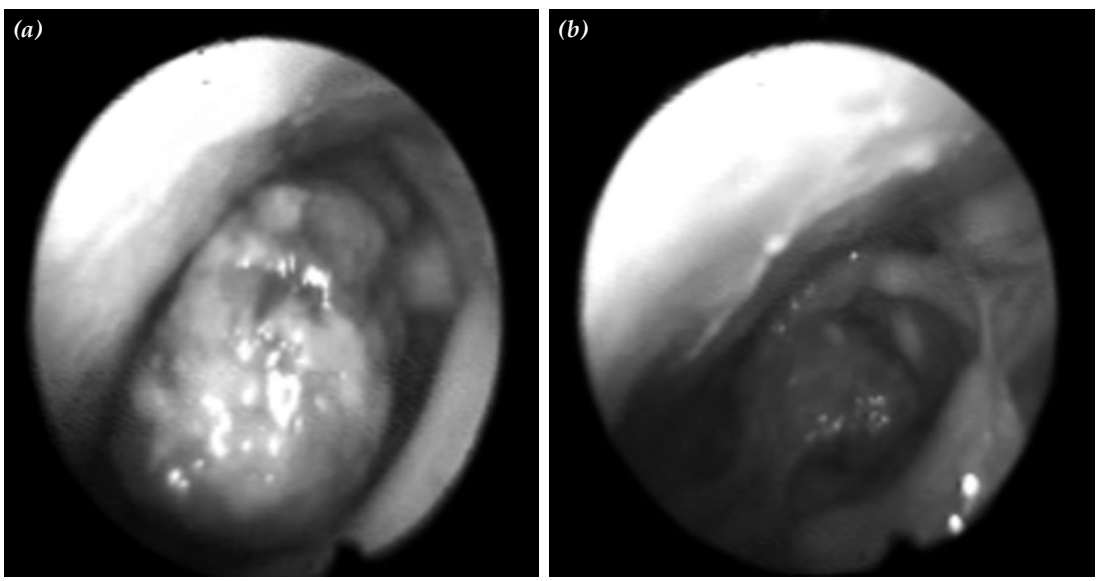

Figure 1. *Flexible fiberoptic laryngoscopic examination a giant hemorrhagic supraglottic mass,* ***(a)*** *that covers the vocal cords and* ***(b)*** *moves briskly respiration.*

Because of the surgical margin was reported as positive after the histological examination, supraglottic laryngectomy with a tracheotomy and right 2nd, 3rd, 4th region neck dissections were performed. The postoperative histopathologic diagnosis was not changed and the surgical margins were tumor-free. The neck dissection material was also tumor free. There were no complications intraoperatively or postoperatively. The tracheotomy was closed on the first month of the surgery. The patient did not receive radiation therapy or chemotherapy after the surgery, because the postoperative histopathological findings did not find any tumor. There was no recurrence during a follow-up period of five months.

DISCUSSION

Neuroendocrine carcinomas of the larynx are rare tumors, although they are the most common non-squamous tumor type of this organ. They are a morphologically heterogeneous group of lesions which are rare, distinct, and share specific immunohistochemical, ultrastructural and morphological characteristics. The prognosis of the carcinoma depends on the type of the tumor.[1] Although the terminology in the literature is confusing and controversial, the World Health Organization (WHO) has identified four different types of neuroendocrine tumor of the larynx. These are; paraganglioma, typical carcinoid tumor, atypical carcinoid tumor and small-cell neuroendocrine tumor.[1] Paragangliomas are tumors with neural origin, whereas three other types are of epithelial origin. The diagnosis of neuroendocrine tumor is based primarily on light microscopy and then confirmed by immunohistochemistry and electron microscopy.[1,7]

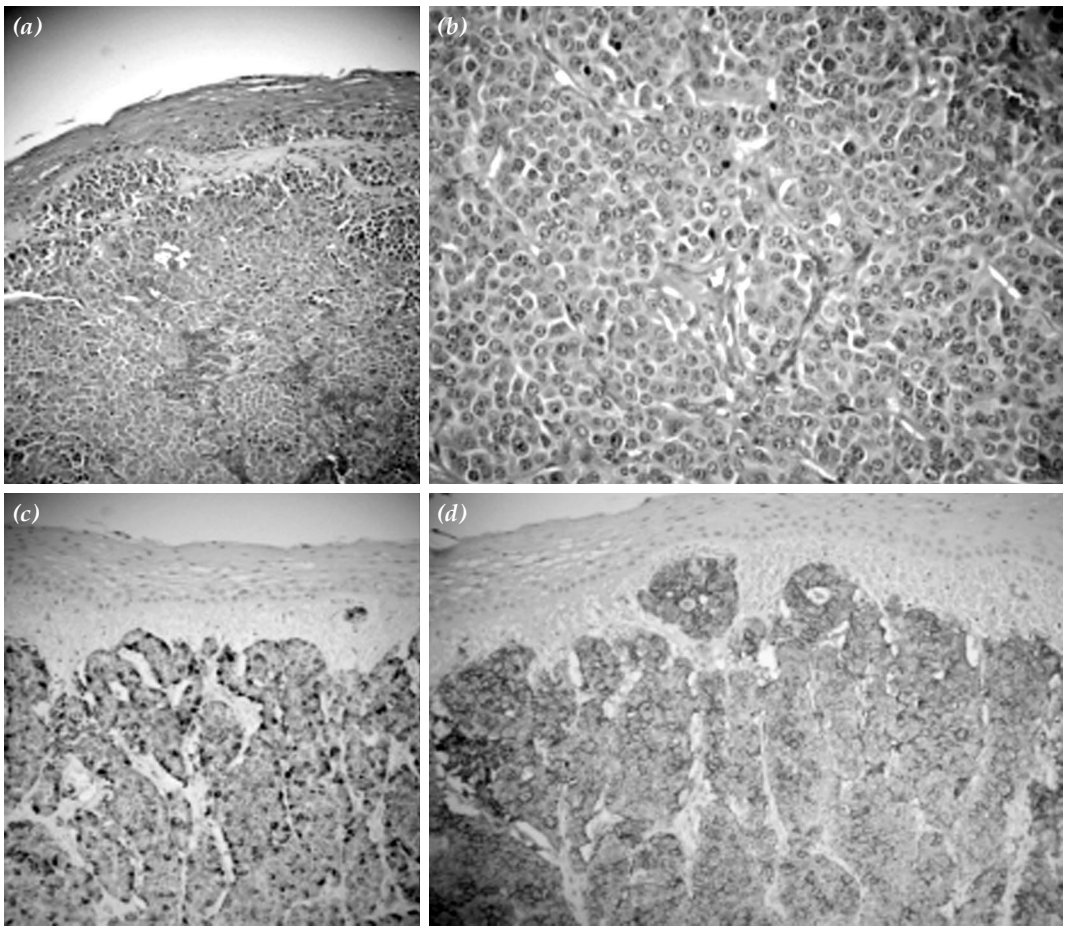

Figure 2. *The histopathologic features of the resected tumor resembled a typical carcinoid tumor with trabecular and "ribbon-like" nests of uniform small round cells* ***(a)*** *H-E x 10,* ***(b)*** *H-E x 40. Tumor cells demonstrated strong and diffuse positivity for Chromogranin A and CD56* ***(c)*** *Chr A x 20,* ***(d)*** *CD56 x 20.*

The histologic type of the neuroendocrine tumors affect the natural history, local recurrence rate and disease-specific survival rate.[2] It has been known that typical carcinoid type tumors appear to be less aggressive nature than the other types of neuroendocrine carcinomas, however late distant metastases that cause death may occur especially in the liver.[8,9] A five year survival rate of 48% for carcinoid tumor of the larynx has been reported in a large series,[2] but this lower survival rate might be related to misdiagnosis of atypical carcinoid tumor as typical carcinoid.

The typical carcinoids are very rare tumors and represent 0.5-1% of all epithelial neoplasms. This type is the least common neuroendocrine tumor of the larynx that often involves the supraglottic portion of the larynx, especially the arytenoids or aryepiglottic fold, because of the generous neuroendocrine cell contents of the supraglottic area.[1,5,6] In our case the tumor was seen in the supraglottic area and it originated from the right aryepiglottic fold with a large pedicle and extended to the right ventricle.

There is male predominance with a male to female ratio of 3:1 in typical carcinoid tumor. The biological behavior of this tumor is benign. The tumor is typically seen in the sixth to eighth decade of life, especially in smokers.[2,6] Our patient was a woman with no smoking history, although her age was typical for the tumor. She had only respiratory distress as a symptom and endoscopic examination revealed a supraglottic mass with a smooth surface.

The treatment of typical carcinoid tumor is conservative surgery (wide local excision, usually partial laryngectomy) unless it spreads and elective neck dissection is not indicated. Chemotherapy or radiotherapy is ineffective in typical carcinoid tumor[5,7] but a combined approach may be beneficial in a few patients with atypical carcinoid tumors.[3] We performed supraglottic laryngectomy and elective neck dissection in this patient because of palpable lymph nodes in the second and third neck regions.

Atypical carcinoid tumors of the larynx are the most common type of neuroendocrine tumors of the larynx.[1,5] The clinical findings and location of these tumors are similar to the typical carcinoid tumors, and their prognosis is not better than typical carcinoid tumors, with five year survival rates of approximately 50%. Thus, more extended surgical resection and elective neck dissections are recommended with addition of radio-chemotherapy.[1]

Small cell type neuroendocrine carcinoma of the larynx is the most aggressive type. Early metastases are common and metastatic disease (cervical lymph nodes, liver, lung, bone and bone-marrow) are seen over 90% of patients.[2] This type of neuroendocrine tumor has poor five-year survival rates of nearly 5%. In this group, the basis of treatment is combined radio-chemotherapy and surgical treatment is not recommended.[1,7]

The paraganglioma type of neuroendocrine tumor has a good prognosis. The majority of this type are supraglottic submucosal masses and suitable for surgical excision. Infraglottic paragangliomas can also be treated with surgical excision. Elective neck dissection is not recommended in this type because cervical lymph node metastases are rare.[7]

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Ferlito A, Silver CE, Bradford CR, Rinaldo A. Neuroendocrine neoplasms of the larynx: an overview. Head Neck 2009;31:1634-46. doi: 10.1002/hed.21162.
2. Ferlito A, Devaney KO, Rinaldo A. Neuroendocrine neoplasms of the larynx: advances in identification, understanding, and management. Oral Oncol 2006;42:770-88.
3. Gillenwater A, Lewin J, Roberts D, El-Naggar A. Moderately differentiated neuroendocrine carcinoma (atypical carcinoid) of the larynx: a clinically aggressive tumor. Laryngoscope 2005;115:1191-5.
4. Barbeaux A, Duck L, Weynand B, Desuter G, Hamoir M, Gregoire V, et al. Primary combined squamous and small cell carcinoma of the larynx: Report of two cases and discussion of treatment modalities. Eur Arch Otorhinolaryngol 2006;263:786-90.
5. Ferlito A, Rinaldo A. The spectrum of endocrinocarcinomas of the larynx. Oral Oncol 2005;41:878-83.
6. McBride LC, Righi PD, Krakovitz PR. Case study of well-differentiated carcinoid tumor of the larynx and review of laryngeal neuroendocrine tumors. Otolaryngol Head Neck Surg 1999;120:536-9.

7. Ferlito A, Shaha AR, Rinaldo A. Neuroendocrine neoplasms of the larynx: diagnosis, treatment and prognosis. ORL J Otorhinolaryngol Relat Spec 2002;64:108-13.
8. Devaney KO, Ferlito A, Rinaldo A. Neuroendocrine carcinomas of the larynx: what do the different histologic types really mean? Eur Arch Otorhinolaryngol 2010;267:1323-5. doi: 10.1007/s00405-010-1318-8.
9. el-Naggar AK, Batsakis JG. Carcinoid tumor of the larynx. A critical review of the literature. ORL J Otorhinolaryngol Relat Spec 1991;53:188-93.