Poorly differentiated neuroendocrine carcinoma originating in the subglottic larynx: a case report with immunohistochemical study

Mahboobe Asadi[1], Milad Elyasi[1], Arvin Shahzamani[1], and Saeedeh Miri[2]

[1]Shahid Beheshti University of Medical Sciences
[2]Tehran University of Medical Sciences

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Introduction

Laryngeal neuroendocrine carcinomas (LNECs) are rare tumors of the larynx with a wide spectrum of clinicopathological manifestations. Generally, laryngeal neuroendocrine neoplasms were divided into 2 categories, epithelial and neural, based on their origin. The epithelial subgroup consisted of typical carcinoid, atypical carcinoid, small cell neuroendocrine carcinoma, and large cell neuroendocrine carcinoma. The neural neuroendocrine neoplasm subgroup is mainly referred to as paraganglioma. [1]

Among these categories, atypical carcinoid is the most common form of neuroendocrine carcinomas in the larynx .Also; prognosis is getting worse from typical carcinoid to small cell neuroendocrine carcinoma.[2] Laryngeal neuroendocrine neoplasms represent 0.5 to 1% of laryngeal epithelial carcinomas, occurring more frequently in the supraglottic region with male predominance. [3]

In this study, we presented a rare case of poorly differentiated NEC (small cell) and described its clinicalopathological presentation. The presentation of this tumor with respiratory distress in a non smoker male patient with a small size mass in subglottic area is the interesting feature of this report.

Case presentation

A 57-year-old non-smoker man referred to our otolaryngology clinic with a history of four-month hoarseness. He also complained of progressive dyspnea since 2 months ago, without cough or aspiration. Direct laryngoscopy revealed a smooth non-ulcerated tumor which was located in the subglottis and vocal cord fixation in the right side. (Figure 1). The mentioned lesion had a red appearance without necrosis. Her general condition was good with unremarkable physical examination. Also, an enlarged cervical lymph node was palpated in level 6.

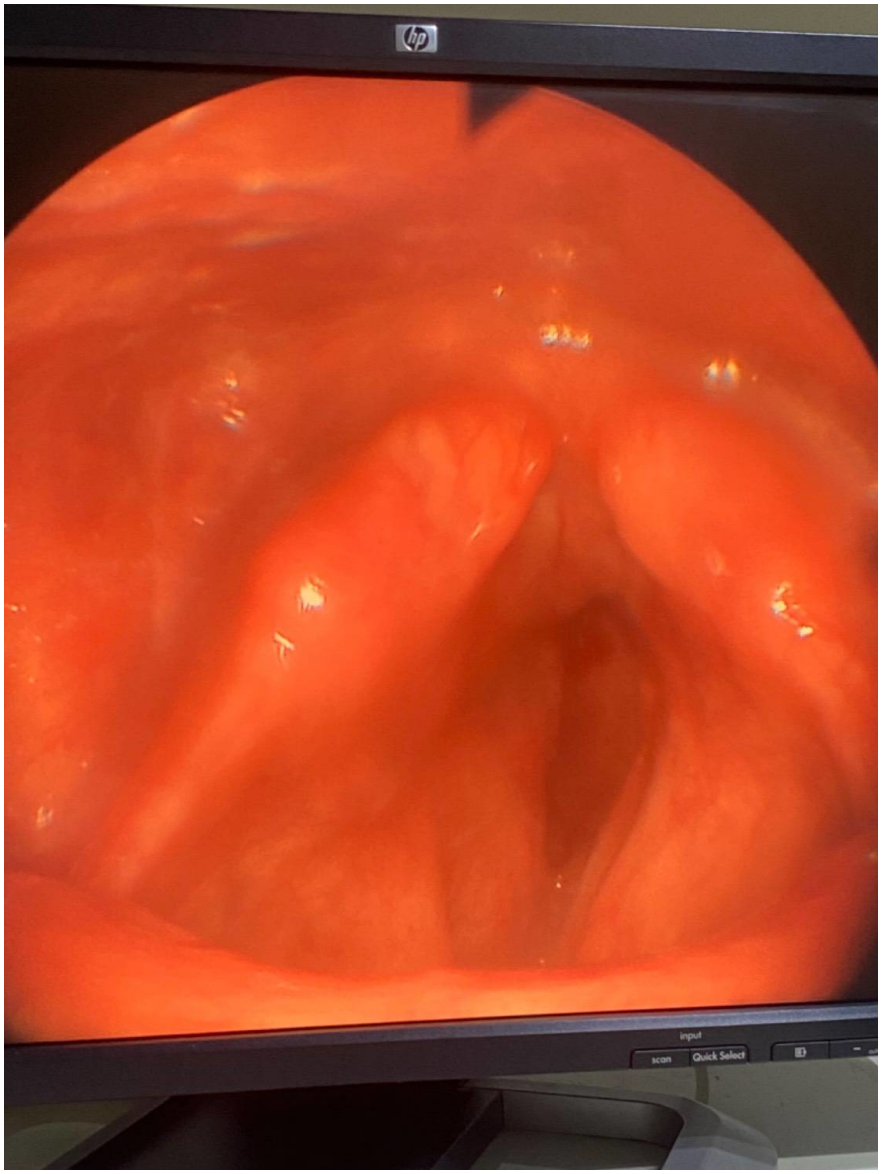


Figure 1: Laryngoscopic images showing a red mass in the sub glottis.

The computerized tomography scan was requested that showed a mass in the subglottic. Glottis and supraglootis were free of tumor.Also, An enhanced metastatic cervical lymph node was detected in pre laryngeal area (Figure 2). Moreover, on the chest, abdominal computerized tomography scan, and bone scan no distant metastatic lesion was noted.

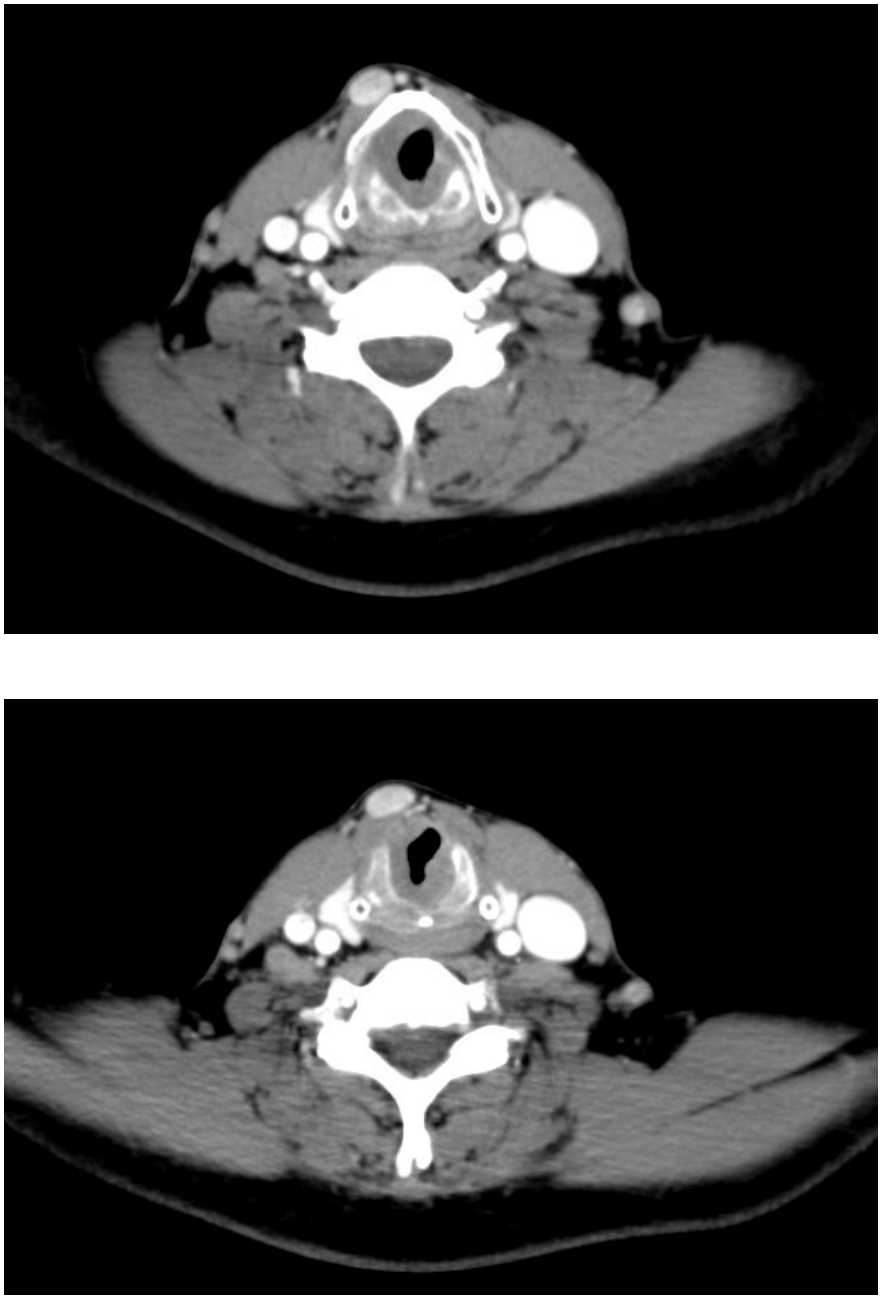
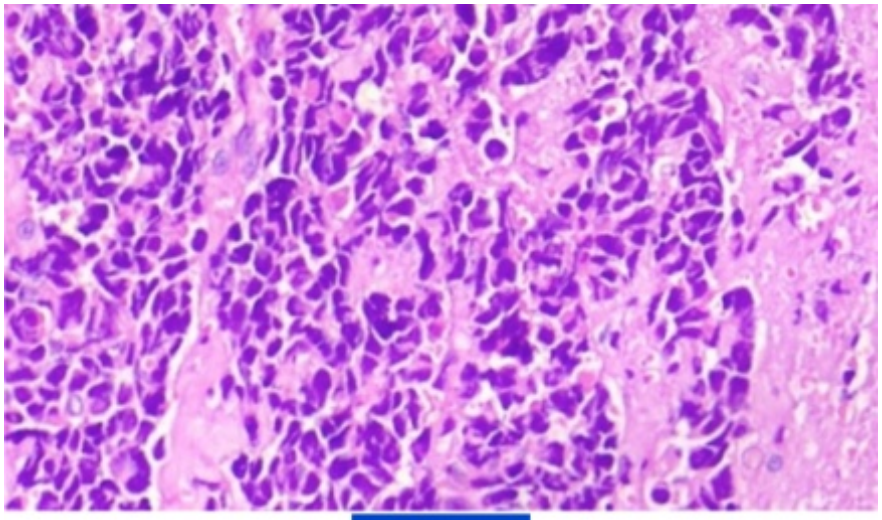
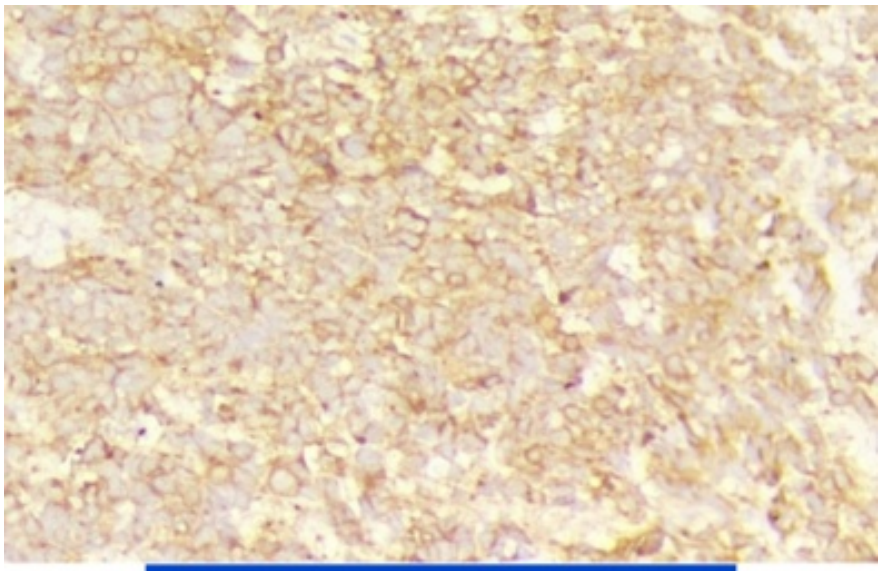


Figure 2.Contrast-enhanced computed tomography scan showing subglottic tumor with an enhanced pre laryngeal node.

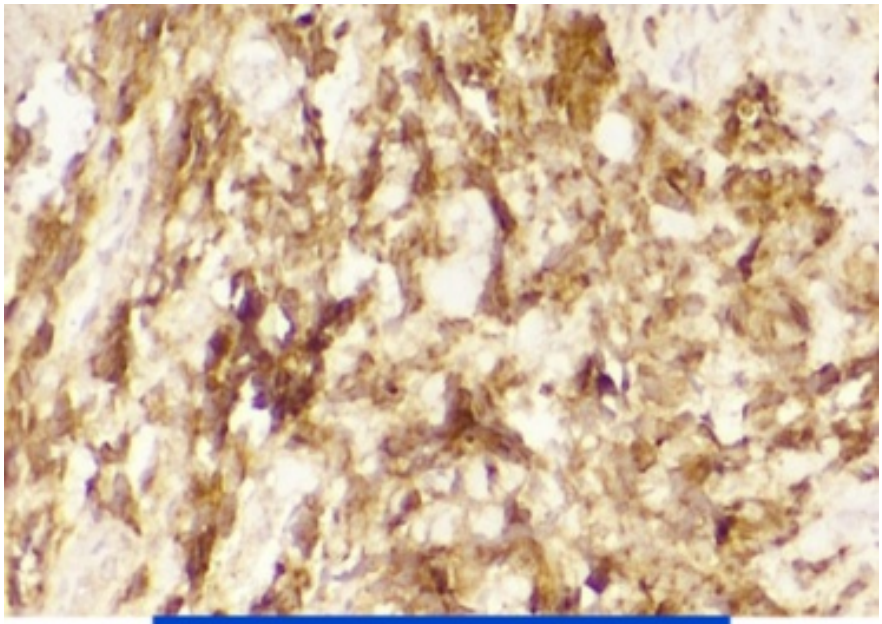
Direct laryngoscopy and biopsy was performed under general anesthesia. The histopathology findings were suggestive for neuroendocrine carcinoma. Microscopic histopathology analysis showed a tumor consist of small size neoplastic cells with acidophilic cytoplasm, coarse chromatin pattern with areas of necrosis and a high mitotic rate (more than 10/mm2).Immunohistochemistry was positive for creatine kinase 7, synaptophysin, chromogranin, Cluster of differentiation (CD) 56, and ki67(Figure 3). The Ki-67 index was 45%. These findings were consistent with the diagnosis of small cell NEC.



H&E

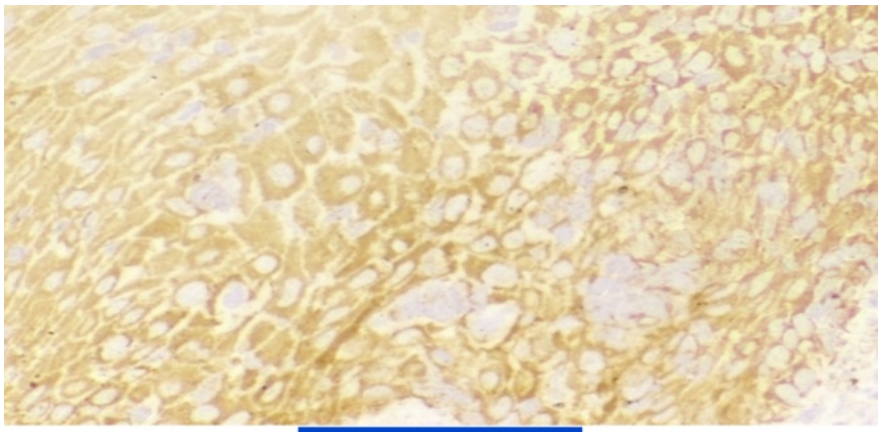


Synaptophysin ×400

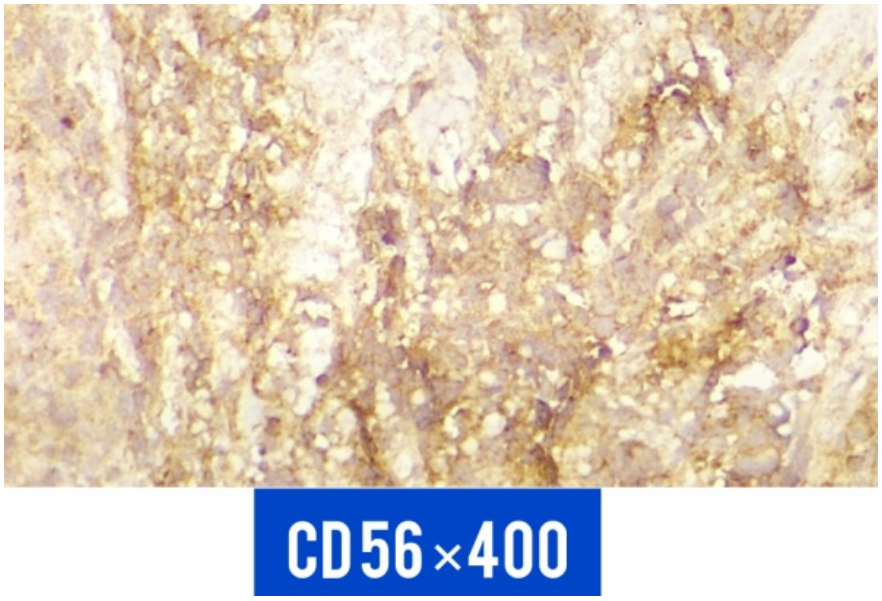


Chromogranin ×400

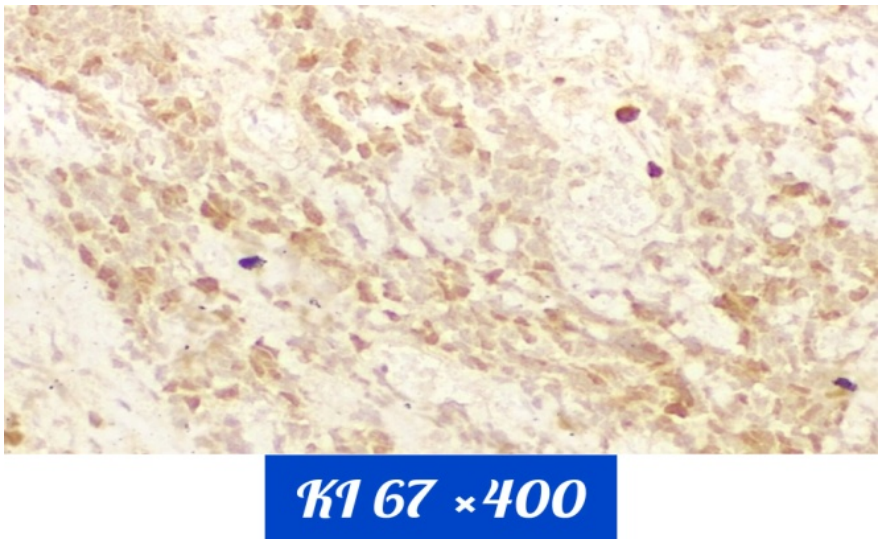
A B C

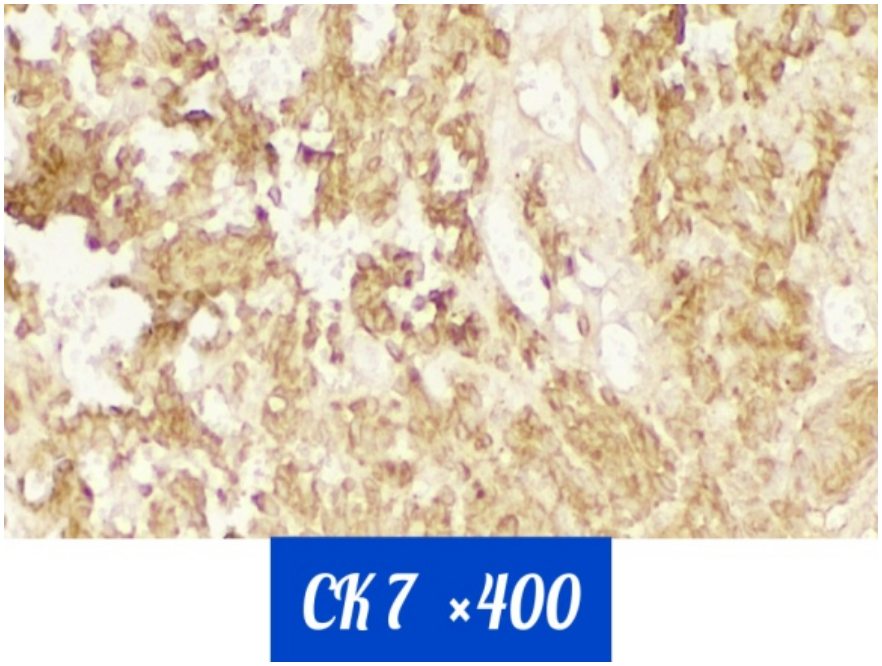


CK ×400



D E





F

F G

Figure 3.A-G H&E stain, ×400. Synaptophysin IHC, ×400. Chromogranin IHC, ×400. CK IHC stain, ×400.CD 56 IHC stain, ×400.KI 67 IHC stain, ×400 . CK 7 67 IHC stain, ×400

Since, chemo radiotherapy is recommended for poorly differentiated NECs, the patient was referred to the radiation oncology department.

Discussion

We describe a rare case of laryngeal NEN in subglottic. While many laryngeal neuroendocrine carcinomas found in the supraglottic, in about 60 to 96 percent of casese.[4]

Although primary neuroendocrine carcinomas are rare, they are the most common non-squamous neoplasm of the larynx. Based on 2017 WHO Classification of Head and Neck Tumors, neuroendocrine tumors of the larynx are classified as well-differentiated neuroendocrine carcinoma: typical carcinoid; moderately differentiated neuroendocrine carcinoma: atypical carcinoid; poorly differentiated neuroendocrine carcinoma: small and large cell neuroendocrine carcinoma, and paragangliomas which have a neural origin. Moreover, based on Neuroendocrine carcinoma (NEC) classification as suggested by the International Agency for Research on Cancer (IARC) and World Health Organization (WHO), in poorly differentiated epithelial neoplasms, Microscopic histopathologic analysis showing tumor necrosis, and mitotic rate of $> 10/2$ mm2.[5]

Atypical carcinoid is the most common neuroendocrine carcinomas of the larynx that represents 0.2% - 0.6% of laryngeal malignancies.[3, 5]Also, atypical carcinoid has more aggressive character that metastasis to cervical lymph nodes, bone, skin, liver, and lung are frequent in their disease nature .[6,7]Laryngeal NENs typically affect middle-aged patients with a history of heavy smoking with a male preponderance.[8]The common clinical manifestations are Hoarseness, dysphagia, and sore throat. In rare cases paraneoplastic syndrome happens. Moreover, cervical lymph node metastases and cutaneous metastases may detect in some cases.[9]

With this in mind, treatment and prognosis of the various NEC groups differ; precise identification of tumor group is critical. Although, surgery is usually the treatment for all tumor type, chemotherapy may be utilized

for moderately to poor differentiated NECs. Laryngeal well-differentiated NEC is treated with wide local excision, generally a partial laryngectomy, without neck dissection. While, in moderately differentiated NECs partial or total laryngectomy with elective or therapeutic neck dissection is necessary. However, adjuvant chemo radiotherapy may be beneficial in some case. Eventually, chemo radiotherapy is recommended for poorly differentiated NECs because surgery is ineffective in these group.[10]Furthermore, tumor prognosis differs among various tumors types. A 5-year disease-specific survival rate is about100%, 53%, 19%, and 15%, in Well-differentiated NEC, Moderately differentiated NEC, small cell NEC, and large cell NEC respectively.[4]

Conclusion:

In conclusion, the differential diagnosis in a patient with hoarseness, dyspnea, and subglottic mass must consist of neuroendocrine carcinomas. Due to tumor rarity, pathological diagnosis should be confirmed by immonohistochemistery. Irradiation and chemotherapy are recommended for treatments in poorly differentiated NEC.This case report of poor differentiated NEC and the corresponding literature review provide useful insight for otolaryngologist to improve their knowledge in the diagnosis and treatment of this aggressive neoplasm.

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