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Case Report
Neuroendocrine tumor

HIDING IN THE GULLET - A Case Report of Neuroendocrine tumor of supraglottic Larynx with brief Literature Review

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Laryngeal neuroendocrine tumours (NET) are infrequent tumors of the head and neck comprising <1% of all laryngeal neoplasms1. These tumors are common in elderly men and often occur in the supraglottic larynx. They have a wide pathologic spectrum ranging from well-differentiated neuroendocrine tumours (NETs) to poorly differentiated neuroendocrine carcinomas(NECs). In this case, the report presents the occurrence of a grade II Neuroendocrine tumor of the supraglottic larynx in an elderly female which is rarely reported in the literature.

Keywords: Larynx, neuroendocrine tumor, well-differentiated

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Introduction

Laryngeal neuroendocrine tumors(NET) are infrequent tumors of the head and neck comprising <1% of all laryngeal neoplasms [1]. These tumors are more common in elderly men and occur in the supraglottic larynx. They are divided into three categories namely well differentiated, poorly differentiated and mixed neuroendocrine and non neuroendocrine neoplasms. Well-differentiated NETs are rare and are further classified into three grades based on mitotic count, ki67 and necrosis.

Case report

A 75-year-old female presented with complaints of dysphagia and hoarseness of voice for two months. There was no cervical lymphadenopathy on examination. CT's neck showed a soft tissue-dense lesion over the right aryepiglottic fold with partial obliteration of the right pyriform fossa. She underwent a laryngeal endoscopy and an excision biopsy of the mass(Fig.1) which was sent for histopathological examination. We received soft tissue in multiple pieces in toto measuring 2x1x0.5cm. Histopathology showed a tumour arranged in small nests and trabeculae with intact overlying lining squamous epithelium(Fig.2a). The tumour cells had moderate eosinophilic cytoplasm mild to moderate nuclear atypia with finely stippled chromatin(Fig.2b) and mitosis 2/sq.mm. No necrosis was made out. IHC showed diffuse strong cytoplasmic positivity for pan-cytokeratin (Fig.3a) and synaptophysin(Fig.3b) diffused weak cytoplasmic positivity for chromogranin(3c). P63 and CK5/6 were negative. The ki67 index was 8%. A diagnosis of grade II neuroendocrine tumor was made. The postoperative period was uneventful and the patient is on regular followup.

Discussion

Neuroendocrine tumors of larynx are broadly divided into epithelial and paraganglionic types based on their tissue of origin [2]. The epithelial-derived tumors are uncommon and account for less than 0.1% of laryngeal malignancies. These tumours arise from dispersed neuroendocrine cells that are found in respiratory mucosa of nasal cavity, paranasal sinuses, nasopharynx, oropharynx and larynx. In larynx, these tumors are second most common after squamous cell carcinoma.

They are more frequent in males in their 6th and 7th decade. Smoking is involved in the aetiology of laryngeal Neuroendocrine neoplasms and is correlated with aggressive behaviour [3]. Pathogenesis is obscure.

The recent WHO(5th edition) classification of neuroendocrine tumors of the larynx divides neuroendocrine neoplasms into well-differentiated (neuroendocrine tumor, NET) and poorly differentiated neuroendocrine neoplasms (neuroendocrine carcinoma, NEC) [4]. Well-differentiated Neuroendocrine tumours are further assigned three grades(G1, G2, G3) based on the presence of necrosis, mitotic rate and ki67 proliferation index. G1 NETs lack necrosis and have <2 mitoses per 2mm2. G2 NETs may have necrosis and/or 2-10 mitoses per 2mm2. The KI67 index for NETs is generally <20%. G2 NET is the most frequent type followed by NEC and G1 NET. Neuroendocrine carcinoma refers only to poorly differentiated NENs and includes both small-cell and large-cell NECs.

Macroscopically NETs present as polypoid nodular pedunculated exophytic masses that may ulcerate. Microscopically, NET G2 tumors are characterized by nest cords and trabeculae of uniform small cells with round nuclei, finely stippled chromatin and inconspicuous mitoses in a fibrovascular stroma. Gland-like structures or rosettes may be seen. Certain studies have identified peculiar ‘glomeruloid structures,’ unique to the NET G2 that may serve as a diagnostic clue in a small biopsy [5]. Some tumors may show a predominance of clear cells, oncocytic, and rhabdoid cells. Occasionally, intranuclear inclusions, nuclear grooves, Leisegang rings(laminated, ring-like structures) and hyaline globules can be identified in these tumors. Our case was a grade II neuroendocrine tumor with mitosis 2/sq.mm, no necrosis and a ki67 index of 8 %.

A panel of IHC markers is necessary to complement the diagnosis and to rule out the differentials [6]. NETs show diffuse nuclear INSM1 immunopositivity and cytoplasmic synaptophysin and chromogranin A staining. They can be positive for keratins including CK7/8 and CAM5.2. Unlike poorly differentiated neuroendocrine carcinomas, NETs do not show aberrant expression of p53 and Rb [7]. Our case showed positivity for pan ck(Fig3a) synaptophysin(Fig.3b) chromogranin(Fig.3c) with a ki67 index of 8%.

The Differential diagnoses that could be considered in a case of G2 NET are Squamous cell carcinoma, low-grade salivary gland neoplasms, Paraganglioma, Medullary thyroid ca and Mixed neuroendocrine and non-neuroendocrine neoplasms(MiNeN) []. Nested architecture and Neuroendocrine marker positivity of NENs overlap with PGL. Unlike NENs, laryngeal PGLs are predominantly seen in females, in the subglottic region and have a favourable clinical outcome. Paragangliomas are CK negative, s 100 and GATA3 positive. Medullary thyroid CA shows diffuse TTF1 positive and can be ruled out by clinical correlation. Both of these were ruled out in our case by negative immunostains and by clinical correlation. Mixed neuroendocrine and non-neuroendocrine (MiNeN) also occur in the nasal cavity and larynx in which case it is a neuroendocrine tumor combined with squamous or adenocarcinoma.

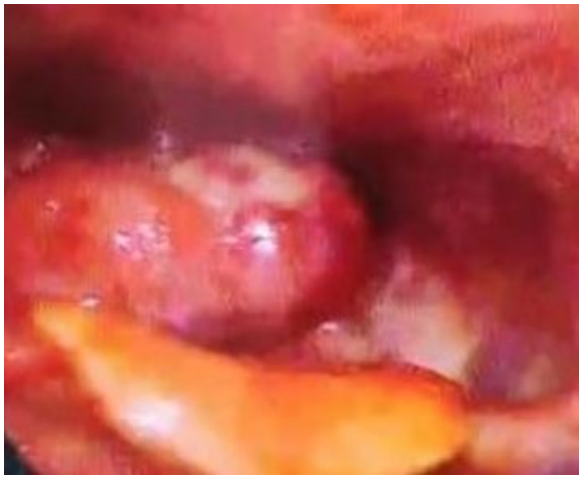

Figure 1: Endoscopic image showing the small polypoidal mass in the larynx

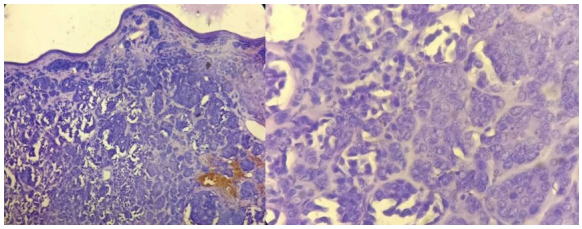

Figure 2(a): Photomicrograph of low power view of the tumor showing intact surface epithelium and tumor cells arranged in small nests in a vascular stroma(H&E, x10). (2b) tumour cells with round nuclei finely stippled chromatin and inconspicuous nucleoli (H&E, x 400)

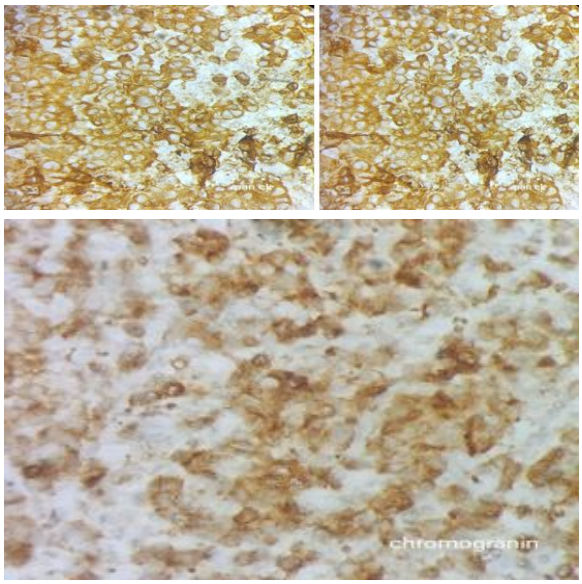

Figure 3(a): The tumor cells are immunoreactive for(a) PanCK (b) Synaptophysin and (c) chromogranin (IHC, x 400)

Treatment of neuroendocrine tumors of the larynx includes surgical resection with neck dissection followed by adjuvant chemo and/or radiotherapy when there is regional lymph node metastasis. Low-grade laryngeal NETs have a reported 5-year survival of approximately 80% after conservative surgical resection.

Lymph node metastasis is infrequent and distant metastasis to the liver has been rarely reported. Laryngeal NETs present with advanced disease in about 20-30% of cases and recur in about 60% of cases [9]. In our case, the patient underwent conservative resection with no residual tumor and is on close follow-up.

Conclusion

Neuroendocrine neoplasms of the larynx are rare and have a wide pathologic spectrum. With a diligent mind, these tumors need to be differentiated from their mimickers as accurate diagnosis and grading are of importance in prognostication and therapy. Grade II NETs of the larynx are rarely reported in the literature and carry a good prognosis for lower-stage tumours.

Contributions

1. Collection of case details, follow-up data, literature review, and prepared manuscript.

2. Literature review, Preparation of figures, prepared manuscript
3. A literature review prepared and edited manuscript and figures

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Disclosure: Nil

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