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Laryngeal Paraganglioma: A Diagnostic Challenge

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ABSTRACT

Paragangliomas are neoplasms of neural crest origin. In the head and neck, they uncommonly involve the larynx. The distinction between paragangliomas and other neuroendocrine tumors can be difficult. Precise diagnosis is important in order to optimize patient treatment. Diagnosis relies mostly on histopathologic examination followed by immunohistochemistry. Here we report a 77-year-old woman with laryngeal paraganglioma that initially misdiagnosed as laryngeal carcinoid tumor.

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Introduction

Ferlito and Friedmann divided neuroendocrine tumors of the larynx into four main types: typical carcinoid, atypical carcinoid, small cell neuroendocrine carcinoma and paraganglioma (1). However, in 1991, Ferlito and Rosai reclassified these tumors into two main groups: tumors with epithelial origin i.e., typical carcinoid, atypical carcinoid, small cell neuroendocrine carcinoma or neural origin i.e. paraganglioma (2). Although neuroendocrine neoplasms are uncommon tumors of the larynx, they represent the most common nonsquamous neoplasms of this organ (3). The larynx contains two sets of normal paraganglia

and paragangliomas are thought to arise from the superior or inferior laryngeal paraganglia (4). It is important that paragangliomas be differentiated from other neuroendocrine tumors of the larynx, including atypical carcinoid, because of differing treatment modalities. Distinguishing laryngeal paraganglioma from other neuroendocrine tumors can be difficult. Immunohistochemistry is an important tool for the correct pathologic diagnosis.

We present a case of laryngeal paraganglioma that initially misdiagnosed as laryngeal carcinoid tumor.

Case Report

A 77-year-old woman presented with a several

days history of hemoptesis. She gave a history of hoarseness since 2 years ago and snoring in the last 6 months. Indirect laryngoscopy revealed a right-sided mucosa-covered supraglottic mass. Fiber optic laryngoscope showed a mass arising from right aryepiglottic fold. Both of the vocal folds had normal movement. On neck examination no lymph node enlargement was observed. The patient underwent an incisional laryngoscopic biopsy.

Microscopically, the specimen was covered by a mucosal layer of stratified squamous epithelium with infiltration of tumoral cells in the stroma. Tumor cells, exhibiting small, round,

homogeneous nuclei and slightly eosinophilic cytoplasm, were arranged as nests. Abundant sinusoidal capillaries were also noted between tumor nests. Mitosis was rarely seen among the cells. According to these histopathologic findings, a provisional diagnosis of neuroendocrine tumor, in favor of carcinoid tumor was made.

Subsequently, the patient underwent an elective supraglottic laryngectomy, without neck dissection, concurrent with laryngeal reconstruction and tracheostomy. Histopathologic examination of the specimen showed a very vascular tumor with nests of cuboidal cells separated by vascularised septa

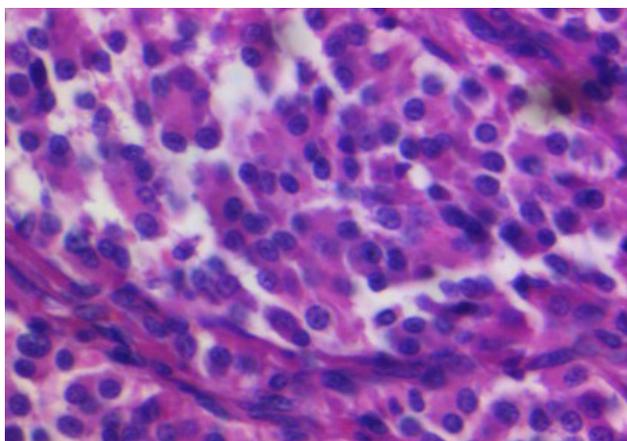


Fig. 1
Section shows nests of cuboidal cells separated by vascularised septae (H&E $\times 40$)

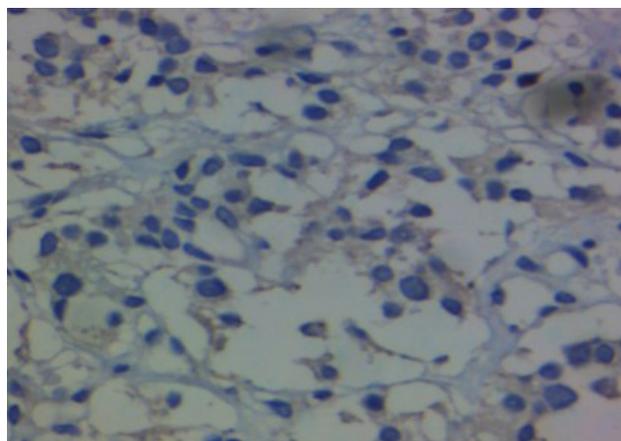


Fig. 2
Tumor cells are negative for pancytokeratin(IHC stain)

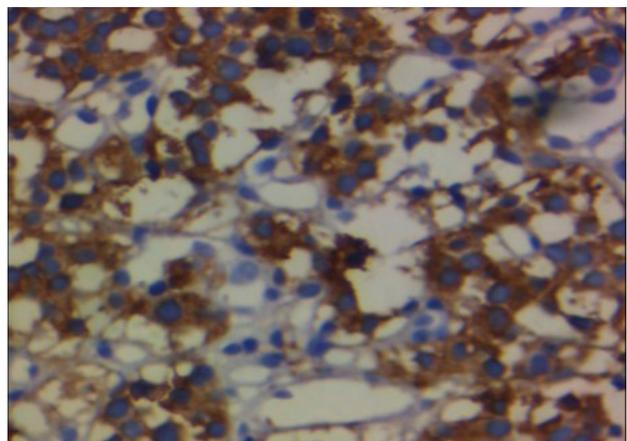


Fig. 3
Tumor cells are positive for chromogranin (IHC stain)

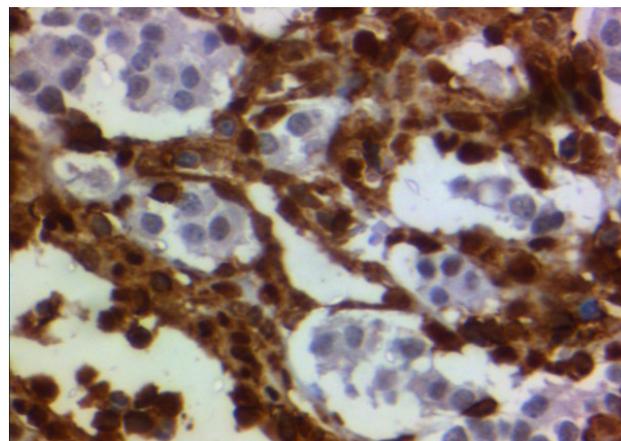


Fig. 4
S100 immunostain marking the sustentacular cells (IHC stain)

(Fig. 1). Mitotic activity was inconspicuous. On immunohistochemistry, tumor cells showed focal expression of neuron specific enolase and chromogranin and were negative for cytokeratin (Fig. 2, 3), whereas sustentacular cells expressed S-100 protein (Fig.4), suggestive of paraganglioma. The patient made an uneventful postoperative recovery. She did not have any evidence of disease at her 7-month follow up after surgery.

An informed consent was from the patient and all ethical issues were observed.

Discussion

Blanchard and Saunders (5) take credit for the first documented description of a paraganglioma of the larynx in 1955. These benign neoplasms have slow growth. Of further interest, Barnes noted a female-to-male ratio of 3:1(6).

Our patient was a 77 years old woman. The majority of laryngeal paraganglioma arise in the supraglottic larynx. It was true in the presented case. The most common presenting symptoms are hoarseness, throat pain, dysphagia, dyspnea, hemoptysis, and airway obstruction. The current case gave a history of hoarseness since 2 years ago, however Beigi et al. presented a case of a supraglottic paraganglioma who presented with intermittent dysphasia to solid foods and dyspnea (7). On the other hand, Olgun Kadir Aribas et al. reported a patient with paraganglioma originating from the inferior laryngeal paraganglion, who had been followed for goiter for 10 years (8).

It is claimed that about 2% of these tumors are malignant (9). However, pathologic findings cannot predict clinical behavior. Joseph R Smolarz et al. reported a 50 year-old man with left supraglottic paraganglioma who underwent laryngectomy but eight months after surgery, he presented with bilateral lung and brain metastases. Although he was treated with systemic chemotherapy but developed spinal metastases and died from his disease 16 months

after diagnosis (10).

The main differential diagnosis is typical carcinoid tumor and atypical carcinoid tumor, which may also have finely stippled chromatin and focally have a Zellballen pattern. However the "Zellballen" pattern is not diagnostic of a paraganglioma as it may also exist in a variety of other tumors including other neuroendocrine tumors and even unrelated neoplasms such as malignant melanoma and medullary carcinoma of thyroid (11). Atypical carcinoid tumor cell has a higher nucleus-to-cytoplasm ratio than paraganglioma. Infiltration, necrosis, or mitotic figures may be appreciated (12).

Barnes reviewed 78 purported cases (6). Of these, 34 were accepted as paragangliomas. The remaining 44 cases were considered to be "unacceptable." Immunohistochemistry is helpful in establishing the correct diagnosis. The presence of chromogranin positivity excludes non neuroendocrine neoplasms (11). Both paragangliomas and typical and atypical carcinoid tumors express neuroendocrine markers, including neuron-specific enolase, chromogranin, and synaptophysin (13). However, the sustentacular cells of paragangliomas will stain strongly for S-100 protein and glial fibrillary acidic protein (13). These cells and this staining are lacking in typical and atypical carcinoid tumors. In contrast, paragangliomas are cytokeratin negative, whereas this marker is usually positive in typical and atypical carcinoid tumors (13).

Surgical resection remains the standard of care for their treatment, although radiotherapy may be considered in selected patients. Limited data is available on the role of external beam radiation therapy for the management of this disease (10).

Conclusion

Close collaboration with an experienced pathologist and special methods are necessary to establish the diagnosis of laryngeal

paraganglioma.

Acknowledgements

The authors declare that there is no conflict of interests.

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