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Case Report · Description de cas · Fallbericht

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3 Paraganglioma of the Larynx

024 Case Report and Literature Review

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Abstract
The laryngeal paraganglioma (LP) is a rare neuroendocrine neoplasm which arises from paraganglionic tissue normally present in the larynx. Immunohistochemistry is essential in the differential diagnosis of the various neuroendocrine neoplasms. The study presents a case of LP arising in an otherwise healthy 30-year-old black woman. Direct laryngoscopy revealed a large mass obstructing the airway almost completely. The patient underwent a total laryngectomy. Histopathological examination showed a population of epithelioid cells arranged in round nests and balls surrounded by a delicate stroma ('Zellballen' pattern). The histological and immunohistochemical patterns were coherent with LP. At 24 months after excision, she shows no evidence of disease.

Paragangliom des Larynx: Fallbericht und Literaturübersicht

Das laryngeale Paragangliom ist ein seltenes neuroendokrines Neoplasma, welches von normalerweise im Larynx vorkommendem paraganglionärem Gewebe ausgeht. Für die Differentialdiagnose der verschiedenen neuroendokrinen Tumoren ist die Immunhistochemie essentiell. Die Studie beschreibt den Fall einer sonst gesunden 30-jährigen Patientin mit einem lanryngealen Paragangliom. Die direkte Laryngoskopie zeigte eine grosse Raumforderung, welche nahezu den gesamten Larynx obstruierte. Es wurde eine totale Laryngektomie durchgeführt. Die Histologie zeigte eine Population von Epitheloidzellen, angeordnet in runden Nestern und Haufen, umgeben von Stroma («Zellballen»-Muster). Die histologischen und immunhistochemischen Befunde bestätigten ein laryngeales Paragangliom. Die Patientin ist 24 Monate nach der Laryngektomie rezidivfrei.

Paragangliome du larynx: à propos d'un cas et revue de la littérature

Le paragangliome laryngé est une tumeur neuro-endocrine rare qui se développe au dépens du tissu paraganglionnaire normalement présent dans le larynx. Un examen immunohistochimique est essentiel pour le diagnostic différentiel des diverses tumeurs neuro-endocrines. Ce travail présente un cas de paragangliome laryngé chez une femme de 30 ans, d'origine africaine, en bonne santé habituelle. La laryngoscopie directe mettait en évidence une volumineuse masse obstruant quasi complètement le fût laryngé. Une laryngectomie totale a été faite. L'examen histopathologique montrait des cellules épithéloïdes en amas circulaires ou sphériques, entourés d'un fin stroma. L'examen histologique et immunohistochimique était compatible avec un paragangliome laryngé. Il n'y a pas de signe de récidive 24 mois après la chirurgie.

Introduction

The laryngeal paraganglioma (LP) is a rare neuroendocrine neoplasm which arises from paraganglionic tissue normally present in the larynx. This tumor is a neuroendocrine neoplasm of neural type, while the epithelial group can be divided into typical and atypical carcinoids and small neuroendocrine carcinomas. More than 90% of the tumors occur in the supraglottic region, in particular in the aryepiglottic region, but may also arise in the subglottic region [1–3].

Immunoistochemistry is essential particularly in the differential diagnosis of the various neuroendocrine neoplasms [4].

Case Report

An otherwise healthy 30-year-old black woman was seen with a severe airway obstruction secondary to an endolaryngeal mass at the North Kinangop Catholic Hospital, Kenia (2,500 m above sea level), where two of the authors were doing a period of voluntary service. The symptoms included hoarseness, dysphagia and weight loss. The medical history revealed that several years prior to admission the patient had undergone an endoscopic excision of a laryngeal mass in another Kenyan hospital, but no documents were available. She underwent an emergency tracheotomy followed by direct laryngoscopy which revealed a large mass involving the right aryepiglottic fold, the adjacent false cord, ventricle, vocal cord and the subglottic region; it obstructed the airway almost completely. Biopsy of the mass was performed, and the histopathological features were coherent with LP. It was not possible to perform CT or MR. The patient underwent a total laryngectomy.

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Definitive histopathological examination, performed in Italy, showed a population of epithelioid cells arranged in round nests and balls surrounded by a delicate stroma ('Zellballen' pattern; fig. 1–3). The tumor stained positive for chromogranin, and S-100 protein was identified in small elongated sustentacular elements present at the periphery of rounded cell nests (fig. 4). The diagnosis was larynx paraganglioma.

Her recovery was uncomplicated, and the patient was discharged after 11 days. At 12 months after excision, she shows no evidence of disease.

Discussion

The LP is a neuroendocrine neoplasm of neural type while the epithelial group can be divided into typical and atypical carcinoids and small neuroendocrine carcinomas. The latter three are malignant, whereas LP seems to be almost exclusively benign with only 1 acceptable case of metastatic paraganglioma in the literature [5]. LP can arise from two pairs of paraganglia in the larynx: one superior glomus in the upper and anterior third of the vestibular folds and an inferior glomus above the division of the recurrent laryngeal nerve into its anterior and posterior branches, at the level of the inferior border if the thyroid cartilage. The superior glomus has a multiple distribution in relation to the aryepiglottic fold and the arytenoid region [6].

More than 90% of the tumors occur in the supraglottic region, in particular in the aryepiglottic region with a preponderance to the right side, but may also arise in the subglottic region [1–3].

Paraganglioma is the only laryngeal neuroendocrine neoplasm with a female prevalence [5], with most cases presenting in the fourth to sixth decades of life [1, 7].

Patients present with a variety of symptoms, including hoarseness, dysphagia, dyspnea, stridor, sore throat or hemoptysis. As a rule, LPs are not catecholamine-producing tumors and they are seldom associated with paragangliomas in other sites; paraneoplastic syndromes have not been reported.

The causes of this neoplasm are obscure; there are reported increases in the incidence of cervical paraganglioma at high altitudes as a consequence of factors leading to chronic hypoxia [8, 9].

Macroscopically the tumors are generally encapsulated, blue or pink with hemorrhagic areas, from few to several centimeters in size. The neoplasm is composed of chief cells arranged in clusters and round cell nests ('Zellballen' pattern) surrounded by a delicate stroma containing numerous vascular channels. The cells have an abundant granular eosinophilic cytoplasm and large vesicular nuclei. Mitoses, necrosis and vascular invasion are infrequent and do not necessarily indicate aggressive or malignant behavior [10]. Dendritic spindle cells or sustentacular cells are seen.

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LP stains positive for chromogranin, synaptophysin, neuron-specific enolase, protein gene product 9.5, met-enkephalin and serotonin. S-100 protein and glial fibrillary acidic protein are not identified in the chief cells but may be present in the sustentacular cells.

LP has been confused with a variety of other primary and secondary laryngeal tumors (carcinoid tumor, melanoma, metastatic renal cell carcinoma, medullary carcinoma of the tyroid); the atypical carcinoid is the neoplasm that has caused the greatest diagnostic confusion.

Immunohistochemistry is among the most significant investigations for the differential diagnosis of the various neuroendocrine neoplasms of the head and neck. Positivity for keratin, epithelial membrane antigen, carcinoembryonic antigen and calcitonin is very common in atypical carcinoid tumor but is incompatible with the diagnosis of paraganglioma [6].

Contrast CT and/or MRI with gadolinium are useful in demonstrating the extent of the lesion. Angiography can also be useful [11].

Immunohistochemistry is essential particularly in the differential diagnosis of the various neuroendocrine neoplasms [4].

Conservative surgery is the treatment of choice, and elective neck dissection is not necessary; very large tumors may require total laryngectomy. Preoperative embolization seems unnecessary. Endoscopic excision should be avoided since bleeding (even from the biopsy) can be difficult to control [10, 12] and laser therapy has not been successful [13].

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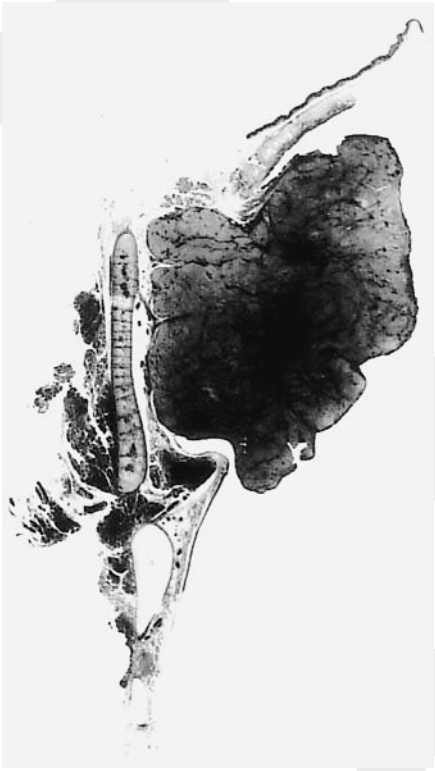
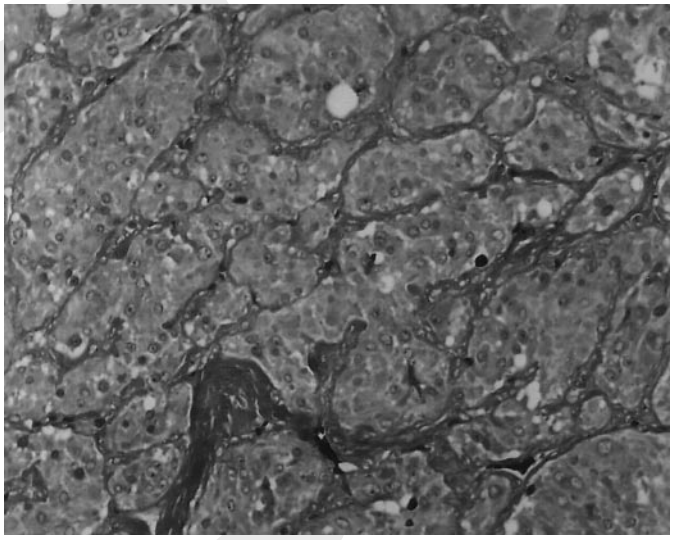


Fig. 1. Surgical specimen: a well-circumscribed solid neoplasm, characterized by a lobulated smooth outline is located subglottically in the laryngeal ventricle. ■■■. ×1.



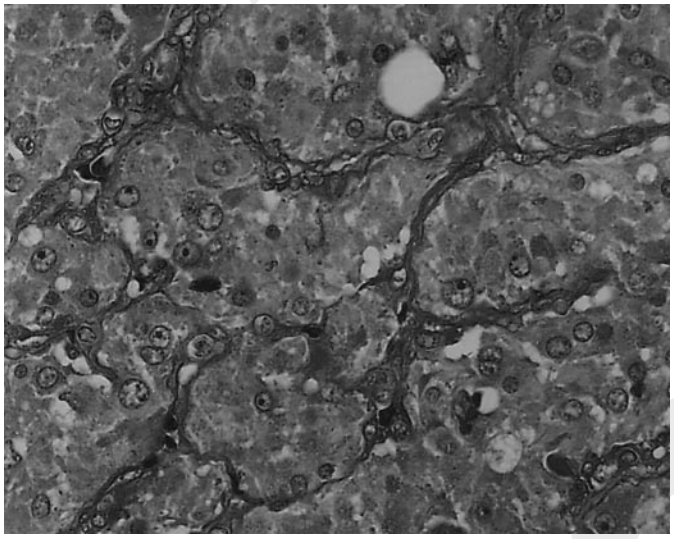


Fig. 2, 3. The tumor cells are arranged in round nests and balls; they are epithelioid, with inconspicuous cell borders and syncytial appearance, the cytoplasm is ample and nuclei are mainly round, can vary in size and sometimes demonstrate a prominent nucleolus. **2** ■■■, ×250; **3** ■■■, ×400.

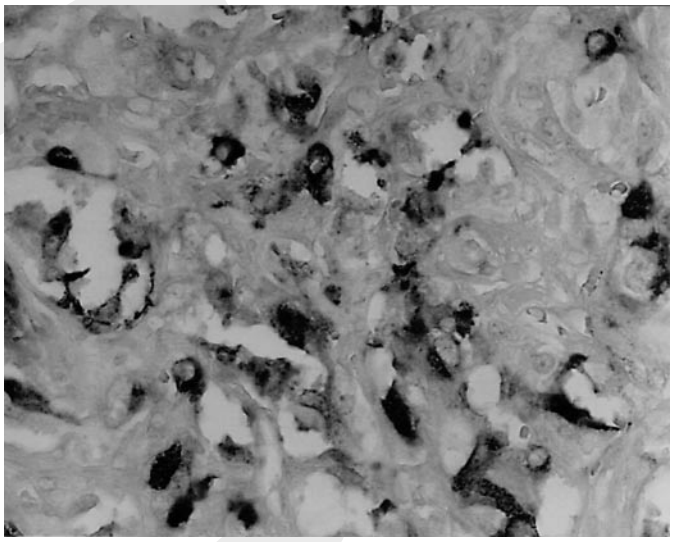


Fig. 4. Positivity for S-100 in small elongated sustentacular cells present at the periphery of rounded cell nests. ×240.

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