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Malignant Paraganglioma in the Left Parotid Region

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Paragangliomas are rare tumors arising from paraganglionic tissue derived from neural crest cells. In the head and neck region, these tumors most commonly originate from the carotid body, vagal paraganglia or the jugulotympanic area, whereas involvement of the parotid gland is extremely uncommon. We report a case of a 54-year-old male patient presenting with a large infiltrative tumor involving the left parotid region. Computed tomography revealed a heterogenous soft tissue mass extending from the skull base to the level of the fifth cervical vertebra, with invasion of surrounding structures and regional lymphadenopathy. Histopathological examination demonstrated tumor cell nests arranged in a characteristic pattern. Immunohistochemical analysis was also performed for confirmation. The findings determined the diagnosis of malignant paraganglioma. Following surgical treatment, the patient was referred to for postoperative radiotherapy. This case highlights the rarity, aggressive behavior and diagnostic challenges associated with parotid paragangliomas, with only isolated cases described in the literature.

Key words: malignant paraganglioma, parotid, head and neck tumor

Introduction

Paragangliomas (also called extra-adrenal or sympathetic paragangliomas) are rare neuroendocrine tumors originating from paraganglionic cells derived from the neural crest [6, 10]. They are closely related to pheochromocytomas, with a histological similarity as well [5]. Paragangliomas can develop in various anatomical locations along the autonomic nervous system.

Within the head and neck region, paragangliomas most commonly arise from the carotid body, jugulotympanic region, and vagal paraganglia [2, 7]. Involvement of

the parotid gland is exceptionally rare and only a limited number of cases have been described in the literature [2, 8]. Although categorization into benign and malignant is discouraged because all paragangliomas have a metastatic potential [4, 9], depending on the tumor presentation, we can predict its behavior to help determine the treatment and prognosis.

Because of their rarity and nonspecific clinical presentation, malignant paragangliomas may pose a significant diagnostic challenge. Imaging tests combined with histopathological and immunohistochemical examination are essential for establishing the correct diagnosis [5, 9]. Our report describes a rare case of malignant paraganglioma involving the left parotid region.

Case Report

We present a case of a case of a 54-year-old male patient with a massive soft tissue tumor formation detected during computed tomography (CT) examination. The lesion had an irregular shape and was located predominantly in the left parotid region. Radiological evaluation demonstrated that the tumor originated from the skull base on the left side and extended caudally to the level of the fifth cervical vertebra (C5). The lesion showed invasive growth with involvement of the surrounding structures, including the pharynx and larynx, which were displaced to the right. The tumor caused lysis of the skull base and infiltration of the left sternocleidomastoid muscle and the left parotid gland. Extension toward the left cerebellar hemisphere was also observed. The mass had an axial dimension of 5.6 x 8.9 cm and a coronal dimensional of 7.9 cm. The lesion demonstrated a native density of approximately 48 HU (Hounsfield units), increasing to 65-130 HU in the arterial phase and 68-104 HU in the venous phase following contrast administration. Additionally, diffuse packages of cervical and submandibular lymph nodes of varying size were detected bilaterally, with maximal diameters up to 1.5 cm. The patient had previously undergone long-term treatment for benign paraganglioma. Following the recurrence of the tumor and subsequent surgical intervention, the histopathological examination revealed a malignant transformation of the lesion.

Tissue specimens were fixed in 10% neutral buffered formalin and embedded in paraffin. Sections of 4 μm thickness were obtained for histological analysis. Further immunohistochemical testing was performed to confirm the diagnosis using the following antibodies – Synaptophysin, Chromogranin, S-100 protein. All the antibodies are supplied by Dako and are ready-to-use (pre-diluted). The staining protocols are validated by Dako.

Hematoxylin and eosin (H&E) staining revealed: Tumor tissue composed of nests and trabeculae of atypical cells arranged within a richly vascularized stroma, consistent with the characteristics of paraganglioma. The tumor cells are invading the capsule and surrounding tissues (**Figs. 1 and 2**).

Immunohistochemical analysis supported this diagnosis: Synaptophysin: diffuse positive staining (++) in tumor cells, Chromogranin: weak diffuse positivity (+) in tumor cells, S-100 protein: positive staining in sustentacular cells surrounding tumor nests (**Fig. 3**).

The extensive imaging tests combined with the information of the tumor behavior, histological and immunohistochemical panel confirmed the final diagnosis of malignant paraganglioma as supported by the images below:

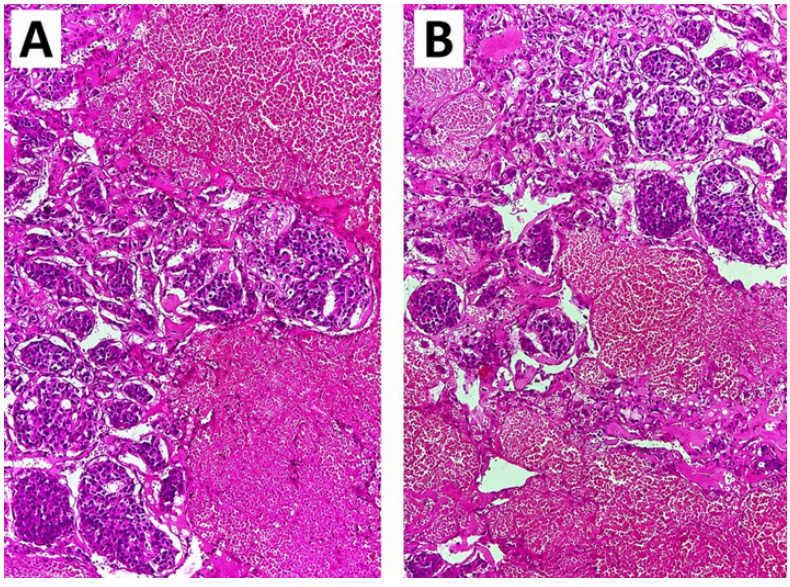

Fig. 1. Both pictures show nests of tumor cells arranged in typical zellballen pattern separated by delicate fibrovascular septa. The cells are polygonal, with eosinophilic cytoplasm and round to oval nuclei. **A.** Vast necrotic areas. (H-E x100). **B.** Lots of hemorrhages (H-E x200).

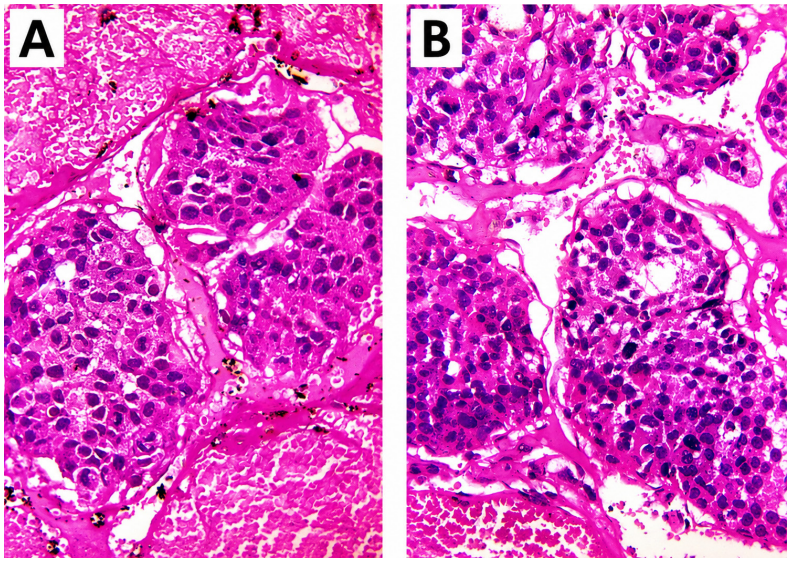

Fig. 2. A. Higher magnification of the same area demonstrates the classic tumor cell pattern, as well as the expressed atypia and mitoses. Necrosis is also seen. (H-E x200). **B.** Emphasis on the vascularized stroma of the tumor. (H-E x400)

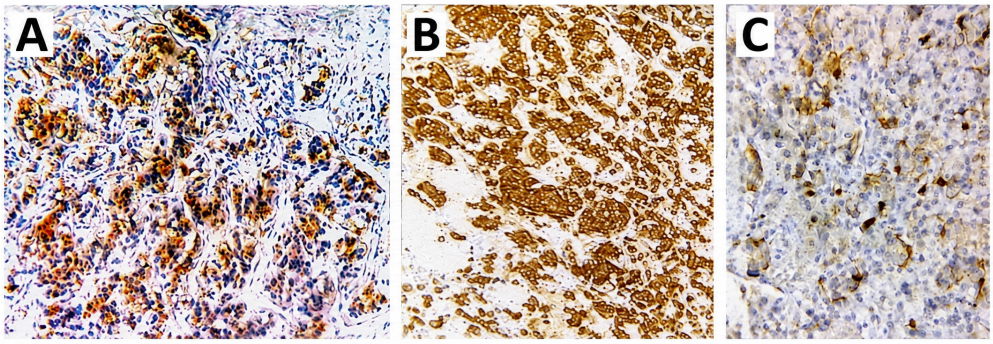

Fig. 3. A. Chromogranin showing diffuse cytoplasmic positivity in tumor cells. **B.** Diffuse cytoplasmic expression of Synaptophysin in tumor cells. **C.** S-100 highlighting sustentacular cells surrounding tumor nests.

Discussion

Paragangliomas of the head and neck represent approximately 0.5% of all tumors in this area [2, 7]. They arise most frequently from the carotid body, jugulotympanic region, and vagal paraganglia [2, 7, 10]. To our knowledge, this is the first reported case of malignant paraganglioma in the parotid region.

Although the majority of paragangliomas exhibit benign biological behavior, malignant transformation can occur in a small percentage of cases [3, 4]. The diagnosis is usually based on imaging, the presence of regional or distant metastases, local invasion, recurrence and histological features.

Radiological imaging plays a crucial role in evaluating tumor extension and its relationship to surrounding structures. Computed tomography and magnetic resonance imaging are particularly useful in assessing the vascularity and extent of the lesions [3, 4].

Histopathological examination is vital for a definitive diagnosis. The typical “zellballen” pattern, consisting of nests of tumor cells separated by fibrovascular septa, is characteristic of paragangliomas [5, 9]. Immunohistochemical markers such as Synaptophysin and Chromogranin confirm neuroendocrine differentiation, while S-100 protein highlights sustentacular cells surrounding tumor nests [5, 9].

Treatment of malignant paraganglioma usually involves surgical resection followed by radiotherapy [4, 8], particularly in cases with incomplete resection or aggressive tumor behavior. Despite treatment, these tumors may demonstrate a tendency for recurrence and metastasis [3, 4].

The differential diagnosis of malignant paraganglioma in the parotid region includes several tumors and tumor-like lesions:

- Vagal schwannoma
- Carotid body paraganglioma
- Metastatic lymphadenopathy

- Medullary thyroid carcinoma
- Hemangioblastoma

Because of the overlapping clinical and radiological features, histopathological examination together with immunohistochemical analysis is essential for establishing the correct diagnosis [7, 8, 10].

The reported 5-year survival of malignant paraganglioma varies depending on the presence of regional or distant metastases, with poorer prognosis in cases with the latter [3, 8].

Conclusion

Malignant paraganglioma of the parotid gland is an extremely rare neoplasm that may present diagnostic and therapeutic challenges. Imaging studies combined with histopathological and immunohistochemical evaluation are essential for establishing the diagnosis. Early detection and appropriate management are crucial due to the potential aggressive behavior, local invasion and recurrence. Reporting rare cases such as this contributes to a better understanding of the biological behavior and clinical management of these tumors, especially in unusual areas like the parotid region.

Patient consent

The authors certify obtaining the patient's consent for using of the information, age and gender, as well as pictures of the microscopic slides.

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