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High-Grade Small Cell Neuroendocrine Carcinoma of the Parotid Gland: A Case Report

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Abstract: ***High-grade small cell neuroendocrine carcinoma of the parotid gland is an uncommon and aggressive malignancy, representing less than one percent of salivary gland tumors (1,2). Distinguishing primary parotid involvement from metastatic disease, particularly pulmonary carcinoma or Merkel cell carcinoma, remains diagnostically demanding (3). An eighty-one-year-old male presented with a left parotid mass and underwent total parotidectomy with facial nerve preservation. Histopathology revealed a small cell neuroendocrine carcinoma confirmed by immunohistochemical markers including chromogranin A, synaptophysin, CD56, INSM1, and a high Ki-67 index. Imaging excluded an alternative primary origin. The patient declined adjuvant therapy. This case underscores the diagnostic value of immunohistochemistry and highlights the clinical course of this rare entity.***

Keywords: Parotid gland carcinoma, Small cell neuroendocrine tumor, Salivary gland malignancy, Immunohistochemistry, Rare head and neck cancer.

1. Introduction

Small cell neuroendocrine carcinoma is a highly aggressive neoplasm that occurs predominantly in males (61.7%), with the highest incidence between the fifth and seventh decades of life, and with primary localization in the parotid gland (83%) (4–6). Due to its aggressive behavior, it is characterized by rapid growth, locoregional infiltration, and frequent involvement of the facial nerve. To date, only a limited number of high-grade neuroendocrine carcinomas arising in the major salivary glands have been reported in the literature, accounting for less than 1% of primary malignant tumors of the parotid gland. Two histologic subtypes are described: small cell and large cell, with differences in the degree of differentiation. In some cases, the tumor originates from Merkel cells or represents metastasis from a primary pulmonary carcinoma (6).

Given the diagnostic overlap with metastatic small cell carcinomas and Merkel cell carcinoma, accurate identification has direct implications for treatment planning and prognosis.

This report aims to describe the clinical presentation, histopathologic features, and diagnostic challenges of high-grade small cell neuroendocrine carcinoma of the parotid gland.

2. Case Report

An 81-year-old male patient from the Caribbean region presented with a hard mass located in the left parotid region. Routine diagnostic studies were performed and ruled out associated comorbid conditions. Computed tomography of the brain, neck, and chest showed no lesions suggestive of a primary tumor in another location or distant metastases (Figure 1).

The patient underwent total parotidectomy under general anesthesia with preservation of the facial nerve. Histopathologic examination revealed a solid tumor measuring 6 X 3 cm, with minimal residual peritumoral parotid tissue. Postoperatively, cervicofacial paresis was observed (Figure 2).

Microscopic evaluation demonstrated preserved serous acini of the parotid gland and a malignant small cell neoplasm composed of cells with scant cytoplasm and nuclei with granular chromatin, arranged in sheets with necrotic areas separated by fibrous stroma (Figure 3).

Immunohistochemical studies were performed using the Ventana BenchMark Ultra platform, yielding the following profile:

- Cytokeratin cocktail (clone AE1/AE3/PCK26): positive, paranuclear dot-like pattern.
- Cytokeratin 20 (clone SP33): negative.
- Chromogranin A (clone LK2H10): positive.
- Synaptophysin (clone SP11): positive.
- CD56 (clone 123C3D5): positive.
- Insulinoma-associated protein (clone BSB-123, BIO SB): positive (Figure 4).
- Cytokeratin 7 (clone SP52): focally positive.
- TTF-1, thyroid transcription factor-1 (clone 8G7G3/1, Cell Marque): focally positive.
- Ki-67 (clone 30-9): 90% (Figure 4).

The final diagnosis was high-grade small cell neuroendocrine carcinoma. It was recommended to rule out its metastatic origin, therefore, whole-body computed tomography was performed and showed no evidence of a primary tumor consistent with pulmonary origin or Merkel cell carcinoma.

The postoperative period was uneventful, with the exception of cervicofacial paresis. The patient was referred to the Oncology Department; however, he declined chemotherapy and expressed his decision to return to his home country, Cuba.

3. Discussion

Neuroendocrine tumors of the parotid gland are extremely uncommon. From an embryological standpoint, they are thought to arise from neural crest–derived cells with neuroendocrine differentiation (7). However, controversy persists regarding whether these tumors are truly primary or secondary to cutaneous or pulmonary carcinomas. Merkel cell carcinoma, first described by Toker in 1972 (8), has been considered one of the potential sources responsible for parotid involvement.

In the literature, most reported cases correspond to small cell carcinomas; less frequently, large cell or well-differentiated (grade 1) tumors are observed, and only a limited number of moderately differentiated cases have been described (7,8).

The WHO Classification of Salivary Gland Tumors divides neuroendocrine neoplasms into two main groups:

- Low-grade neuroendocrine tumors (NETs) with well-established differentiation, classified as G1, G2 or G3, according to their degree of differentiation and biologic aggressiveness.
- High-grade neuroendocrine carcinomas (NECs), which are invariably aggressive and may be of small cell or large cell type (9,10).

Several authors have reported a higher prevalence in males (61.7%), with an age range between 50 and 70 years, and an unfavorable prognosis (6). A high proportion of patients develop local recurrence or distant metastases. According to a published analysis, overall survival is significantly reduced in primary tumors larger than 3 cm in diameter ($p = 0.032$) (10).

In conclusion, small cell neuroendocrine carcinoma of the major salivary glands is a highly aggressive tumor; however, its prognosis may be relatively better than that observed in neuroendocrine neoplasms arising at extra-salivary sites (10).

4. Conclusion

High-grade small cell neuroendocrine carcinoma of the parotid gland represents a rare and diagnostically complex malignancy. Immunohistochemical analysis plays a central role in differentiating between primary salivary gland tumors and metastatic disease.

Although the prognosis is usually unfavorable, the limited number of cases presented in the literature makes it difficult to draw firm conclusions about the biological behavior and clinical course of this entity.

Conflicts of Interest

The authors declare no conflicts of interest.

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Figures

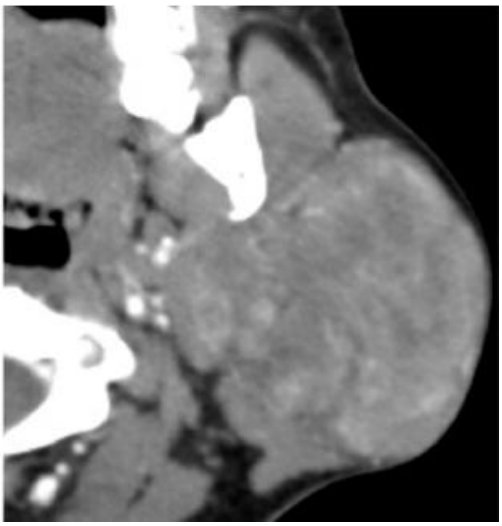

Figure 1: Computed axial tomography. Left parotid tumor

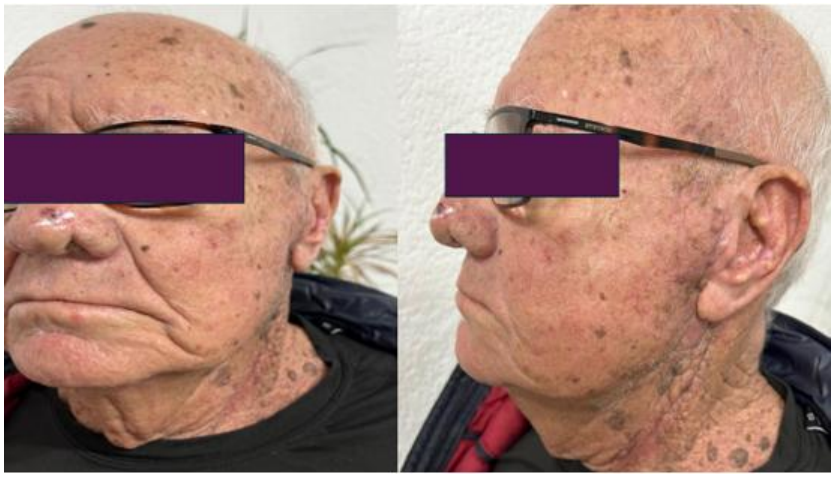

Figure 2: Postoperative period day 15

Figure 3: A: 4× magnification. Right side shows preserved serous acini of the parotid gland; left side shows a malignant small cell neuroendocrine neoplasm arranged in sheets with areas of necrosis, separated by fibrous tissue (capsule). B: 10×

magnification. Malignant neuroendocrine neoplastic proliferation arranged in sheets with focal areas of necrosis. C: 10× magnification. Tumor and serous acini separated by fibrous connective tissue.

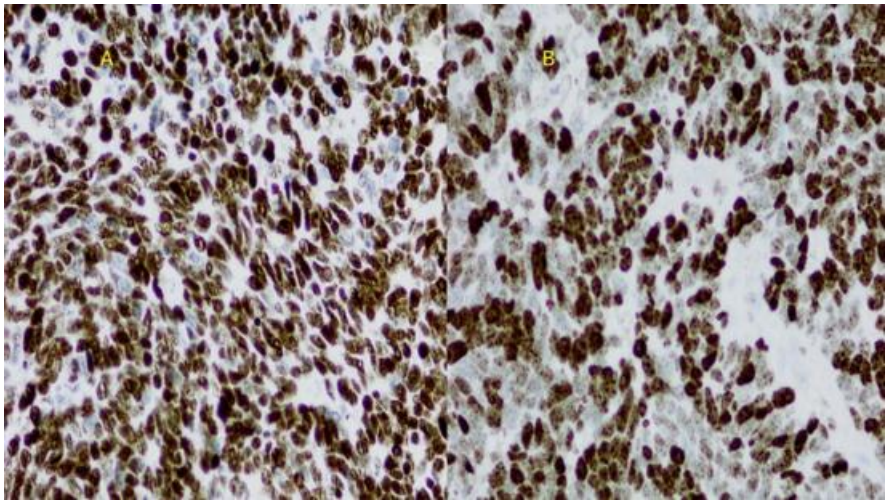

Figure 4: A: 40× magnification. High nuclear Ki-67 expression. B: 40× magnification. INSM1 with positive nuclear staining.