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Basal Cell Adenocarcinoma Arising from the Parotid Gland

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Established Facts

- Basal cell adenocarcinoma (BCAC) is a rare neoplasm affecting the salivary glands, predominantly the parotid gland.
- The definitive diagnosis requires the exclusion of other more frequent entities with a different prognosis.
- Given the rarity of BCAC, the therapeutic approach is an extrapolation of other salivary gland tumors.

Novel Insights

- In this clinical report, the use of adjuvant radiotherapy was controversial but was considered taking into account the histological characterization.
- The approach to rare entities should take into account the particularities of each case, not allowing for a global approach to other tumors.

Keywords
Parotid tumor · Basal cell adenocarcinoma · Parotid gland · Salivary gland tumor

Abstract
Basal cell adenocarcinoma (BCAC) is a rare malignant tumor of the salivary glands, representing 1–2% of salivary gland neoplasms. It is considered a low-grade tumor, often associated with a good prognosis. We report a case of a 60-year-old man with 3-month history of a growing, painless mass in the right ascending ramus of the mandible. Ultrasound and CT scan showed an asymmetry between parotid glands, depicting a nodular structure on the right side. A parotid fine needle aspiration cytology revealed neoplastic cells suggestive of adenoid cystic carcinoma. The patient underwent a total parotidectomy with lymph node dissection. Histopathology result was reported as BCAC. The patient concluded adjuvant radiotherapy and continued follow-up surveillance without evidence of relapse. The adjuvant approach in this case was decided by a multidisciplinary team given the absence of classically known risk factors. We highlight the importance of considering BCAC in the differential diagnosis in salivary gland tumors.

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Introduction

Basal cell adenocarcinoma (BCAC) is a rare malignant tumor of the salivary glands, representing approximately 1–2% of salivary gland neoplasms. This entity is relatively recent, being first introduced to World Health Organization (WHO) classification of tumors in 1991 [1]. As an histological entity, basal cell tumors include basal cell adenomas (BCA), the solid type of cystic carcinomas, and BCAC. The BCAC, as a malignant tumor, has more aggressive features like frequent mitoses and an infiltrative growth [2]. BCAC is more common in caucasians, does not have a gender predilection, and targets the major salivary glands with higher frequency, as more than 80% are found in the parotid gland. Since it is considered a low-grade tumor, it is often associated with a good prognosis. However, recent studies suggest a possibility of local recurrence up to 50%, highlighting the importance of a long-term follow-up [3].

Case Report

A 60-year-old man with a medical history of transient ischemic attack, an accident at work resulting in loss of the right eye and facial paralysis, arterial hypertension, and diabetes mellitus type 2 noninsulin-dependent, presented with a 3-month history of a slow-growing, painless mass in the right ascending ramus of the mandible. There was no history of difficulty chewing, change in voice or salivation, difficulty breathing, or other compressive symptoms. Physical examination demonstrated a solid, semi-mobile, 15 × 20 mm mass in the right parotid gland. There were no palpable cervical lymph nodes, and the general examination was unremarkable.

An ultrasound image revealed an heterogeneous nodule in the right parotid with 19.3 × 14.5 mm and a cervical level IIA adenopathy. A CT scan of the neck, thorax, and abdomen showed an asymmetry between parotid glands, with two nodular structures in the right parotid gland, 23 × 14 mm and 17 × 17 mm. Peri-parotid adenopathies of approximately 10 mm were also described (shown in Fig. 1). A parotid fine needle aspiration cytology revealed neoplastic cells suggestive of adenoid cystic carcinoma. A PET-CT scan was performed and showed a right parotid lesion with fluorodeoxyglucose avid with a standardized uptake value of 14.8 (shown in Fig. 2).

The patient underwent a total parotidectomy with a supraomohyoid lymph node dissection (20 lymph nodes evaluated), identification, sacrifice, and reconstruction of the facial nerve. Pathological report was compatible with a BCAC, with 21 mm of dimensions, perineural and lymphovascular invasion, no lymph node metastases (pT2N0R0) (shown in Fig. 3). Ki67 proliferative index was estimated at 20% of the neoplastic cells. After surgical recovery, adjuvant radiotherapy was recommended; the treatment plan included irradiating the parotid region and cervical lymph nodes levels II and III at a total dose of 60 Gy and 54 Gy, respectively. The complications were mucositis and radiation dermatitis, with progressive resolution in the following weeks.

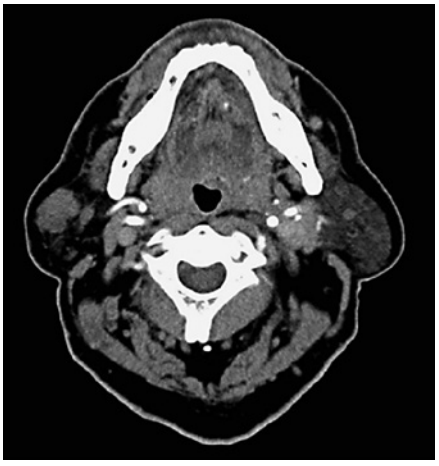

Fig. 1. Axial section of contrast-enhanced computed tomography scan showing nodular structures in the right parotid gland.

Currently, 9 months after the surgery and radiotherapy treatment, the patient remains well and without evidence of relapse. The patient will continue follow-up surveillance with frequent clinical evaluation and scans.

Discussion/Conclusion

According to the World Health Organization (WHO) classification, there are more than 20 histological subtypes of malignant salivary gland tumors. BCAC is a rare entity, a frequently low grade with indolent behavior. Most tumors will arise in the major salivary glands, mainly in the parotid gland, with a few being reported in the minor salivary glands [4]. The differential diagnosis can be challenging, considering the overlapping features between both, benign and malignant entities. Basal cell tumors include BCA, the solid type of cystic carcinomas and BCAC. The distinction with the benign partner, the BCA, based only on cytomorphology can be difficult due to their shared similarities on architectural and cytological morphology. BCAC shows significant cytological atypia and an increased mitotic rate compared with BCA; however, these differences are insufficient to distinguish the two entities. The pattern of invasion of the surrounding gland and soft tissues, with a propensity to perineural and vascular invasion, is more frequently associated with BCAC [2, 5].

One crucial differential diagnosis is the pleomorphic adenoma, the most typical benign tumor of salivary glands. These lesions have a smooth outer surface and surrounded by a capsule. Even though, considered be-

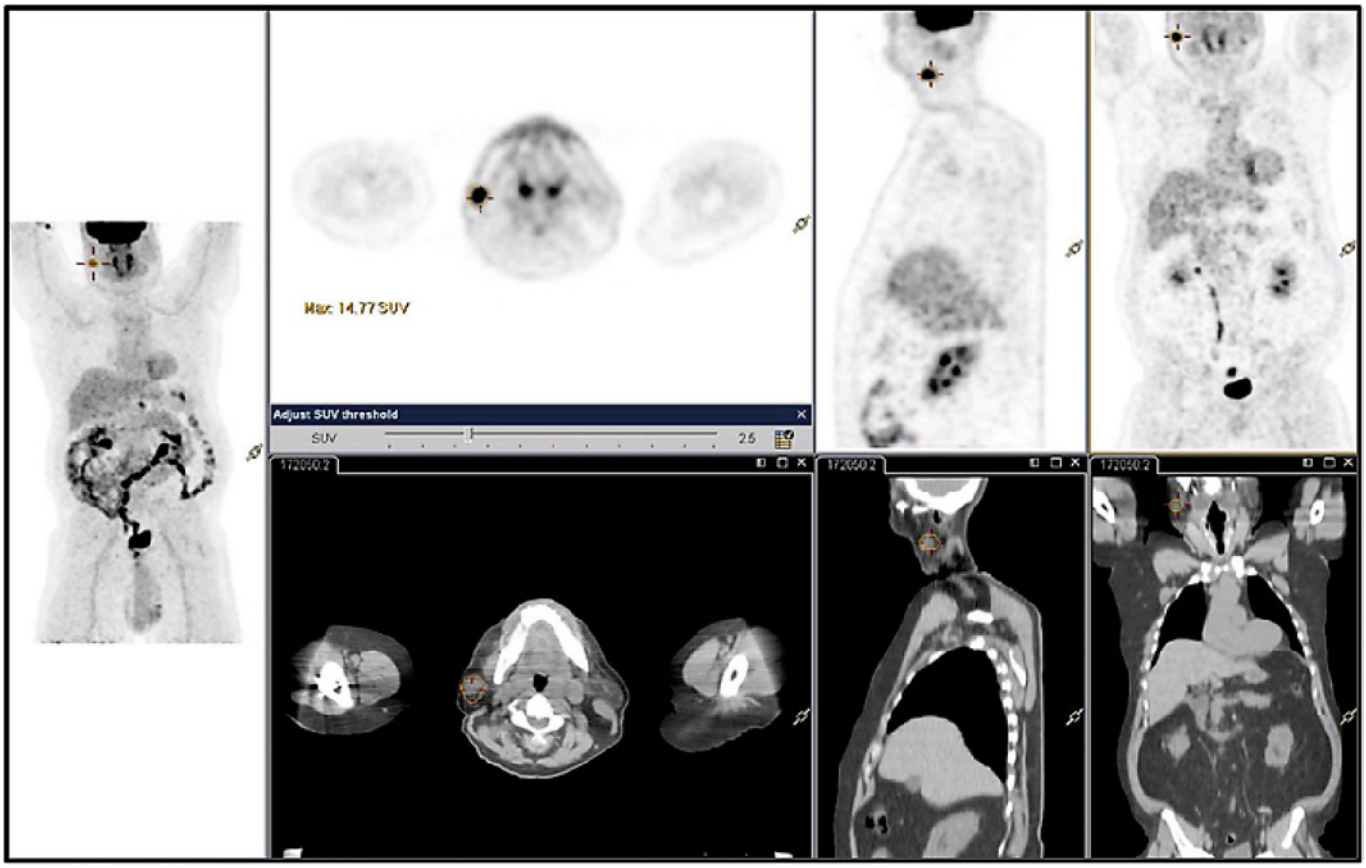

Fig. 2. PET-CT images demonstrating transverse and coronal plane identifying high 18F-FDG (18F-fluorodeoxyglucose) uptake in right parotid lesion.

nign, there is a propensity for recurrence after treatment. Other benign entities critical to the differential diagnosis are canalicular adenoma, myoepithelioma, oncocytoma, and cystadenoma [6]. The malignant behavior of BCAC can be a confounding factor in distinguishing this entity from other neoplasms. Regarding the malignant options of salivary gland tumors, the most frequent are mucoepidermoid carcinoma and adenoid cystic carcinoma. Other important, but rare malignant tumors, are basaloid squamous cell carcinoma and polymorphous adenocarcinoma [6]. In our case, the first proposed diagnosis was adenoid cystic carcinoma based on FNAC. In contrast to BCAC, adenoid cystic carcinoma is a more aggressive tumor that needs a different approach mainly from the surgical standpoint. The presence of central necrosis and MYB expression will suggest the diagnosis of adenoid cystic carcinoma since they are uncommon in BCAC. Thus, the distinction between BCAC and adenoid cystic carcinoma should be clarified since it has clinical and prognostic implications. The 10-year survival rate for BCAC is above 75%, whereas the 10-year survival rate for adenoid cystic carcinoma is around 30%, with a propensity to more lung metastasis [4, 7].

Also, a different genetic profile contributes to the tumorigenic mechanisms. Basal cell neoplasia is related to CYLD tumor-suppressor gene due to somatic mutations and less commonly due to germline mutations. Basal cell salivary neoplasms tend to have CYLD exon 9–11 and 12–20 mutations, but the exon 12–20 mutations are only seen in malignant tumors [3].

In general, due to the rarity of this entity, there is no consensus regarding the treatment of BCAC, with some reports recommending surgical excision alone, others suggesting radiation alone, and other a combination of both, especially for patients with some high-risk features. However, the definition of high-risk characteristics is not yet well established. Despite recent advances that add value to the genetic background, the most determined pre-

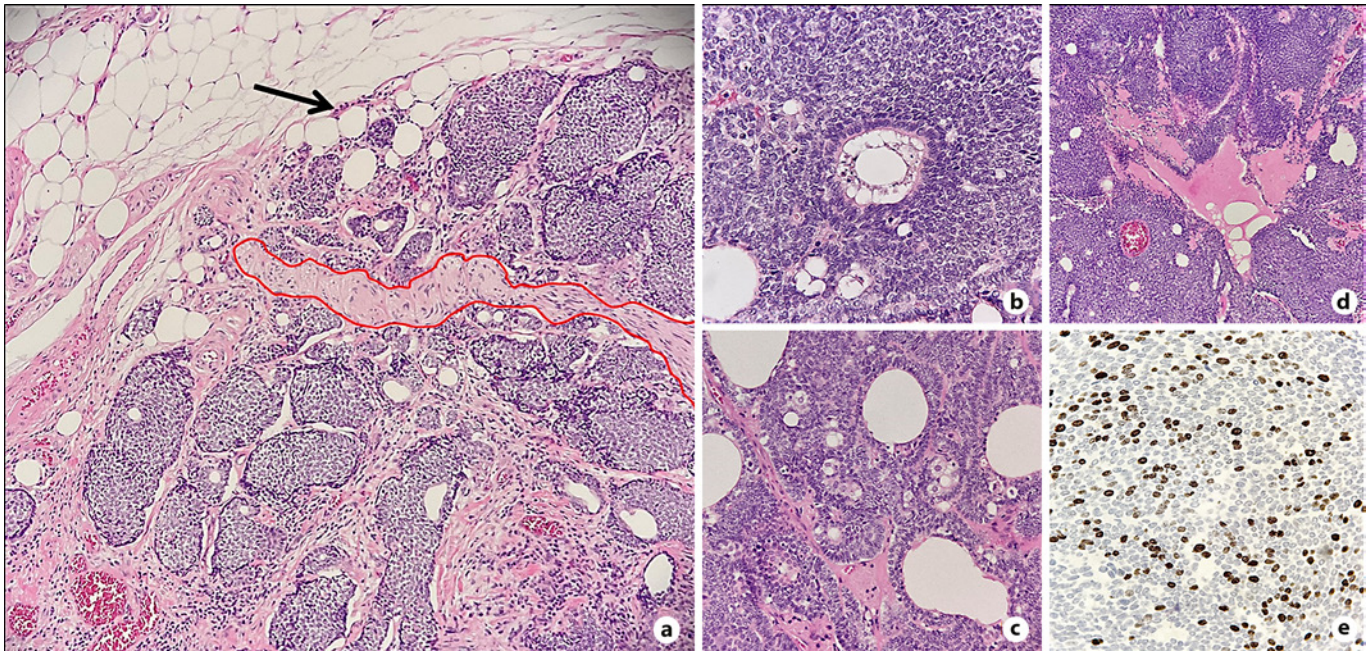

Fig. 3. Histopathological images of BCAC. **a** H&E (×100) – Unencapsulated tumor showing obvious infiltrative growth of small solid nests, with a few tubule-like structures, creeping out of the normal salivary gland parenchyma into surrounding adipose tissue (arrow). Note the perineural invasion (contour). **b** H&E (×400) – Tumor showing evidence of its biphasic composition: ductal component lined by cells with moderate eosinophilic cytoplasm and round to ovoid nuclei; surrounded by basal-looking cells of scant cytoplasm. **c** H&E (×200) – Solid and tubular growth patterns of tumor showing sebaceous differentiation. **d** H&E (×200) – Area with basement membrane-like eosinophilic material separating the tumor nests. **e** The proliferation index (Ki67) was estimated at 20% (hotspot).

dictors of adverse prognosis are tumor size (T3 or T4 tumors) and perineural invasion [8].

The best surgical approach in this entity is unclear. Some authors recommend local excision or parotidectomy, mainly depending on the tumor size (greater or smaller than 4 cm) and the extraglandular extension. A surgery with clear margins is always the goal and is the curative method for most patients. However, lymphadenectomy can be an option for patients with clinically positive lymph nodes or if there is imagological suspicion for node extension. In other salivary glands tumor entities, the nodal dissection approach is well established; therefore, it is also considered in BCAC. Both surgery and lymphadenectomy can have some long-lasting consequences. Due to the proximity and possibility of facial nerve involvement, complications like nerve damage, epidermolysis, wound dehiscence, or chyle leak can occur [9].

The role of radiotherapy in BCAC also remains controversial. Some authors recommend the use of radiation after surgery only in patients with high-risk features, like high T-stage (T3 and T4), perineural and lymphovascular invasion, close surgical margins, local recurrences, or involvement of minor salivary gland [2, 10].

In this case, the patient underwent major surgery with total parotidectomy and supraomohyoid lymph node dissection (20 lymph nodes evaluated). During the procedure, a facial nerve involvement was detected, becoming necessary for its identification, sacrifice, and reconstruction of some branches. A microsurgical reconstruction was performed with transposition and anastomosis of facial nerve branches. In the postoperative period, the patient sustained mobility limitations of the facial and cervical muscles. The chewing movements and, consequently, the ability to eat were also affected. With targeted physiotherapy exercises, the patient showed almost full recovery from his facial muscle movements.

In the pathology report, perineural and lymphovascular invasions were considered risk features and contributed to deciding on combined treatment. Besides the primary tumor T-stage was a T2, not considered as a risk T-stage, this case was discussed in a multidisciplinary

meeting and was proposed for added radiotherapy. A factor contributing to this decision was the lack of histologic grade establishment in the pathology report. Some reports suggest the importance of grading BCAC and its role in determining the therapeutic approach [11].

One of the most recent series of BCAC was reported by Ahsanuddin et al. [2], in which they described 322 cases diagnosed between 1996 and 2015. In this report, the parotid gland was the most frequent primary site of BCAC, with 71.7%. Regarding treatment options, most patients underwent surgery alone (51.9%), followed by surgery and radiation (41.0%). A 5-year overall survival of 81.9% confirms the good prognosis of this entity.

Zhan and Lentsch [12] also describe a series of 509 BCAC cases, with most of the cases affecting the parotid gland. The prognosis, in this study, was associated with the age of patients and the primary tumor (T) stage. In patients with a high T-stage disease, surgery in combination with radiation had significantly better survival than surgery alone.

In several studies, the follow-up of BCAC patients is described as a long-term process that can reach up to 10 years. While local recurrence can occur and is well documented, regional lymph nodes and distant metastasis are rare. Besides clinical and imagiological surveillance for possible recurrence, these patients must also be surveilled over time regarding facial muscles motor function, especially in cases where surgery involved the complete excision of the salivary gland and lymphadenectomy.

Despite the initial difficulties in characterizing the entity, later pathological evaluation of the surgical specimen allowed the establishment of a robust diagnosis. Given the absence of classically known risk factors, a multidisciplinary team opted for the adjuvant approach. The patient was successfully managed with surgery and adjuvant radiotherapy, showing no evidence of disease at the follow-up.

Acknowledgments

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Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. This retrospective review of patient data did not require ethical approval in accordance with local/national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Marina Vitorino and Andreia Filipa Chaves developed the treatment strategy for this patient, proposed and coordinated the multimodal treatment, and wrote the article. Joaquim Tinoco performed histopathology and immunohistochemistry. All authors contributed to the writing process, reviewed, and approved the manuscript.

Data Availability Statement

The authors declare that data supporting the findings of this study are available within the paper. Further inquiries can be directed to the corresponding author.

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