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CASE REPORT
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Extensive Basal Cell Adenocarcinoma Involving Minor Salivary Gland of the Hard Palate: A Rare Entity

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Abstract

Basal cell adenocarcinoma (BCAC) is a very rare slow-growing malignant basaloid tumour of the minor salivary gland. We reported a case of BCAC of the minor salivary gland of the hard palate occurring in a 56-year-old man. BCAC shares overlapping histopathological features with the other oral basaloid cell neoplasms which carries different prognosis and treatment modality. We emphasized on the histomorphologic features and the role of immunohistochemistry panel in the differential diagnosis of BCAC in incisional biopsies.

Keywords: Basal cell adenocarcinoma, basaloid morphology, hard palate, immunohistochemistry, minor salivary gland.

Introduction

BCAC accounts for 1.6% of all salivary gland neoplasms and 2.9% of all malignant salivary gland neoplasms with the majority of the cases occurring in the parotid gland (Gnepp *et al*., 2009). The occurrence in minor salivary gland is exceedingly rare (< 1%) and commonly involves the palate, buccal mucosa, nasal cavity, floor of mouth and upper lip. To the best of our knowledge, there are only 25 cases of palatal BCAC that have been reported in the literature (Jayakrishnan *et al*., 2003; Toida *et al*., 2005; Yamagata *et al*., 2006; Ward *et al.*, 2009; Venkata and Irulandy, 2011; Akiyama *et al*., 2012; Cuthbertson *et al.*, 2015; Tursun *et al*., 2019). The majority of BCAC develops *de novo* but 23% of cases may arise from a pre-existing basal cell adenoma (BCA) (Muller and Barnes, 1996). While BCAC is morphologically similar to BCA, the presence of infiltrative growth, lymphovascular and perineural invasion will help to distinguish between these two neoplasms. However, the assessment of the lymphovascular and perineural invasion is a limitation in small incisional biopsies. Thus, we aimed to emphasize the importance of histomorphological and immunohistochemical analysis in the diagnosis of BCAC.

Case report

A 56-year-old Malay male, an active smoker, presented with five years history of a painless hard palate mass which was gradually increasing in size. It was associated with anosmia, unprovoked epistasis, dysphagia and intermittent difficulty in breathing for the past one year. The patient also experienced pain during mastication for the past month and had lost 15 kg of body weight within four months. The physical examination revealed a midline mass with an irregular border and ulcerated surface at the hard palate extending to the soft palate (Fig. 1a). A few palpable small right cervical lymph nodes were detected. An axial computed tomography (CT) scan revealed a locally aggressive large expansile hard palate tumour (10.3 cm x 8.3 cm x 7.6 cm) with local tumour extension, complete nasal occlusion and narrowing of the oral cavity. A magnetic resonance image (MRI) (Fig.1b and 1c) of the brain showed no intracranial extension.

An incisional biopsy displayed solid and trabecular nests of basaloid tumour cells with peripheral nuclear palisading (Fig. 2). The tumour cells were monotonous with oval to round basophilic nuclei and scanty cytoplasm. An intercellular and peripheral membranous pattern of eosinophilic hyalinized material was noted. Foci of squamous eddies were present. A prominent stellate reticulum-like pattern was noted within the tumour islands. Mitosis was about 8 per 10 high power field (HPF). There was no dysplasia of the overlying oral mucosa. There was no evidence of lymphovascular invasion while perineural invasion was non-assessable due to absence of nerve bundle.

The neoplastic cells were positive for pan cytokeratin (CKAE1/AE3), cytokeratin 7 (CK7) (Fig. 3a), P63, cytokeratin 5/6 (CK5/6) and vimentin with focal positivity for P53 (Fig. 3b), epithelial membrane antigen (EMA), S100 and P40. They were negative for CD117 (Fig. 3c), smooth muscle actin (SMA), carcinoembryonic antigen (CEA), CK20 and CD10 stains. The Ki67 proliferative index was about 10% (Fig. 3d). Increase in mitotic count and Ki67 proliferative index and positivity of P53 gave a final diagnosis of BCAC.

Subsequently, the patient underwent right total maxillectomy, left partial maxillectomy, right modified radical neck dissection and left selective neck dissection. A diagnosis of basal cell adenocarcinoma was confirmed. Post-operatively, the patient underwent adjuvant radiotherapy with tumour doses of 60 Gy delivered by fraction of 1 Gy, 5 days a week for 6 weeks. There was no evidence of recurrence after 1 year of follow-up since the radiotherapy.

Discussion

BCAC of minor salivary gland is extremely rare. It typically occurs in adults in their sixth or seventh decade of life and has no gender predominance (Fonseca *et al.*, 2017). The patients usually presented with a slow growing painless mass that had been present for weeks and could be up to 10 years (Jayakrishnan *et al*., 2003). BCAC have been reported to present with enhancing mass within the salivary gland on CT scan examination (Warrick *et al.*, 2000). Whereas, on MRI examination, BCAC reportedly show a mean ADC value of 0.96 +/- 0.29 (SD) which can be used to distinguish it from its benign counterpart (Habermann *et al*., 2009).

It is a challenge to differentiate BCAC of minor salivary glands with other basaloid neoplasms in a simple incisional biopsy due to overlapping microscopic features. Histomorphological analysis with a panel of immunohistochemical stains will help in determining the accurate diagnosis of BCAC. The histological differential diagnoses include basal cell adenoma (BCA), adenoid cystic carcinoma (AdCC), intra-oral basal cell carcinoma (IOBCC), basaloid squamous cell carcinoma (BSCC) and basal cell ameloblastoma (Bajpai and Pardhe, 2017).

On histopathological examination, the tumour may exhibit solid, tubular, trabecular, cribriform and membranous patterns. The solid pattern is the most commonly encountered pattern in BCAC. Microscopically, it has a dual population of cells, comprising small, dark basaloid cells with scanty cytoplasm, and larger polygonal cells with eosinophilic to amphophilic cytoplasm and pale basophilic nuclei. Stellate reticulum-like pattern and squamous differentiation may be observed. Depositions of eosinophilic basement membrane are seen within and surrounding the tumour nests. Mitotic figures of more than 4 per 10 HPF has been reportedly used as a feature to indicate malignancy (Nagao *et al*., 1998). Perineural and vascular invasion are found in approximately a quarter of cases (Parashar *et al*., 2007).

BCAC stains for both epithelial and myoepithelial immunohistochemistry markers, highlighting the dual population of cells. However, the expression for BCAC is non-specific, variable and dependent on the patterns of growth. Thus, a panel of immunohistochemistry markers is an important complementary in the diagnostic process. The epithelial markers that are typically expressed in BCAC include CKAE1/AE3, CK7, CK5/6, CEA and EMA. The markers of myoepithelial differentiation such as SMA, S100, P63 and vimentin may be expressed in BCAC particularly by cells at the periphery of tumour nests (Williams *et al.*, 1993; Kim *et al*., 1997; Andreadis *et al*., 2005; Farrell and Chang, 2007). CEA stain was negative in the present case as well as in several other case reports (Raslan *et al*., 1995; Parashar *et al*., 2007; Sarafraz *et al.*, 2015). Although SMA is a marker of myoepithelial differentiation, it has

been reported as negative in several reports, including the present one (Andreadis *et al*., 2005; Farrell and Chang, 2007; Parashar *et al*., 2007; Jung *et al*., 2013).

BCAC is distinguished from BCA by means of invasion of local structures, and perineural as well as lymphovascular invasion. Nagao *et al.* (1998) described Ki-67 proliferative index of greater of than 5% as a strong indication of malignancy, despite the absence of infiltrative growth, while Yamagata *et al.* (2006) suggested a cut-off point of 10%. The lack of P53 immunoreactivity in BCA may also be useful in differentiating it from its malignant counterpart.

The cribriform-like pattern of BCAC is rarely observed although it can mimic AdCC. The major distinguishing factor is the cytomorphologic features of AdCC which include the presence of pale, clear cells with dark hyperchromatic angulated nuclei, absence of peripheral palisading, higher mitotic activity and necrosis. Strong positivity of CD117 is a recognized marker for AdCC (Jung *et al.*, 2013).

Unlike in BCAC, the squamous differentiation in BSCC involves the mucosal epithelium which may demonstrate dysplasia or carcinoma in-situ. BSCC has far greater mitotic activity than BCAC and usually demonstrate a strong p53 and high Ki67 immunoreactivity. BSCC is negative for CK7, CK20, S100 protein and vimentin as compared to BCAC (Andreadis *et al*., 2005).

Woods *et al*. (2014) had described a case of IOBCC involving the hard palate, with history of painful erythematous growth of one-year duration. The histological features of IOBCC are similar to its cutaneous counterpart. However, the current case is lacking the usual feature of IOBCC which is the prominent artefactual cleft from the surrounding stroma. Furthermore, the mitotic figures and apoptotic bodies are significantly higher in IOBCC as compared to BCAC. Immunohistochemically, IOBCC is positive for the cytokeratin, P63, P53 and negative for EMA (Shumway *et al*., 2011; Woods *et al.*, 2014). Leon *et al*. (2006) reported SMA is positive in 89% of BCC cases in the oral and maxillofacial region with the Ki-67 proliferative index in between 6 to 35%. Yada *et al.* (2004) reported a strong expression of CD10 in 86% cases of IOBCC which was negative in the present case.

Ameloblastoma of basal cell type is the least common histological variant of the ameloblastoma, accounting for 2.02% of the cases (Reichart *et al.*, 1995). We considered the peripheral ameloblastoma of basal cell type as a differential diagnosis because of the basaloid feature of the tumour cell despite the lack peripheral gingival soft tissue involvement in the present case. Histologically, the tumour exhibits nests of basaloid cells that shows dark basophilic nuclei with little cytoplasm and peripheral palisading. The stellate reticulum-like areas in the central portion of tumour nest which is the feature of ameloblastoma is absent in

this variant and the areas are occupied by the basaloid cells. They are negative for CK7, EMA and CD117 (Sridhar *et al*., 2015). Furthermore, the site for this case is not consistent with odontogenic neoplasm.

BCAC is a low-grade malignant tumour, with a good long-term prognosis (Eveson and Thompson, 2012). The distant metastasis and disease related death are uncommon in BCAC. However, it is a locally destructive and tends to recur (Yamagata *et al*., 2006). Thus, a complete surgical resection with wide margins is warranted as the primary treatment for BCAC. Frozen section is recommended to assess the margins intraoperatively to ensure the complete surgical resection (Cuthbertson *et al*., 2015). With the adequate resection, additional measure is not necessary. Routine neck dissection is indicated only when the regional lymph node is involved and the adjuvant radiotherapy is recommended for cases with close or positive resected margins (Farrell and Chang, 2007). BCAC involving the minor salivary gland has a higher recurrence rate and poorer prognosis due to poor resectability of the tumour caused by its location (Gnepp *et al*., 2009). The other poor prognostic factors of BCAC include advanced stage at presentation, residual tumour at surgery and tumour recurrence.

In conclusion, BCAC of the minor salivary gland is a rare salivary gland tumour. Histomorphologic features with the aid of a panel of immunohistochemical analysis comprising of CK7, CK5/6, vimentin, S100, P63, P53, CD117 and Ki67 in BCAC is helpful in establishing the diagnosis of BCAC.

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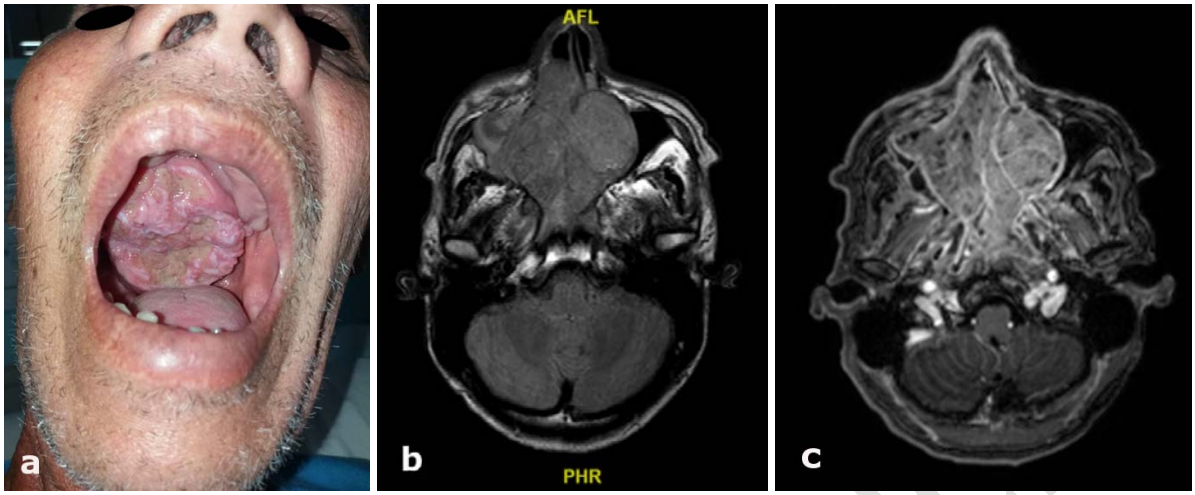

Fig. 1: (a) A large fungating ulcerated mass of the hard palate extending posteriorly. (b) Axial view of MRI of brain shows there is presence of large multilobulated mass with hypo-to-isointense signal on T1, (c) heterogenous hyperintense signal on T2 and heterogeneously enhanced post contrast. The mass extends anterosuperiorly to abut the frontal sinus and involve the right maxillary sinus, anterior ethmoid air cells, right posterior ethmoid air cells, sphenoid sinus and bilateral nasal cavities.

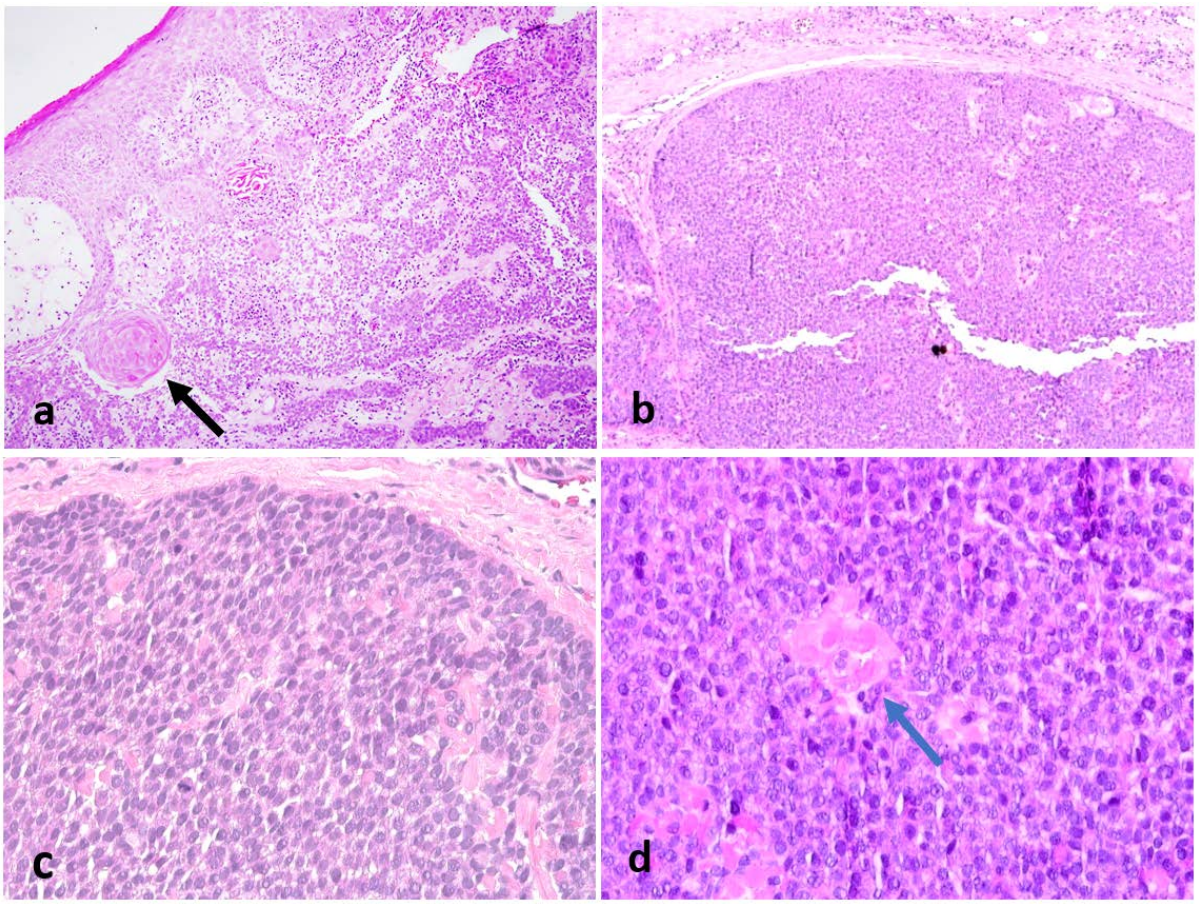

Fig. 2 Histopathological image of the incisional biopsy: (a) The basaloid tumour cells are arranged in infiltrating anastomosing trabecular pattern. There is squamous differentiation seen (black arrow) (b) The tumour cells are circumscribed and arranged in solid pattern (H&E stain, x40). (c) The peripheral palisading by smaller cells with scant cytoplasm and round to oval deeply basophilic nuclei are appreciated (H&E stain, x400). (d) There are eosinophilic basement membrane-like materials (blue arrow) seen within the tumour (H&E stain, x400).

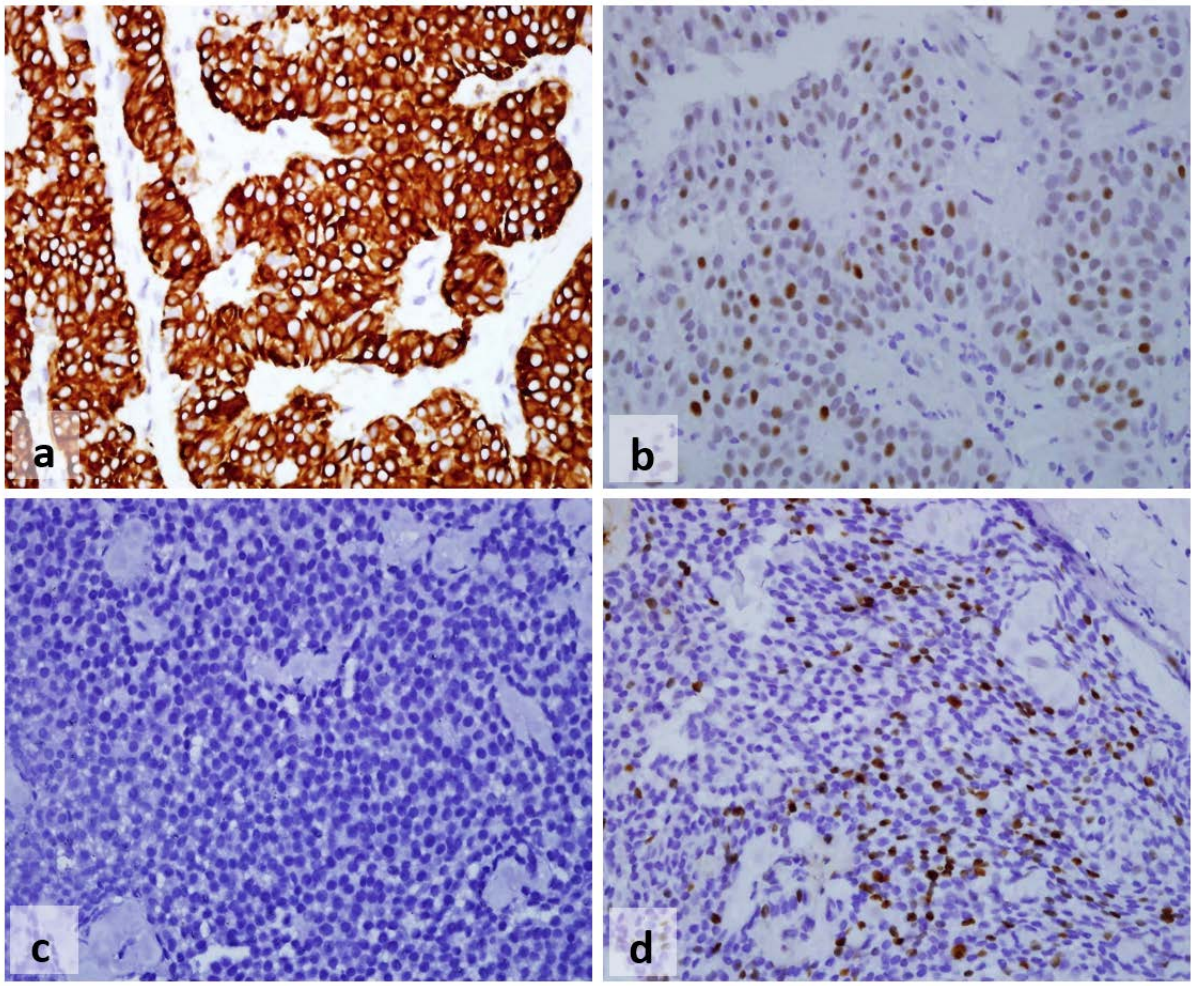

Fig. 3 Immunohistochemical findings of the incisional biopsy: (a) The tumour cells are positive for CK7. (b) Focal positivity for P53. (c) Negative for CD117. (d) Ki-67 proliferative index of 10% (Magnification x400).

