Basal Cell Adenoma-Clinicopathological, Immunohistochemical Analysis and Surgical Considerations of a Rare Salivary Gland Tumor with Review of Literature

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ABSTRACT

Introduction: Basal cell adenoma (BCA) of the salivary glands is a rare benign salivary gland tumour. Differentiation of BCA from varied entities involving maxillofacial area is mandatory. **Aim:** To analyze the clinicopathological, histopathologic features, immunohistochemcal analysis and surgical considerations of this rare entity. **Materials and Methods:** This study included 12 cases of BCA from archives of department reported over the period of 13 years. All the pertaining clinicopathologic features such as incidence, age, sex and site of lesions were assessed. Tissue sections were stained by using panel of immunohistochemical markers, i.e. Pan CK, CK 5/6 and S100, Calponin, p63, CD 117 and smooth muscle actin. **Results:** BCA was observed in 26-52 years age group (mean age, 38.75 years) with female propensity of 7:5 male to female ratio. It is seen more commonly in parotid gland, followed by upper lip, buccal mucosa and palate. Solid type is the most common histopathologic type followed by tubular, membranous and trabecular. Only one case of membranous type of BCA showed recurrence. Pan CK, CK 5/6 showed strong immunoreactivity, calponin showed moderate staining, p63 and Ki-67 mild staining, whereas CD 117 and SMA showed negative immunostaining. **Conclusion:** Vigilant comprehensive analysis of all the pertaining clinicopathologic and histopathologic features and immunohistochemical analysis are required for differentiating from other lesions with basaloid differentiation having varying prognosis.

KEYWORDS: Basal cell adenoma, basal cell adenocarcinoma, monomorphic adenoma

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INTRODUCTION

Basal cell adenoma (BCA) of the salivary glands is a rare benign tumor with a high recurrence rate and, in general, good prognosis is recognized as an independent entity in the Second Edition of the Salivary Gland Tumors Classification of the World Health Organization (WHO).[1] The most frequent location is the parotid gland, followed by upper lip, buccal mucosa, lower lip and palate. These tumors frequently affect patients between their fifth and seventh decades. Histologically, four characteristic patterns have been described: Solid, trabecular, tubular and membranous.[2-4] Due to prognostic implications, differential diagnosis with basal cell adenocarcinoma, basaloid squamous cell carcinoma (BSCC) and adenoid cystic carcinoma (AdCC) is mandatory. Considering the rarity of this lesion, histologic paradox regarding its diagnosis and lack of descriptive studies in literature directed us to analyze the clinicopathological factors, immunohistochemcal analysis and surgical considerations of this rare entity.

MATERIALS AND METHODS

This study included 12 cases of BCA from patients referred to the Department of Oral Pathology between 2002 and 2012. All the pertaining clinic-demographic characteristics such as incidence, age, sex and site of lesions were collected for descriptive assessment. Three micrometer tissue sections were taken for histopathologic and immunohistochemical (IHC) evaluation. After confirmation of the

previous diagnosis by two independent pathologists, tissue sections were subjected to IHC analysis by using Pan CK, CK 5/6 and S100, calponin, p63, CD 117 and SMA markers. Immunoreactivity was independently assessed by all study participants and graded into negative staining (<10%), weak, (10%-25%), mild (26%-50%), moderate (51%-75%) and strong staining (76%-100%).

Results

A total of 12 cases of BCA of maxillofacial region over the period of 13 years were selected for assessment and results obtained were correlated with the findings of differential lesions found in literature. BCA was observed in 26 - 52 years age group (mean age, 38.75 years) with female propensity. It was observed more commonly in parotid gland (8) followed by upper lip (2), buccal mucosa (1) and palate (1). Solid type is most common histopathologic type followed by tubular, membranous and trabecular. [Table 1] None of the cases showed facial nerve involvement and treatment was local excision. Follow-up from two to six years revealed only a single case of recurrence of membranous type of BCA. The lesions typically are slow growing, firm, non-tender, asymptomatic masses with minimal chances of recurrence [Table 1]. Pan CK and CK 5/6 showed strong immunoreactivity [Figure 1d and 1e], calponin showed moderate staining [Figure 1f], p63 and Ki-67 mild staining [Figure 2d and 2c], whereas CD 117 [Figure 2e] and SMA showed negative immunostaining [Figure 2a and Table 2].

Discussion

Present study focused on differentiation of BCA from other lesions of varied prognosis. PA is the most common benign tumor involving parotid glands and palate as the most common intraoral site (42.8 - 68.8%), followed by the upper lip (10.1%) and cheek (5.5%). It is seen commonly in females of 4 - 6th decade.[5] Sometimes, it is even difficult to differentiate PA and BCA histologically. In PA, palate is the most common intra-oral site but in contrary to BCA palate is the rarest site of occurrence. PA shows strong immunoreactivity for calponin and moderate for Pan CK and SMA indicating myoepithelial cell proliferation. It shows weak staining for Ki-67, which is a proliferative marker and mild staining in BCA [Table 2].

Differential diagnosis must be established with some unfavorable entities, such as the basal cell adenocarcinoma, AdCC and BSCC. In contrast to BCA, an infiltrative growth, more mitotic figures (>4 mitotic count/10 HPF) and Ki67-staining of 5% of the cells are observed in basal cell carcinoma.[6]

Sometimes pathologists face a diagnostic challenge in differentiating AdCC and BCA because both the entities show proliferation of basaloid cells. According to literature, AdCC is seen commonly in mean age of 52 years and have high

Table 1: Clinicopathologic characteristics of 12 cases of basal cell adenoma

IHC markers	Basal cell adenoma	Pleomorphic adenoma	Basal cell adenocarcinoma	Adenoid cystic carcinoma	Basaloid squamous cell carcinoma
PAN CK	Strong	Moderate	Strong	Strong	Moderate
CK 5/6	Strong	Mild	Mild	Moderate	Moderate
Calponin	Moderate	Strong	Mild	Moderate	Negative
CD 117	Negative	Negative	Negative	Strong	Negative
p 63	Mild	Mild	Strong	Strong (peripheral)	Mild (diffuse)
Ki-67	Mild	Weak	Strong	Strong	Strong
SMA	Weak	Moderate	Negative	Moderate	Negative
S-100	Variable	Mild	Mild	Strong	Negative
PCNA	Mild	Mild	Strong	Strong	Strong

PAN CK: Pan cytokeratin, SMA: Smooth muscle actin, PCNA: Proliferating cellular nuclear antigen, IHC: Immunohistochemistry

Table 2: Immunohistochemical analysis of lesions with basaloid proliferation

Age (years)	Gender	Site	Histopathologic type	Treatment	Follow up
36	Female	Parotid gland	Solid	Local excision	No recurrence
32	Female	Parotid gland	Solid	Local excision	No recurrence
26	Female	Parotid gland	Membranous	Total parotidectomy	Recurrence after 9 months
52	Male	Palate	Solid	Local excision	No recurrence
30	Male	Parotid gland	Tubular	Local excision	No recurrence
45	Female	Parotid gland	Solid	Local excision	No recurrence
28	Female	Upper lip	Membranous	Total parotidectomy	No recurrence
38	Male	Parotid gland	Solid	Superficial parotidectomy	No recurrence
46	Female	Parotid gland	trabecular	Local excision	No recurrence
52	Male	Buccal mucosa	Solid	Superficial parotidectomy	No recurrence
42	Female	Upper lip	Tubular	Local excision	No recurrence
38	Male	Parotid gland	Solid	Local excision	No recurrence

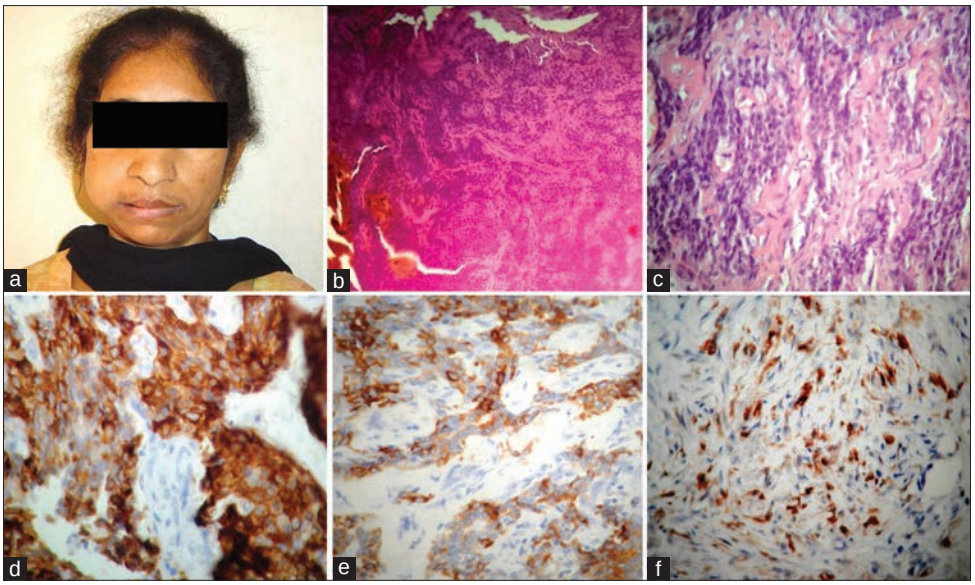

Figure 1: (a) Clinical photograph showing swelling at parotid gland region; Photomicrograph showing: (b) Cells arranged in solid and tubular pattern in hyalinized stroma (H and E, ×10); (c) Basaloid cells in hyalinized stroma (H and E, ×10); (d) Strong Pan CK immunostaining; (e) Strong CK 5/6 immunostaining; (f) Moderate calponin immunostaining

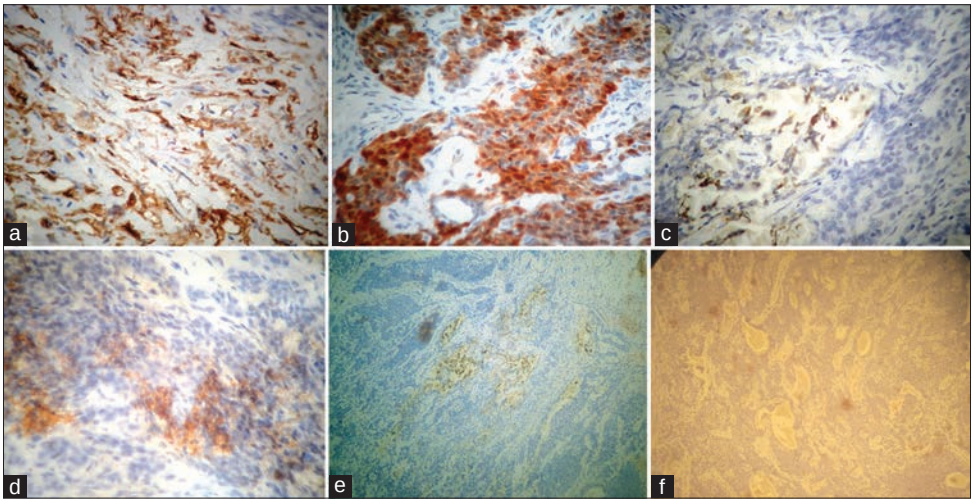

Figure 2: Photomicrograph showing: (a) Weak smooth muscle actin immunostaining; (b) Moderate S100 immunostaining; (c) Mild Ki-67 immunostaining; (d) Mild p63 immunostaining; (e) Negative CD117 immunostaining; (f) Mild PCNA immunostaining

propensity for parotid glands. In AdCC there are high chances of perineural invasion,[7] whereas the present study showed that none of the cases of BCA demonstrated perineural invasion. In the AdCC whirlpool of epithelial cells, dark external cells in a stockade pattern and a thick basal membrane-like structure are observed. Moreover, vascularization in the microcystic areas is absent, in contrast to BCA, in which multiple endothelial canals are present.[8] IHC analysis showed that CD117(c-Kit) is a specific marker for AdCC[9] and the present study showed that it is negative for BCA. Ki-67 and p63 markers are indicative of proliferative activity of tumor tissue. P63 is a selective IHC marker of basal/stem cells of stratified epithelium and of myoepithelial cells.[9] Current study showed that they are strongly expressed in AdCC and weak-mild expression in BCA. So these markers can be reliable in differentiating BCA and AdCC.

BSCC is an aggressive variant of squamous cell carcinoma (SCC), which predominantly occurs in men between the age of 60 and 70. Differentiation of it from other entities is mandatory as it carries a very poor prognosis. It is characterized by the presence of solid cells in a lobular fashion, which are small and have scarce cytoplasm with hyperchromatic nuclei without nucleoli. In this latter entity, both populations of basal cells are not observed, in contrast to BCA. Continuity of tumoral cells with epithelium of the surface and squamous dysplasia are also observed, in contrast to BCA.[10,11] Tumoral nests are clearly differenced from inter-epithelial stroma because of an intact basal cell membrane. This delimitation is observed neither in the pleomorphic adenoma nor in the AdCC. Present study showed that Pan CK and CK 5/6 are strongly expressed in BCA and Ki-67 and p63 show high immunoreactivity in BSCC.

Other benign lesions such as the mucocele, sebaceous cyst, lipoma and nasolabial cyst are also considered in the differential diagnosis. Clinical appearance of BCA may simulate a mucocele of the oral mucosa. Generally, the mucocele usually appears in the lower lip of young people, whereas BCA appears in the upper lip of the elderly.[12]

Basal cell adenocarcinoma is a malignant counterpart of BCA. Ki-67 and p63 are expressed intensely in case of basal cell adenocarcinoma, basaloid squamous cell carcinoma and AdCC but in our study only focal/Mild staining was observed in BCA. [Table 2] Additionally BCA was positive for S100 and Pan CK indicating its relation to myoepithelial cells. However some authors suggest the existence of these markers in neoplastic cells of BCA independent of their lineage.[13]

BCA can be unencapsulated, therefore, the best treatment is adequate local excision rather than enucleation.[14] They are amenable to conservative resection such as superficial parotidectomy. Extracapsular excision is performed in cases in which there is effect on minor salivary glands in the oral mucosa. It is mandatory not to disrupt the capsule, in order to minimize the risk of recurrence, which is observed in rare occasions.[10] The recurrence rate for the solid and trabecular-tubular variants is almost nonexistent. The membranous type is most commonly associated with recurrence (25% to 37%), and this may be a result of the multicentricity of this lesion rather than because of true recurrences, although rare, malignant transformation is more common in the membranous type than in the other types. So, total parotidectomy rather than superficial parotidectomy has been proposed in the membranous type of BCA. Multicentric development, unencapsulation in 50% of cases, association with eccrine tumors and malignant transformation have led some investigators to classify separately.[10,15]

Conclusion

Vigilant comprehensive analysis of all the pertaining clinicopathologic, histopathologic features and IHC analysis are required for differentiating lesions with basaloid differentiation which can sometimes pose challenge to pathologist. With increased awareness and acceptance of this lesion as a separate entity by pathologists, we perhaps can expect an increase in its diagnosis.

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