

Simplifying Predicament around Monomorphic Adenomas: Report of Two Cases

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Abstract

Monomorphic adenomas are rare benign epithelial tumours of salivary gland. This term was originally used to describe a group of benign salivary gland tumours demonstrating a more uniform histological pattern than the most common benign salivary neoplasm pleomorphic adenoma. In this article we are presenting two cases of monomorphic adenomas. The first case is of basal cell adenoma and the second one is of canalicular adenoma. Since the inception of the group monomorphic adenoma, there has been lot of confusion related to its usage as a common term. In support of recent WHO recommendation to discontinue the usage of term monomorphic adenoma, we have discussed the clinical, macroscopic and histopathological features of various benign salivary gland neoplasms to simplify the diagnostic dilemma along with IHC markers to confirm the diagnosis.

Keywords: Basal cell adenoma; Canalicular adenoma; IHC markers for benign salivary gland tumour; Monomorphic adenoma,

Introduction

Salivary gland neoplasms are rarest neoplasm of oral cavity constituting 2-6.5% head and neck neoplasms and are of various types and subtypes posing diagnostic challenges.¹ The presence or absence of stromal changes in benign salivary gland tumours such as chondroid or myxoid components are used to distinguish pleomorphic and monomorphic adenoma.² Monomorphic adenomas include benign salivary gland neoplasm with uniform histological pattern.³ Although this terminology was discontinued by WHO,⁴ usage of the term and histopathological dilemma still persist. Different types of monomorphic adenomas based on histological pattern are not easy to discern.

Case Report

Case 1: A 41 year old woman reported with a diffuse swelling of anterior maxillary region since last 1 year. On palpation a diffuse, firm to hard, non-tender swelling involving upper labial vestibule was found measuring 2cmx3cm extending toward palate leading to displacement of maxillary anteriors and elevation of upper lip [Figure 1(A &B)]. Provisional diagnosis of benign salivary gland tumour, Giant cell lesion, Periapical cyst and Ameloblastoma was made. Excisional biopsy was done under LA and tissue was subsequently processed for histopathological examination.

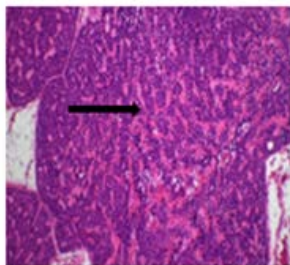
H&E stained sections revealed the presence of small uniform cuboidal cells with deep basophilic nuclei and scant cytoplasm arranged in small islands and cords in an interconnected or retiform pattern. The intervening scant stroma is loose fibrovascular in nature. The neoplastic aggregates were well separated from the surrounding stroma by an eosinophilic amorphous area [Figure 1(C &D)]. A Diagnosis of “Basal Cell Adenoma” was made.



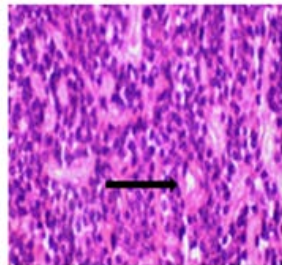
1A



1B



1C



1D

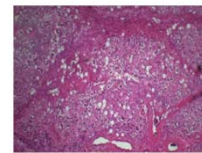
Figure 1 : 1A Intraoral photograph showing palatal swelling ; 1B Intraoral photograph showing swelling respect to upper labial vestibule; 1C Photomicrograph 4x view showing neoplastic cells arranged in cords and islands; 1D Photomicrograph 40x view showing small uniform cells with deep Basophilic nuclei

Case 2: A 40 year old male reported with a painful swelling during meal in the left floor of mouth since last 3 months. On palpation a well demarcated immobile, firm, tender swelling having a smooth texture with normal overlying mucosa was noted. There was no regional lymphadenopathy [Figure 2A]. Clinical differential diagnosis of Benign salivary gland neoplasm, Sialolith and Mucocele was made. Excisional biopsy of the lesion was done under GA and tissue was processed for histopathology.

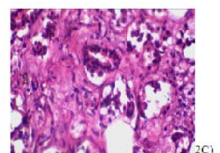
Histological examination revealed the presence of well capsulated glandular neoplasm characterized by uniform cuboidal cells with prominent nuclei and inconspicuous cytoplasm arranged in single or bilayered pattern in tubules and small islands. The stroma was loose fibrovascular with numerous thin wall dilated blood capillaries [Figure 2 B&C]. A diagnosis of Canalicular Adenoma was made.



2A)



2B)



2C)

Figure 2: 2A) Extra oral photograph showing submandibular swelling, 2B) Photomicrograph 10x view shows Aggregates of capsulated neoplastic tumor mass, 2C) Photomicrograph 40x view Tumor cells arranged in small tubular pattern

Discussion

The usage of term monomorphic adenoma is under debate since last few decades due to the ambiguity around its

origin, histopathologic features and prognosis. Monomorphic adenoma was first described by Rauch, Seifert and Gorlin in 1970 as those tumours which do not come under category of the pleomorphic adenoma. Broadly they included basal cell adenoma, sebaceous lymphadenoma and sebaceous adenoma, adenolymphoma, oxyphilic adenoma (oncocytoma), cystadenoma under monomorphic category. Later Thackray, Sobin and Lucas described monomorphic adenomas as benign glandular epithelial growth with scant insignificant intervening mesenchymal tissue.⁵In 1981 Batsakis and Branon classified monomorphic adenoma on the basis of origin which has been tabulated below.

It has been suggested that various benign tumours included under monomorphic category should be referred by its specific histopathological names and use of the term monomorphic adenoma be discontinued which was further accepted by WHO in 2017. The term monomorphic adenoma appears insignificant as a specific histological entity because of the wide array of tumours included under the classification of salivary gland tumours. Few commonly accepted Classifications of Monomorphic Adenomas have been given in Table 1.

To understand and differentiate between various entities included under benign salivary adenomas their basic clinical features have been described.

Table 1: Commonly accepted Classifications of Monomorphic Adenomas

WHO Classification (1972) ⁵	Batsakis and Branon classification (On the basis of origin) ¹	WHO Classification (2017.) ⁴
1) Adenolymphoma (papillary cystadenoma lymphomatosum) 2) Oxyphilic adenoma (Oncocytoma) 3) Other types a) Basal cell adenoma b) Canalicular adenoma c) Sebaceous adenoma and Sebaceous lymphadenoma d) Intraductal papilloma and Sialadenoma Papilliferum e) Salivary gland neoplasm, not yet further classified	1. Tumor of terminal duct: Basal cell adenoma and canalicular adenoma 2. Tumors of terminal or striated duct: Sebaceous adenoma and Sebaceous lymph adenoma 3. Tumors of Striated duct :Oncocytoma and Papillary cystadenoma lymphomatosum 4. Tumors of Excretory duct: Sialadenoma Papilliferum and Inverted ductal papilloma	1. Term Monomorphic adenoma was removed from the classification due to controversies around it

Basal cell Adenoma

The term basal cell adenoma was first used by Klessner and Klein in 1967 to describe encapsulated slow growing, epithelial neoplasm composed of basal cells. Originally Klessner and Klein classified basal cell adenoma into tubular, solid and trabecular variants. Subsequently, Gorlin et al in 1970 have included basophilic and omitted

trabecular type while C Crumpler et al. in 1976 included Basaloid variant.⁵

Basal cell adenoma represents 54% of monomorphous adenomas. It usually presents as a unilateral, well-circumscribed, round to oval mass frequently affecting female patients in their fifth to seventh decade of life. The most common site is the parotid gland followed by upper

lip, buccal mucosa, nasal septum and palate.⁶ Macroscopically, tumours in major salivary gland have a well-defined capsule whereas those in minor salivary gland are less well defined. The cut surface is homogeneous with gray to brown colour, with occasional cystic degeneration.⁷

Canalicular adenoma

In 1955 Bhaskar and Weinmann defined and illustrated the clinical and histological feature of a tumour that is now referred as canalicular adenoma. It was first considered as a separate entity until Rauch, Siefert and Gorlin in 1970 described that canalicular adenoma and trabecular type of basal cell adenoma are one and same entity. Daley et al 1984 gave evidence that canalicular adenoma is a separate entity from basal cell adenoma.⁵

Canalicular adenoma is an uncommon benign salivary gland tumour and constitutes 1-3% of all salivary gland tumours. Most commonly it involves the upper lip of female patient above 50 years of age and it appears as a slow growing, painless, sub mucosal solitary or multiple nodule not exceeding more than 3cm with its colour varying from pink to blue.⁸

Sebaceous adenoma

Sebaceous adenomas constitute 0.1% of salivary gland neoplasm and slightly less than 0.5% of all salivary adenomas. This tumour commonly involves parotid gland in male patients in sixth decade of life and tumour may range in size from 0.5-3.0 cm. Macroscopically, Sebaceous adenoma are commonly encapsulated mass and varies in colour from greyish white to pinkish white.⁷

Oncocytoma (Oxyphillic adenoma)

In 1977 Batkasis and Sylvest omitted oncocytoma from the monomorphic group.⁵ Oncocytomas are rare and constitute 0.4-1% of all salivary gland neoplasms. It occurs primarily in parotid of female older than 50 years

of age. They usually present as slow growing, painless, solid mass not exceeding more than 4cm in diameter.⁹

Papillary cyst adenoma lymphomatosum

Batkasis and Sylvest in 1977 omitted Papillary Cystadenoma Lymphomatosum from the monomorphic adenoma group. Papillary Cystadenoma Lymphomatosum represents 10 to 14% of all salivary tumours. This tumour commonly affects the parotid of males between 5th and 7th decade of life. This tumour is mostly superficial and represent as painless swelling at the lower pole of parotid gland. Macroscopically, most of the tumours are oval to round encapsulated mass, 2 to 5cm in diameter. Transection shows a pale grey surface punctuated by narrow cystic or cleft-like spaces filled with serous or mucinous secretions.¹⁰

Sialadenoma papilliferum

Sialadenoma papilliferum is classified under the ductal papillomas constituting less than 1% of all minor salivary glands tumours. This tumour commonly involves palate of male patient over 40 years of age. Intraorally, it presents as a painless, well circumscribed papillary growth most commonly at the junction of hard and soft palate followed by buccal mucosa, retro molar pad, lips, faucial pillars, parotid gland and rarely on floor of the mouth.¹¹

Inverted ductal papilloma

Inverted ductal papilloma is a rare minor salivary gland tumour. This tumour appears most commonly on lower lip followed by buccal mucosa as sub mucosal nodule of 0.5 to 1.5 cm between 4th and 5th decade of life with no gender predilection. Macroscopically, the lumen of the tumour is often narrow and occasionally communicates with the exterior of mucosal surface through constricted opening.⁷

A tabulated summary of histological features and IHC markers of various benign salivary gland neoplasms has been enumerated to act as a guiding tool to arrive to the

most appropriate diagnosis and simplify the dilemma around monomorphic adenoma. (Table 2)

Table 2: Key histopathological features along with associated IHC markers as a diagnostic aid for benign salivary gland neoplasms.

Neoplasm	Origin	Epithelium	Cytoplasm	IHC marker
Basal cell adenoma	Intercalated duct cell	<ul style="list-style-type: none"> Mainly consist of polygonal or cuboidal cell exhibiting peripheral palisading with basophilic or ampophillic cytoplasm. Hyaline droplet in island of epithelial cell are seen Thick hyalinised eosinophillic distinct basement membrane. 	<ul style="list-style-type: none"> Fibrous with less amount of blood vessels 	<ol style="list-style-type: none"> Pan cytokeratin Ck5/6 Calponin P63 Ki67 SMA S-100
Canalicular Adenoma	Duct reserve cell specially those of minor salivary glands	<ul style="list-style-type: none"> Mainly consist of bilayered columnar cell with eosinophillic or ampophillic cytoplasm Characteristic periodic separation of the bilayered epithelial cell known as beading pattern 	<ul style="list-style-type: none"> Highly vascular with few fibroblast and little collagen 	<ol style="list-style-type: none"> pan cytokeratin S100 EMA CK19 P63
Sebaceous adenoma	Salivary duct inclusion within parotid lymph nodes	<ul style="list-style-type: none"> Island of epithelium showing minimal atypia scattered in hypeplastic lymphoid tissue 	Fibrous stroma	<ol style="list-style-type: none"> CD15 Androgen receptor EMA
Oncocytoma	Oncocytes lining the duct of salivary gland	<ul style="list-style-type: none"> Large cells with eosinophillic cytoplasm and distinct cell membrane arranged in narrow row or cords 	Little stroma in the form of thin fibrovascular septa	<ol style="list-style-type: none"> Cytokeratin p63
Adenolymphoma	It develop from salivary duct inclusion in the lymph nodes ,after the embryonic	<ul style="list-style-type: none"> Bilayered Inner cells are tall, columnar, granular due to mitochondrial presence and outer layer of cells are 	Lymphoid stroma with germinal centre formation	<ol style="list-style-type: none"> CK7 Ck5/6 Ck19 P63

	development of parotid gland	oncocytic triangular and occasionally fusiform or basiloid in appearance		5) AMA 6) S100
Sialadenoma papilliferum	Excretory duct	<ul style="list-style-type: none"> Exophytic and endophytic proliferation of the ductal epithelium. Surface of the lesion is formed by papillary projection of epithelium supported by fibrovascular core 	Infiltration of chronic inflammatory cells like lymphocytes plasma cells and neutrophils	1) EMA 2) P63 SMA
Inverted Ductal Papilloma	Excretory duct	<ul style="list-style-type: none"> Consist of basaloid and squamous cell arrange in thick bulbous papillary projection that fill ductal lumen 		1)CK 2)EMA 3) Calponin 4)S100 5) alpha SMA 6) ki67

Conclusion

Due to different pathologic features and prognostic implications associated with different benign salivary gland lesions we support the WHO recommendation of usage of various variants separately rather than a more generic term “Monomorphic adenoma”. A tabulated summary of histological features and IHC markers of various benign salivary gland neoplasms has been enumerated to act as a guiding tool to arrive to the most appropriate diagnosis and simplify the dilemma around monomorphic adenoma.

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