

Oncocytic pleomorphic adenoma of palatal salivary gland with macrophages and giant cells associated with cholesterol crystals

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Abstract

Pleomorphic adenoma (PA) is the most common salivary gland tumor characterized by histo-morphological diversity in the form of myxoid, hyalinized, chondroid, osseous, and squamous areas. In this paper, we report a rare case of predominantly oncocytic variant of PA in a 45-year-old male patient on the posterior palatal region. Microscopic examination showed homogenous eosinophilic cellular mass composed of epithelial components arranged in the form of tubular and solid patterns. The polygonal and oval cells showed abundant dark eosinophilic granular cytoplasm. The cell borders were distinct with a central nucleus showing prominent nucleoli. Interestingly at few places, cholesterol clefts were seen surrounded by macrophages and giant cells. The tumor was surgically excised with no evidence of recurrence after 2 years.

Introduction

Salivary gland tumors are known for their varied histomorphological appearance, which sometimes poses a diagnostic challenge for pathologists. One of such appearances is the oncocytic change in tumor cells of benign and malignant salivary gland tumors.¹ Morphologically, oncocytes are characterized by abundant eosinophilic granular cytoplasm with pyknotic nuclei, which is usually centrally placed or shifted towards one side.² Oncocytic nature of tumor has been associated with Warthin's tumor, oncocytoma, and oncocytic

carcinoma.¹ Pleomorphic adenoma (PA) is the most common salivary gland tumor and accounts for 70% of all the tumors of major salivary glands.³ As the name suggests, PA is characterized by plethora of morphological appearances including myxoid, hyalinized, chondroid, osseous, squamous etc. However, predominantly oncocytic cells in PA are extremely rare to occur.²⁻⁵ Literature search indicates only 18 cases reported till date with largest case series (9 cases) reported by Skalova *et al.*² in 1999 (Table 1).

In the present paper, we report a case of PA showing predominantly oncocytic cells with cholesterol clefts and macrophages.

Case Report

A 45-year-old male patient reported with a slow growing asymptomatic swelling on the hard palate region since 5 months. His medical and family history was unremarkable. Physical examination revealed 4 cm × 4.5 cm, diffuse, non-tender, smooth-surfaced, and soft to firm non-fluctuant swelling involving the posterior region of the palate (Figure 1). Mucosal ulceration and cervical lymphadenopathy was not detected. Radiographic examination revealed intact palatal bone. Based on the clinical and radiographic findings, a presumptive diagnosis of PA of palatal salivary glands was made. The lesion was biopsied and sent for histopathologic examination.

Microscopic examination showed homogenous eosinophilic cellular mass composed of epithelial components in the form of tubular and solid pattern. The solid areas were present in the form of small islands and strands. The cells showed predominantly polygonal and oval shape with vesicular nuclei. Stroma at majority of areas showed hyalinization (Figure 2). The abluminal polygonal and oval cells showed abundant dark eosinophilic granular cytoplasm (Figure 2). Even some clear oval cells displayed eosinophilic granular cytoplasm (Figure 3). The cell borders were distinct with centrally placed nucleus showing prominent nucleoli. Cholesterol crystals were evident at few places associated with large oval macrophages showing faint granular eosinophilic cytoplasm along with giant cells (Figure 4). The tumor was very cellular and devoid of chondromyxoid stroma. Based on these findings, a final diagnosis of oncocytic PA of minor salivary glands of palate was made. Tumor was surgically excised under general anaesthesia via intra-oral approach. Histopathological findings of excisional biopsy were consistent with that of incisional biopsy specimen. There was no evidence of recurrence after 2 years.

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Discussion

In 1931, Hamperl coined the term oncocyte (Onkocytin) to describe a cell having abundant eosinophilic granular cytoplasm and a centrally located hyperchromatic nucleus.⁶ Oncocytic metaplasia of ductal and acinar cells is commonly encountered in normal salivary glands in persons over 50 years of age,^{7,8} but primary oncocytic neoplasms and tumour-like lesions are comparatively rare, accounting for less than 1% of salivary tumours.⁷

Histomorphological appearance of oncocytes is attributed to abundant mitochondria present in the cytoplasm of cell.⁹ Presence of oncocytes in salivary gland tumors is not a rare phenomenon as they are considered as a prominent feature of Warthin's tumor, oncocytoma, and oncocytic carcinoma. Even some non-oncocytic tumors like myoepithelioma, acinic cell carcinoma, mucoepidermoid carcinoma, basal cell adenoma, polymorphous low-grade adenocarcinoma, and sebaceous adenoma can show predominantly oncocytic histomorphologic feature.^{1,10} However, their presence in PA is regarded as an extremely rare phenomenon and can cause diagnostic pitfall in the differential diagnosis.²⁻⁵

To our knowledge, only 18 cases of oncocytic PA were reported till date including present case (Table 1). The age ranged from 20 to 75 years with a mean of 45.44±16.38 years. The male to female ratio was 1:1.25. Most common site was parotid gland (14 cases) followed by submandibular (2 cases), para-pharyngeal

area¹ and palate.² The size of the lesion ranged from 1.5 cm to 4.7 cm. Recurrence and metastasis has not yet been reported in the literature. In the present case, we have reported cholesterol cleft formation at few places associated with prominent macrophages and giant cells (Figure 4). Macrophages were large oval cells showing faint granular eosinophilic cytoplasm with centrally or peripherally placed pyknotic nuclei. Macrophages were clearly distinct from the oncocytes based on the intensity of eosinophilic stain. Since cholesterol clefts act as foreign material, they are usually surrounded by macrophages and giant cells. Only one case of PA (non-oncocytic) associated with cholesterol crystals and macrophages have been reported in the literature till date.¹¹ In the present case, we observed clear change in the cytoplasm of oncocytic cells, which again can be regarded as a rare phenomenon in oncocytic PA. Oncocytic metaplasia has long been regarded as affecting both secretory and ductal epithelial cells in salivary glands,^{7,8} although Askew *et al.*¹² provided ultrastructural and light microscopic evidence of both epithelial and myoepithelial oncocytes. In agreement with this, Feiner described a case of an oncocytic adenoma of the parotid gland revealing immunohistochemical co-expression of S-100 protein and cytokeratins (Cks), which was interpreted as an indication of myoepithelial differentiation of oncocytes.¹³⁻¹⁶

Oncocytic PA showed positivity for Ck5/6, Ck8/18, Ck14, vimentin, alpha-smooth muscle actin, S100 protein, p63, epidermal growth factor receptor and b-catenin. However, oncocytic cells in PA usually show a luminal phenotype, expression of anti-mitochondria antibody and reduced b-catenin staining.⁴ In normal age related oncocytic metaplasia, both luminal and abluminal cells show similar oncocytic morphology indicating similarity with the molecular pathogenesis of oncocyte formation in PA.

In oncocytic PA, Mariano *et al.*³ reported pos-

itivity for high molecular weight Ck in luminal cells and myoepithelial cells. However, myoepithelial cells were negative for Ki67, S-100 and p53. This suggests that mitochondrial phenotype is present in both the luminal and myoepithelial cells and mutation occurs in more differentiated cells during tumor formation. All the oncocytic salivary gland lesions are usually biologically indolent. Hence, oncocytic change in PA is likely to have any prognostic importance. The surgical treatment is complete wide excision with good safety margins.^{2,6} The prog-



Figure 1. Photograph showing diffuse swelling on the posterior palatal region with smooth surface.

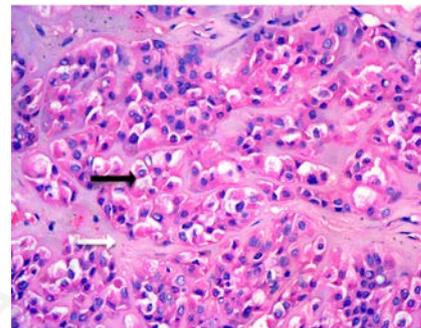


Figure 2. Photomicrograph showing oval to polygonal oncocytic cells with dark granular eosinophilic cytoplasm (Black arrow) and hyalinized connective tissue stroma (White arrow). (Hematoxylin and Eosin stain, Total Magnification X400).

Table 1. Reported cases of oncocytic pleomorphic adenoma.

Author	Year	Age (years)	Sex	Location	Size (cm)	Treatment	Follow-up	Recurrence
Gray <i>et al.</i> ¹⁴	1976	27	F	Parotid	3.5×2.5×2.5	NA	1 year	No
		70	F	Parotid	3×3×2	NA	1 year	No
		28	M	Submandibular	2×1.5×0.5	NA	1 year	No
Pulitzer and Reitmeyer ⁵	1987	55	M	Parotid	2.5	Superficial PE	6 months	No
Ferreiro and Stylopoulos ¹⁰	1995	75	F	Parotid	2.5	Superficial PE	10 months	No
Skalova <i>et al.</i> ²	1999	42	M	Parotid	3.5×3×3	Superficial PE	2 years	No
Skalova <i>et al.</i> ²		31	F	Parotid	1.5	Superficial PE	5 years	No
Skalova <i>et al.</i> ²		20	M	Parotid	NA	Superficial PE	5 years	No
Skalova <i>et al.</i> ²		56	F	Parotid	NA	NA	3 years	No
Skalova <i>et al.</i> ²		49	M	Parotid	2×2.5×3	PE	2 years	No
Skalova <i>et al.</i> ²		38	F	Parotid	2	PE	14 years	No
Skalova <i>et al.</i> ²		58	F	Para-pharyngeal mass	4.5×5×3.5	Excision, RT	12 years	No
Skalova <i>et al.</i> ²		20	F	Submandibular	-	Excision	5 years	No
Skalova <i>et al.</i> ²		39	M	Parotid	4.7×3.7×2.5	PE	4 years	No
Jiménez-Heffernan <i>et al.</i> ¹⁵	2001	61	M	Parotid	2.3	NA	NA	NA
Di Palma <i>et al.</i> ⁴	2006	44	F	Parotid	NA	NA	NA	No
Mariano <i>et al.</i> ³	2011	60	F	Parotid	NA	Superficial PE	NA	No
Kaur and Bhogal ¹⁶	2015	15	M	Palate	3×2	Excision	2 years	No
Present case	2016	45	M	Palate	4×4.5	Excision	2 years	No
Total	19 cases	20-75 (43.8±17.4)	10F 9 M	Parotid (14), Submandibular (2) Parapharyngeal (1), Palate (2)	Range: 1.5-4.7 cm		6 mon.-14 years	No recurrence (18/18)

F, female; M, male; PE, parotidectomy.

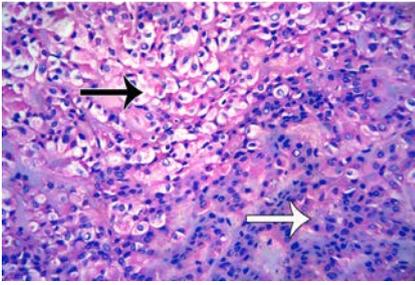


Figure 3. Photomicrograph showing two cell populations; clear cells showing oncocytic appearance (black arrow) and non-oncocytic cells (white arrow). (Hematoxylin and Eosin stain, Total Magnification X400).

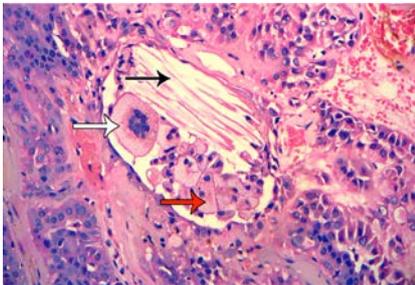


Figure 4. Photomicrograph showing cholesterol clefts (black arrow) surrounded by macrophages with faint granular eosinophilic cytoplasm (red arrow) and giant cells (white arrow). (Hematoxylin and Eosin stain, Total Magnification X400).

nosis is good and no recurrent cases have been reported till date.

In conclusion, we have reported a rare case of oncocytic PA with histopathological evidence of cholesterol crystals, macrophages and giant cells. Presence of clear cell change in oncocytic cells can also be regarded as a rare event in oncocytic PA as it has not yet been reported in the literature.

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