

Clear Cell Morphology in a Salivary Gland Tumor - Clearly a Morphological Dilemma

Nisha J Marla* and Poorni Bharathi T

Pathology, Father Muller Medical College

ABSTRACT

Primary salivary gland tumors with clear cell morphology comprise an uncommonly encountered subgroup of salivary gland neoplasm. Clear cell morphology is a known feature in both benign and malignant salivary gland tumors. Oncocytomas are uncommon tumors of the salivary gland. They have an abundance of mitochondria, which is manifested as granular eosinophilic cytoplasm by light microscopy with presence of cytoplasmic glycogen. Fixation artifact can impart cytoplasmic clearing and oncocytomas with a predominance of clear cytoplasm are labeled Clear cell oncocytomas. Accurate diagnosis of salivary gland tumors can be challenging because of the many diagnostic entities, extensive morphologic overlap, and the rarity of most tumor types. Here we report a case of Clear cell salivary oncocytoma which was confirmed by Immunohistochemical markers by excluding morphological differential of Clear cell myoepithelioma.

Keywords: Clear Cell Change, Oncocytoma, Myoepithelioma, Benign Tumors, Salivary Gland Tumors

Introduction

Primary salivary gland tumors with clear cell morphology comprise an uncommonly encountered subgroup of salivary gland neoplasm. **Oncocytomas are benign neoplasms composed of oncocytes with large eosinophilic cuboidal to columnar cells with more than 60% of their cytoplasm occupied by mitochondria.** Clear cell morphology is a known feature in both benign and malignant salivary gland tumors and this feature has been studied extensively.^[1] The term “clear cell tumor” is not a diagnostic category but a description of one of the several tumors and tumor-like lesions of the salivary glands, histologically characterized by a significant population of cells possessing clear cytoplasm. Clear-cell tumors of salivary glands constitute 1% of all primary salivary gland tumors.^[2] Oncocytes sometimes have clear cytoplasm. This is often the case in multifocal nodular oncocytic hyperplasia, which may be bilateral. The cytoplasm shows granular positivity with phosphotungstic acid hematoxylin (PTAH) stain and antimitochondrial antibody, and large numbers of mitochondria are seen on ultrastructural examination.^[3,4] Here we report a rare case of Clear cell salivary oncocytoma.

Case Report

A 33yr old female patient presented with a swelling in the parotid region since 3 years. On ultrasonography showed intraparotid isoechoic lesion with a radiological impression of Chronic sialadenitis/Benign salivary gland tumor. Fine needle aspiration cytology was reported as Warthins Tumor.

She underwent resection of the superficial lobe of the parotid gland. Grossly it was well defined, 2 x2 cm tumor with grey white cut surface (Fig 1). Microscopy showed a well defined and noninfiltrative tumor predominantly composed of cells with clear cytoplasm and a bland nucleus (Fig 2). Extensive sampling was performed to rule out Warthins tumor as a diagnosis of Warthins was made on FNAC. There was absence of lymphoid cells however few cells with granular cytoplasm, suggestive of oncocytes were noted. (Fig 3). PAS stain showed positivity, suggesting glycogen in these granular cells (Fig 4, represented as inset). PTAH stain was noncontributory.

On microscopy, differentials of Clear cell salivary Oncocytoma and a Clear cell variant of Myoepithelioma were rendered and IHC was suggested for further evaluation as PTAH was noncontributory in our case. On IHC, CK was positive, SMA, Calponin, Caldesmon, CD10, Desmin were negative and Ki 67 was 1%. With this a final diagnosis of Clear cell salivary oncocytoma was rendered after ruling out a morphological differential of Clear cell myoepithelioma.

Discussion

Oncocytoma accounts for approximately 0.4–1% of all salivary gland neoplasms, **majority of them occur in the parotid glands**, with only a small percentage occurring in minor salivary glands of palate, tonsillar fossae, larynx, nasal cavity, maxillary sinus, and the lacrimal gland. It occurs primarily in persons older than 50 years of age. Among oncocytic major salivary gland tumors, 84% occurs in the parotid gland with male to female ratio of 1:1.^[4,5]

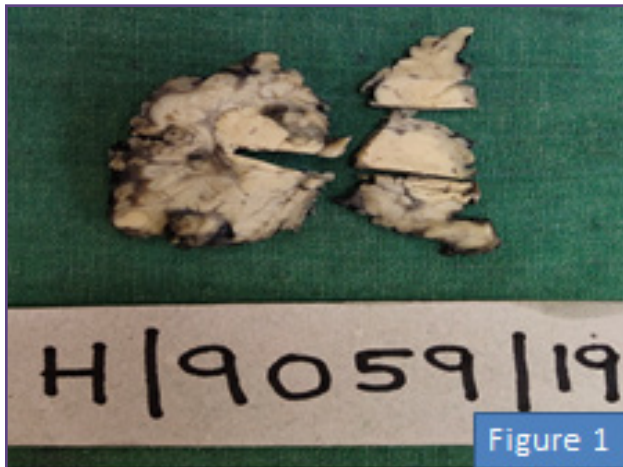


Figure 1

Fig. 1: Gross specimen of Parotidectomy with well defined grey white tumor.

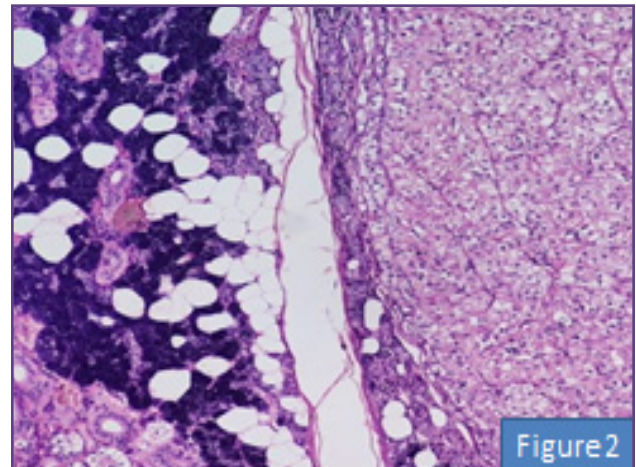


Figure 2

Fig. 2: Well defined tumor showing clear cell morphology with normal salivary gland tissue. (100x).

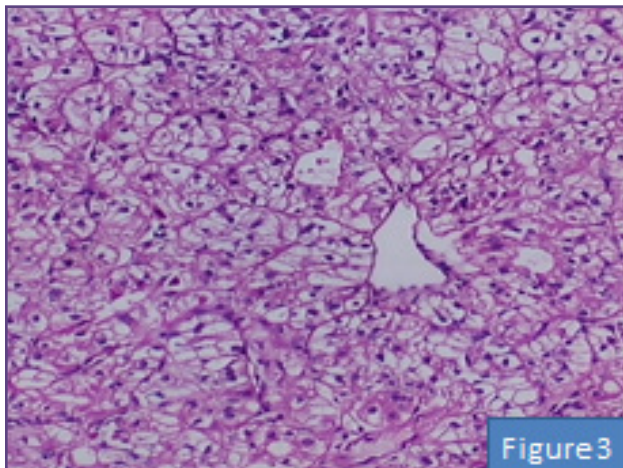


Figure 3

Fig. 3: Clear cells with well defined cell border and centrally placed nucleus. (400x).

Most salivary gland tumors can be diagnosed purely on hematoxylin and eosin stained slides but clear cell tumors are an exception and generally require special stains, immunohistochemistry and even electron microscopy. Warthin's tumor without significant lymphoid cells can be misinterpreted as an Oncocytoma. Adequate sampling with presence of lymphoid cells and epithelial cells will help in arriving at the diagnosis. At times one may require immunohistochemistry for confirmation as seen in our case. [6,7]

In literature clear cells have been reported in a number of benign tumors such as Pleomorphic Adenoma, Myoepithelioma, and Oncocytoma, and in malignant tumors like Clear cell Carcinoma, Epithelial-Myoepithelial Carcinoma, Oncocytic Carcinoma, Mucoepidermoid Carcinoma, Acinic cell Carcinoma, Polymorphous Low Grade Adenocarcinoma and Adenoid Cystic Carcinoma. [7,8]

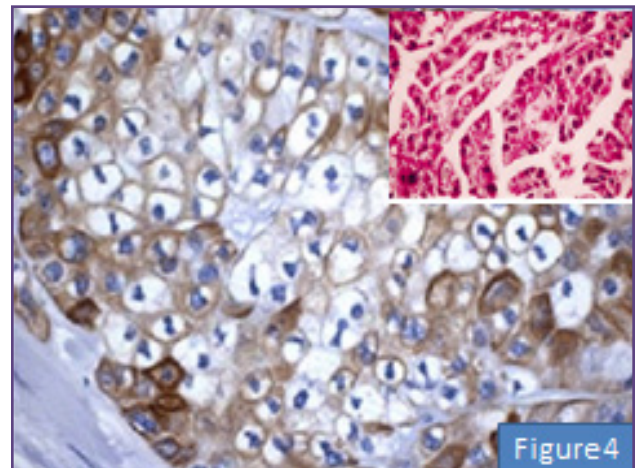


Figure 4

Fig. 4: Inset showing pink PAS positive substance. (400x).

Majority of clear cells are noted in malignant tumors and in benign tumors it is noted in variants of oncocytoma and myoepithelioma. Most of the Clear cell carcinomas of salivary glands are low grade. Salivary gland tumors showing features of clear cell change are contributed by the myoepithelial cells. Based on this, primary salivary clear cell neoplasias can be divided into those that diagnostically require evidence of myoepithelial differentiation, i.e., clear cell myoepithelioma/myoepithelial carcinoma and epithelial-myoepithelial carcinoma and those that do not. Clear cell variants of salivary gland tumors such as acinic cell carcinoma, mucoepidermoid carcinoma and oncocytoma also do not have myoepithelial differentiation. In this context, immunohistochemistry with calponin can be an important diagnostic tool. [9,10]

Conclusion:

Despite the well-recognized morphology of this tumor, there is a wide range of neoplasms that may mimic Oncocytoma and hence one needs to be consider it in differential diagnosis. It is important to recognize Oncocytomas, including the clear cell variant, because of its favorable prognosis compared to other clear cell neoplasms of the salivary gland. An awareness of all the possible “mimickers” of Clear cell salivary oncocytoma becomes more significant in view of the fact that most are malignant neoplasms with a poor prognosis.

Acknowledgements

Dr Jayaprakash C S. Professor and HOD, Department of Pathology

References

1. Ellis GL. “Clear cell” oncocytomas of salivary gland. Hum Pathol. 1988;19; 862–867.
2. Ellis GL. Clear cell neoplasms in salivary glands: clearly a diagnostic challenge. Ann Diagn Pathol. 1998;2:61–78.
3. Saqi A, Giorgadze T A, Eleazar J, Remotti F et al. Clear Cell and Eosinophilic Oncocytomas of Salivary Gland: Cytological Variants or Parallels? Diagnostic Cytopathology DOI 10.1002/dc
4. Rito M, Fonseca I. Salivary Gland Neoplasms: Does Morphological Diversity Reflect Tumor Heterogeneity ? Pathobiology 2018;85:85–95.
5. Majumdar A B, Paul S S , Sarker G, Ray S. Oncocytoma of Oral Cavity Mimicking as Jaw Tumor. Hindawi Publishing Corporation Case Reports in Otolaryngology Volume 2014, Article ID 315058, 5 pages.
6. Kar A, Pattnaik K, Kar T, Biswal P et al. Clear cell lesions in pathology: Histomorphologic approach to diagnosis. Indian Journal of Pathology and Microbiology 2020; 63(2): 177-187.
7. Said-al-Naief N, Klein MJ. Clear cell entities of the head and neck: a selective review of clear cell tumors of the salivary glands. Head and Neck Pathol. 2008;2:111-5.
8. Brandwein M, Huvos A. Oncocytic tumors of major salivary glands: a study of 68 cases with follow-up of 44 patients. Am J Surg Pathol. 1991;15:514–528.
9. Shrestha P, Yang LT, Liu BL, et al. Clear cell carcinoma of salivary glands: immunohistochemical evaluation of clear tumor cells. Anticancer Res. 1994;14:825–836.
10. Woods T, Fitzpatrick S, Cohen D, Islam M et al. Clear cell changes in salivary gland neoplasms: A 20-year retrospective study. Oral Patol Oral Cir Bucal. 2017 May 1;22 (3):e276-81.

*Corresponding author:

Dr Nisha J Marla. Postal Address: W/O Dr Jayashankar Marla, Suraj, 3-5-514/2, Kadri Kambala Road, Kadri Mundana, Mangalore – 575004, Karnataka
Phone: +91 9481148975
Email: nishajmarla@gmail.com

Financial or other Competing Interests: None.

Date of Submission : 13/09/2020
Date of Acceptance : 11/11/2020
Date of Publication : 30/12/2020