

CLEAR CELL TUMORS- A REVIEW

A.BANU JOTHI, M.DHARSHINI VIRUTHIKA, M.INDHU DEEPIKA, Dr. P.POOJA SRI,
Dr. MARY TRESA JEYAPRIYA

^{1,2,3}CRRI, ⁴Post Graduate, ⁵Reader
KARPAGA VINAYAGA INSTITUTE OF DENTAL SCIENCES

ABSTRACT:

Clear cells are either epithelial or mesenchymal cells composed of pale or clear cytoplasm with a distinct nucleus. These tumours are heterogenous group of both benign and malignant neoplasm of epithelial, mesenchymal, melanotic and hematopoietic derivation. The biological behaviour may range from indolent to aggressive. Clear cells can be observed in any type of benign and malignant salivary gland tumours, including benign mixed tumours, myoepithelioma/myoepithelial carcinoma, oncocytoma/oncocytic carcinoma, mucoepidermoid carcinoma, acinic cell carcinoma, polymorphous low-grade adenocarcinoma, and adenoid cystic carcinoma.

KEYWORDS: Clear cell tumors, oncocytoma, Mucoepidermoid carcinoma, Myoepithelioma, Adenoid cystic carcinoma.

INTRODUCTION:

Clear cells are either epithelial or mesenchymal cells composed of pale or clear cytoplasm with a distinct nucleus. Clear cells are associated with physiological and pathological conditions. Pathologic conditions can arise from clear cells like, the remnants of dental lamina can give rise to odontogenic cysts, melanocytes give rise to melanomas, and adipocytes are associated with lipomas and liposarcomas.⁽¹⁾

It is possible for intraosseous salivary gland tumours to develop from ectopic salivary tissue, the neoplastic transformation of the mucous cells lining dentigerous cysts, embryonic remnants of submandibular glands located within the mandible, the bony entrapment of mucous cells of the retromolar pad during embryogenesis, or theoretically, salivary tissue present in lingual cortical defect of the mandible. (2-4). Any type of benign and malignant salivary gland tumour, such as benign mixed tumours, myoepithelioma/myeloma, oncocytoma/oncocytic carcinoma, mucoepidermoid carcinoma, acinic cell carcinoma, polymorphous low-grade adenocarcinoma, and adenoid cystic carcinoma, can be distinguished by the presence of clear cells..⁽⁵⁻¹⁰⁾

CLASSIFICATION:

PHYSIOLOGIC CLEAR CELL:

Keratinocytes make up the majority of the oral epithelium's histologic cells, with clear cells such as Melanocytes, Langerhans cells, Merkel cells, and lymphocytes making up the remaining 10%. These cells, which are found at various levels of the oral epithelium, lack a significant number of tonofilaments and desmosomes, and none of them take part in the maturation process. In addition to being physiological clear cells, epithelial derivatives of glandular or secretory cells also contain unique compounds such as mucins, mucoids, and sebum. The cytoplasm of adipocytes in connective tissues is transparent and empty, and their nucleus is pushed to the periphery because the common fixative formalin and the dye xylene used during histological preparation change how the adipocytes interact with the protein.⁽¹¹⁻¹⁶⁾

PATHOLOGIC CLEAR CELL

Focused or widespread clear cell changes can be caused by neoplastic or non-neoplastic diseases, as well as artificial or degenerative changes. The odontogenic apparatus, tissues of the salivary glands, connective tissues, and metastatic cancers are responsible for the majority of significant clear cell lesions in the oral and maxillofacial region. The tumour origin, knowledge of the frequency, and patterns of clear cell presentation of the lesion may be useful in making a diagnosis and differentiating between benign and malignant clear cell tumours.⁽¹⁷⁻²⁶⁾

I. CLEAR CELL ODONTOGENIC LESIONS

1) Odontogenic cysts

1. Gingival cyst of adults

2. Lateral periodontal cyst

3. Clear cell calcifying odontogenic cyst

2) Odontogenic tumors

1. Clear cell odontogenic carcinoma

2. Clear cell odontogenic ghost cell tumor
3. Clear cell calcifying epithelial odontogenic tumor

II. CLEAR CELL SALIVARY GLAND TUMORS

1. Clear cell myoepithelioma
2. Clear cell oncocytoma
3. Clear cell mucoepidermoid carcinoma
4. Clear cell acinic cell carcinoma
5. Clear cell myoepithelial carcinoma
6. Epithelial myoepithelial carcinoma
7. Hyalinizing clear cell carcinoma

III. CLEAR CELL VARIANT TUMORS:

Some clear cell variant tumors also present in the oral cavity such as clear cell variant of ameloblastoma, clear cell variant of mucoepidermoid carcinoma, clear cell variant of oncocytoma, clear cell variant of acinic cell carcinoma, clear cell variant of sebaceous adenoma and lymph adenoma and clear cell variant of squamous cell carcinoma.

CLEAR CELL ODONTOGENIC LESIONS:

It is extremely rare for odontogenic neoplasms to contain a considerable amount of clear cells.⁽²⁷⁾ Clear cell odontogenic cysts are: Calcifying odontogenic cyst (CCOC), gingival cyst of adults (GCA) and lateral periodontal cyst (LPC). Except for the CCOCa which consists primarily of clear cells, all the other odontogenic lesions contain areas bearing histologic features characteristic of the respective entities which help in differentiation of one from another.⁽²⁸⁾ Numerous studies have shown that the occurrence of clear cells may prove to be a sign of increased tumor aggressiveness indicating a more radical surgical approach.⁽²⁹⁻³¹⁾

CLEAR CELL SALIVARY GLAND TUMORS:

Clear cells constitute less than 1% of all primary salivary gland tumors.⁽³²⁾ Clear cell salivary gland tumors are almost invariably malignant in nature but they do include two benign lesions namely: Clear cell variant of oncocytoma (CCO) and myoepithelioma (CCM). Clear cells in acinic cell carcinoma (CACC) seldom comprise a significant portion of the tumor whereas clear cell mucoepidermoid carcinoma (CMEC) can readily be identified by an admixture of clear-squamoid, mucous and intermediate cells.⁽³³⁾ Primary salivary tumors should be distinguished from clear cell metastatic tumors since they have diagnostic and therapeutic consideration.⁽³⁴⁾ With respect to biological behavior, clear cell salivary gland tumors are considered low grade malignancies because in spite of their benign appearance they are capable of local infiltrative growth and destruction as well as metastasis with poor prognosis.⁽³²⁾

PREDOMINANT CLEAR CELL TUMORS:

1) CLEAR CELL MYOEPITHELIAL CARCINOMA:

Myoepithelial tumors arise from myoepithelial cells, and is characterized by absence of ductal differentiation and both epithelial, Smooth muscle cell character. In head and neck region, the parotid glands are mostly affected in malignant state extremities in head and neck region are affected in benign lesion as well as, paranasal sinus and nasal cavity of head region are also affected.⁽³⁵⁾

2) ACINIC CELL CARCINOMA:

Parotid gland is mostly affected by acinic cell carcinoma. The tumour originates from intercalated duct reserve cell. Bilateral involvement of Parotid gland is seen in 3% of cases. In 80% of cases the carcinoma develops from the superficial lobe and

inferior pole of the parotid Gland. Many acinic cell carcinomas reveal clear cell element zones, as a result of inadequate Fixation. ⁽³⁶⁾

3) **EPIMYOEPITHELIAL CARCINOMA:**

It is a malignancy of salivary gland which has clear cells and darkly stained cells forming a lumen. Usually greater than 3 cm lesions can recur and is an intermediate grade tumour. ⁽³⁶⁾

4) **HYALINIZING CLEAR CELL CARCINOMA (HCCC):**

Myoepithelioma, acinic cell carcinoma, Oncocytoma, mucoepidermoid carcinoma are predominantly composed of clear cells. there are two subgroups according to their morphology: 1) Biphasic- eosinophilic and clear cells with a double layer arrangement 2) Monophasic- composed of only clear cells. Clear cells arranged in solid sheets or nests, cords around hyalinized Bands. ^(37,38)

5) **CLEAR CELL CARCINOMA:**

It is a low-grade tumour that predominantly affects minor salivary glands. Both Clear cell carcinoma and epimyoeplithelial carcinoma shows clear cell changes that are due to cytoplasmic accumulation of glycogen and myofilaments. Uniformly bland cells compose predominantly clear cell cytoplasm. ⁽³⁶⁾

6) **MUCOEPIDERMOID CARCINOMA:**

Mucoepidermoid carcinoma is a most common salivary gland neoplasm. The typical features of mucoepidermoid carcinoma are the presence of clear cells, epidermoid Cells and cystic spaces lined by mucus cells. Clear cell Cytoplasm is seen and it appears as watery clear cytoplasm with centrally placed pyknotic nuclei. ⁽³⁹⁾

7) **ONCOCYTOMA:**

Oncocytoma is a clear cell variant tumour and is a benign salivary gland tumour. Most of the tumours are completely clear and some tumours have eosinophilic granular cytoplasm. The Transformation to clear cells from eosinophilic oncocytes is visible. ⁽³⁷⁾

II. ODONTOGENIC ORIGIN:

1) **CALCIFYING EPITHELIAL ODONTOGENIC TUMOR: (CEOT)**

CEOT is a Benign epithelial odontogenic tumour. The epithelial cells are polyhedral in shape with foamy Clear cytoplasm and variation in nuclei size. According to Abrams and Howell out of 11 clear cell neoplasms, 7 patients had clear cell variant of CCCEOT. ⁽⁴⁰⁾

2) **CLEAR CELL ODONTOGENIC CARCINOMA: (CCOC)**

CCOC is a rare neoplasm that affects maxilla and mandible and mostly affects females more than 60yrs of age. It is a poorly circumscribed tumour with clear cytoplasm which is locally aggressive. It often metastases to lung and regional lymph nodes and has a recurrence rate of more than 50%.

3) **CLEAR CELL AMELOBLASTOMA:**

Ameloblastoma is the most common odontogenic neoplasm in the oral cavity. Martinez and Robinson in 1977, first brought out the difference between clear cell ameloblastoma and Unicyclic ameloblastoma. Waldron et al in 1995 and NG and Siar described Clear cell ameloblastoma as an intraosseous lesion and extraosseous lesion. Microscopically Islands of clear cells are seen which are polygonal in shape. ^(41,42)

4) **CLEAR CELL VARIANT OF LATERAL PERIODONTAL CYST:**

Lateral periodontal cyst is a developmental nonkeratinised cyst occurring lateral to the root of the tooth. The cyst is lined by thin, non-Keratinized epithelium and clusters of glycogens- rich voluminous clear epithelial cells. Lateral periodontal cyst has a variant known as Botryoid Odontogenic cyst (BOC). ^(36,43)

CONCLUSION:

Clear cell tumours are a diverse group of benign and malignant neoplasms with origins in the epithelium, mesenchyme, melanocyte, and haematological system. The biological behaviour can be anything from passive to hostile. Yet, the majority of the time, the presence of clear cells may indicate a more aggressive tumour. Derivations from clear cells are crucial for the diagnostic hints. Hence, understanding histomorphology and immunohistochemical staining features is crucial.

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