

Clear Cell Tumors Of The Oral Cavity

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ABSTRACT:

Clear cell lesions are heterogeneous groups of odontogenic and salivary gland having its origin derived from epithelial, mesenchymal, hematopoietic and melanocytic components. Clear cells are found in different tumors and these clear cells are usually identified by the histopathological sections. Benign and malignant clear cell tumors are rare in oral cavity (2%). Pathologically H and E staining method is a gold standard method for histological examination for various human diseases. Identifying the clear cell is one of the clue or proof of accurate diagnosis. There are also some other structures observed in histopathological sections like grooves, Islands, granules, inclusions, globules, halo or clearing which enables the pathologist to find out the proper and accurate diagnosis. Clear cell changes are seen in various benign, malignant and non neoplastic conditions. Clear cell tumors affect other body parts also including CNS, skin, female urogenital tract, head and neck areas rarely bone and soft tissue region. For an approach to clear cell tumors the pathologist must identify if the change is from artifactual or mimic like the clear cell tumors, or originally clear cell tumors from appropriate origin. This Article gives idea of the clear cell tumors and various differential diagnosis of the clear cell tumors that affect the oral cavity.

KEYWORDS: *Clear Cell Lesions, clear cell, benign and malignant and non- neoplastic lesions, grooves, Islands, globules.*

INTRODUCTI

Clear cell tumors are infrequent in oral cavity. Clear cells are observed in many different tumors that are usually odontogenic, salivary and metastatic in origin. Clear cells are polyhedral cells with clear cytoplasm with distinct nuclei¹. Initially Merkel cells are called as a HELLE ZELLEN (clear cells) named after merkel in 1875², the cells are located in the basal layer of the epidermis. In salivary gland, the term 'clear cell carcinoma' was first described by Batsaki in 1980³. Finally in 1985 Hansen et al named it as a clear cell odontogenic neoplasm. These clear cells are result from fixation artifacts and cytoplasmic accumulation of glycogen, lipids in sebaceous cells, mucin in mucous cells, tonofilaments in epidermoid clear cells, zymogen in clear acinar cells, that is not stained by hematoxylin and eosin stain. This is the most common reason for the cell to appear as a clear cell^{1,2}. There are two types of clear cells. 1) physiologic clear cell 2) pathologic clear cell.

PHYSIOLOGICAL CLEAR CELL

Clear halo cells around the nuclei, present in various parts of the body like remnants of dental lamina, rests of Malassez, myoepithelial cells, mucous acinar cells, secretory cells in the epithelium, and nonkeratinocytes (melanocytes, langerhans cells, merkel cells)^{5,6}. During the processing, cytoplasm around the nuclei shrinks and becomes halo. It gives a clear cell appearance⁷.

PATHOLOGICAL CLEAR CELL:

Pathologically clear cells are rare in salivary glands, oral cavity and jaws (1- 2%). Clear cells -++++ are considered a minor element of other tumors¹. Clear cells can be noticed and derived in any malignant, benign,

epithelial, mesenchymal, hematopoietic and melanocytic tumors⁸. focal clear cell changes are more progressive and extensive in tumors which is more challenging in diagnosis.

1. Salivary gland tumors- glycogen in their cytoplasm which is causes of cytoplasmic clearing
2. Acinic cell adeno carcinoma- Alterations in the cytoplasmic organelles and fixation artifacts causes clearing the cell⁹
3. Muco epidermoid carcinoma-mucin with glycogen causes clearing¹⁰.
4. Metastatic renal cell carcinoma-accumulation of glycogen and lipids causing clear cell.

CLEAR CELL TUMORS OF THE ORAL CAVITY¹¹

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.

PREDOMINANT CLEAR CELL TUMORS:

1) CLEAR CELL MYOEPITHELIAL CARCINOMA:

Myoepithelial tumors are arising from myoepithelial cells, absence of ductal differentiation and both epithelial, smooth muscle cell character. Parotid glands are mostly affected in malignant state and 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. Myoepithelial cells are arranged in various patterns like epitheloid, plasmacytoid and clear cell patterns. CCMC lesions are more aggressive, 50% recurrence rate and 40% metastatic rate¹. These tumors characteristically reacts with anti S-100 protein, vimentin, high molecular weight cytokeratin, muscle specific actin (MSA) and alpha smooth muscle actin (SMA). Calponin is the most specific marker for this tumor when compared to the MSA and SMA¹².

2) ACINIC CELL CARCINOMA :(Fig 1)

Acinic cell carcinoma predominantly occurs in major salivary glands mostly parotid. The origin of the tumor is from the intercalated duct reserve cell and although it retains the potential for neoplastic transformation¹³. These tumor found in all age groups including children, no gender predilection. In 3% of cases bilateral involvement of parotid gland is seen .80% of cases carcinoma develops from the superficial lobe and inferior pole of the parotid gland ¹³.It is a slow growing lesion less than 3 cm in diameter. Pain is a common symptom. Tumor cells are uniform and well differentiated, contain cytoplasmic PAS–positive, diastase digestion–resistant granules normally found in acinic Cells. Many acinic cell carcinomas reveal clear cell element zones, as a result of inadequate fixation.

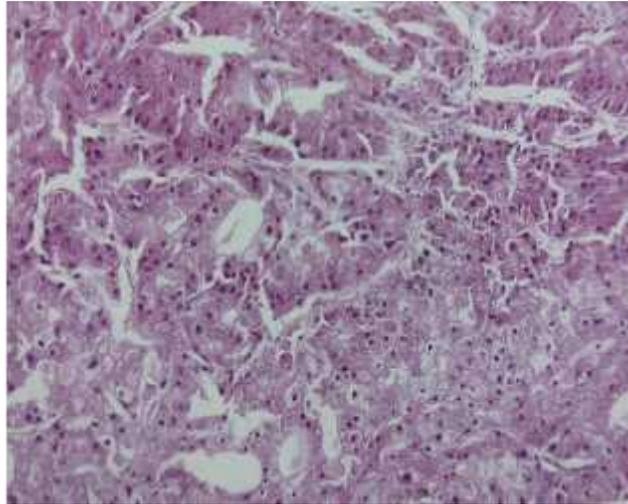


Fig:1 Acinic cell carcinoma with clear cell area

3) EPIMYOEPITHELIAL CARCINOMA¹³: (Fig 2)

Epimyoeptelial carcinoma is a clear cell containing malignancy of salivary gland (major glands) .affected by 7-8 decades of life and two- to- one female predilection. A lobular pattern of growth composed of 2 cell types 1)abundant clear cells with islands of cuboidal 2)darkly staining cells forming a lumen.S-100 protein ,Glycogen,actins are present in these cells supporting their myoeptelial origin. It is an intermediate grade tumor usually greater than 3 cm lesions can recur.

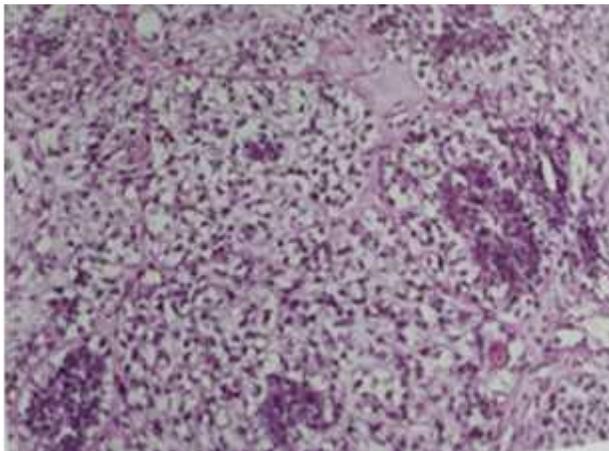


fig ;2 Epimyoeptelial carcinoma ;clear cells surrounding darker staining tumor ductal cells

4) HYALINIZING CLEAR CELL CARCINOMA (HCCC):

Salivary gland tumors are predominantly composed of clear cells, such as myoepithelioma, acinic cell carcinoma, oncocytoma, mucoepidermoid carcinoma. These tumors are identified by their specific histological findings. According to their morphology there are two subgroups 1) Biphasic- eosinophilic and clear cells with a double layer arrangement 2) Monophasic- composed of only clear cells. Later it subgroups as hyalinizing clear cell carcinoma.^{1,3}. HCCC shows microscopically clear cells arranged in solid sheets or nests, cords around hyalinized bands.

5) CLEAR CELL CARCINOMA: (Fig 3)

Clear cell carcinoma and epimyoeplithelial carcinoma –exhibit clear cell changes that are due to cytoplasmic accumulation of glycogen and myofilaments. Formally called as hyalinizing cell carcinoma, is a low grade tumor mostly affected in minor salivary glands. Microscopically predominant clear cell cytoplasm composed of uniformly bland cells¹³. Areas of nest and sheets of cells are seen. Tumor stained positive for glycogen, negative for mucin, s-100protein, MSA (muscle -specific protein)

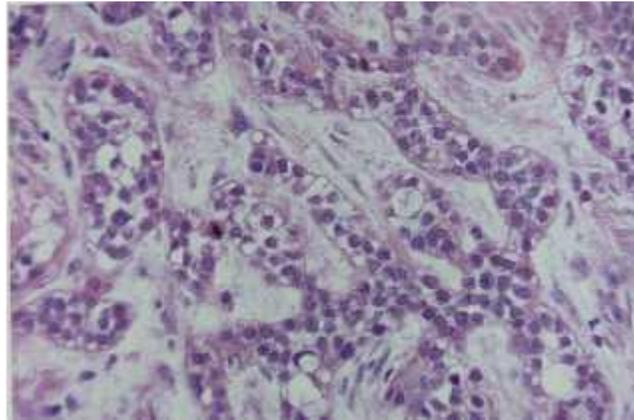


Fig :3 clear cell carcinoma Trabecular arrangement of clear cells

6) Mucoepidermoid carcinoma (MEC): (Fig 4)

Mucoepidermoid carcinoma is a most common salivary gland neoplasm. Presence of clear cells, epidermoid cells and cystic spaces lined by mucus cells are the typical features of mucoepidermoid carcinoma. Clear cell cytoplasm can be seen in MEC .It appears watery clear cytoplasm with centrally placed pyknotic nuclei¹⁴.

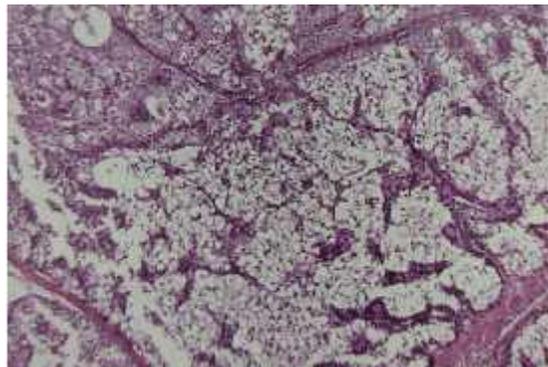


Fig: 4 mucoepidermoid carcinoma (intermediate grade)with a focus of clear cell change

7) ONCOCYTOMA: (Fig 5)

It is a benign salivary gland tumor. Oncocytoma is a clear cell variant tumor. Most of the tumors completely clear and some tumors have eosinophilic granular cytoplasm. Transformation from eosinophilic oncocytes to clear cells can be visible ¹.

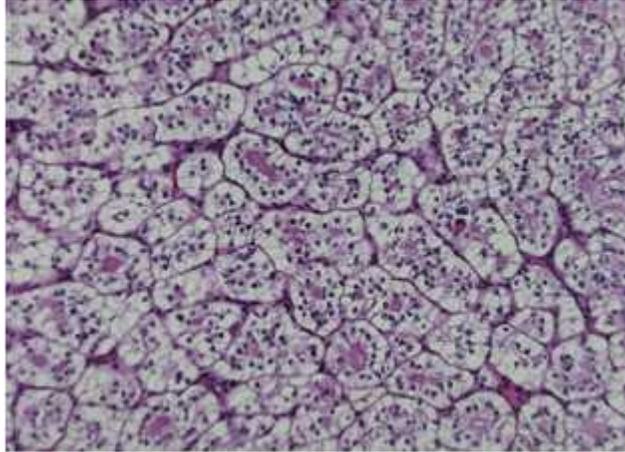


Fig: 5 oncocytoma with clear cell change

II ODONTOGENIC ORIGIN:

1) CALCIFYING EPITHELIAL ODONTOGENIC TUMOR: (CEOT)

It is a benign epithelial odontogenic tumor. According to Abrams and Howell out of 11 clear cell neoplasms, 7 patients had clear cell variant of CCCEOT¹⁵.microscopically epithelial cells are polyhedral in shape with foamy clear cytoplasm and variation in nuclei size.

2) CLEAR CELL ODONTOGENIC CARCINOMA: (CCOC) (Fig 6)

CCOC is a rare neoplasm of the mandible and maxilla. Usually affected by females more than 60 years of age. It is a locally aggressive, poorly circumscribed tumor with clear cytoplasm. The rate of recurrence is more than 50% and metastases to lung and regional lymphnodes.differential diagnosis of other clear cell component such as calcifying epithelial odontogenic tumor, central mucoepidermoid carcinoma, metastatic renal carcinoma, metastatic acinic cell carcinoma.

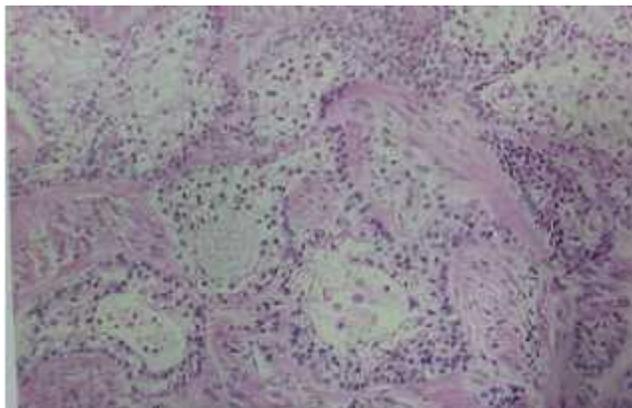


Fig :6 clear cell odontogenic tumor as nest of odontogenic epithelium with relatively clear cytoplasm

3) CLEAR CELL AMELOBLASTOMA:

In 1977 Martinez and Robinson first brought out the difference between clear cell ameloblastoma and unicystic ameloblastoma¹⁶. Ameloblastoma is a most common odontogenic neoplasm in the oral cavity. Clear cell ameloblastoma as an intraosseous lesion and extraosseous lesion¹⁷ described by Waldron et al in 1995 and NG and Siar. Microscopically Islands of clear cells with polygonal in shape. The reason for clear cells in odontogenic tumors are from the origin of dental lamina.

4) CLEAR CELL VARIANT OF LATERAL PERIODONTAL CYST:

A lateral periodontal cyst is a nonkeratinised developmental cyst occurring lateral to the root of the tooth. Both gingival cyst and lateral periodontal cyst are pathologically similar lesion¹³. Both the cyst are lined by thin, non keratinized epithelium and clusters of glycogen-rich voluminous clear epithelial cells are present. Botryoid odontogenic cyst (BOC) is observed to be a variant of lateral periodontal cyst¹⁸.

III CLEAR CELL METASTATIC TUMORS:

1) RENAL CELL CARCINOMA:

Renal cell carcinoma is a most frequent metastatic tumor in the oral cavity. Usually metastatic tumors are uncommon in oral cavity. Only 1% of cases reported in oral cavity. Primary tumor which metastasize in oral cavity are lung carcinoma in male predominance, Breast carcinoma in female cases¹⁹. Renal cell carcinoma (RCC) are the third most common neoplasm affected in the head and neck region. It is difficult to identify that renal cell carcinoma metastasis and salivary gland origin clear cell carcinomas.

CONCLUSION:

Clear cell tumors of the oral cavity are heterogeneous groups of both benign and malignant neoplasm of epithelial, mesenchymal, melanocytic and hematopoietic derivation with variable histopathological findings. Clear cell changes associated with the malignancies are important for the diagnostic clues. Clear cells are special features help to diagnose certain clear cell tumors. Clear cells are preponderance to clear cell tumors. Apart from pathological clear cells artifactual clear cells can lead to misdiagnosis of tumors. So it is vital for the pathologist to know the histomorphology and immunohistochemical staining characteristics.

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