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CLEAR CELL LESIONS OF ORAL CAVITY-AN INSIGHT

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Abstract
The clear cell lesions of head and neck region are rare and both benign and malignant lesions are observed. The usual factors attributing to clear cells in a pathology are accumulation of glycogen, mucopolysaccharides, lipids, mucin, foreign material in cytoplasm, hydropic degeneration of cell organelles, artifactual changes and improper cell preservation. Physiologically certain cells having rich glycogen content of the cytoplasm such as remnants of dental lamina, rests of malassez and eccrine sweat gland have clear cytoplasm. Lipids of adipose tissue is lost during processing with organic solvents(xylene) and thus appear clear. Pathologic clearing of cells happen if the tumour cells having glycogen/mucin/lipid content and hydropic degeneration of neoplastic cells. Clear cells found in tumours of head and neck are commonly of odontogenic cysts and tumours, salivary gland tumours and metastatic tumours. The appearance of clear cells may be due to fixation artifacts, lesser cell organelles giving an empty appearance and accumulation of substances such as glycogen, mucin, lipids, immature granules intracellularly. Cellular contents mentioned above may be washed during tissue processing that gives a clear appearance.

Keywords – Clear cells, Clear cell lesions, glycogen/lipid/mucin accumulation.

INTRODUCTION

The clear cell lesions of head and neck region are rare and both benign and malignant lesions are observed. The usual factors attributing to clear cells in a pathology are accumulation of glycogen, mucopolysaccharides, lipids, mucin, foreign material in cytoplasm, hydropic degeneration of cell organelles, artifactual changes and improper cell preservation.[1] The clearing of cells happens both physiological and pathological as well. Physiologically certain cells having rich glycogen content of the cytoplasm such as remnants of dental lamina, rests of malassez and eccrine sweat gland have clear cytoplasm. Lipids of adipose tissue is lost during processing with organic solvents(xylene) and thus appear clear. Pathologic clearing of cells happen if the tumour cells having glycogen/mucin/lipid content and hydropic degeneration of neoplastic cells.[2]
The clearing of cells in pathology could be due to dental lamina origin.[3] The accumulation of glycogen/mucin or lipids in various odontogenic cysts, tumours, salivary gland neoplasms, malignant and benign tumours result in clearing of cytoplasm.[4,5]

Types of clear cells

Physiologic clear cells- The oral ectoderm lining the stomadeum(primitive oral cavity) contain cells having cytoplasm which are rich in glycogen and thus gives clear appearance. Thus the remnants of these cells after development are seen as clear cells.[6] The cells in epithelium which are not involved in keratin production are referred to as Nonkeratinocytes. These nonkeratinocytes (Melanocytes and Langerhans cells) have clear halo around the nucleus due to shrinkage of cytoplasma during tissue processing as they lack desmosomal attachment

with adjacent keratinocytes. Though merkel cells are nonkeratinocytes due to presence of tonofilaments and occasional desmosomes they do not show clear cell appearance.[7]

Pathological clear cells- The presence of glycogen/mucin and lipid content in the cytoplasm of cells in various cysts and tumours show clear cell appearance. Such clear cells are seen in tumours of epithelial, mesenchymal and melanocytic/hematopoetic origin.[8]

Apart from glycogen/mucin and lipid content of the cells, the scarcity of organelles in salivary duct cells and immature zymogen granules of serous acinar cells also result in clear cell appearance.[9]

Clear cells in head and neck region

Clear cells found in tumours of head and neck are commonly of odontogenic cysts and tumours, salivary gland tumours and metastatic tumours. The appearance of clear cells may be due to fixation artifacts, lesser cell organelles giving an empty appearance and accumulation of substances such as glycogen, mucin, lipids, immature granules intracellularly. Cellular contents mentioned above may be washed during tissue processing that gives a clear appearance.[9]

Clear cell lesions of Oral cavity

Clear cells are cells with clear cytoplasm and prominent nuclei. The lesions with clear cells account about 1% to 2% cases in the oral cavity.[9]

Classification of clear cell tumours of head and neck [2]

Osseous tumours with clear cell features- Osteosarcoma
Clear cell chondrosarcoma
Chordoma

Non-neoplastic reactive conditions and storage diseases-As differential diagnosis of clear cell entities(Based on histomorphological presentation)- Rosai Dorfman disease
Gaucher's disease
Langerhans cell histiocytosis
Erdheim-chester disease

Classification of clear cell tumours of salivary glands(Cardina and Alos,WHO 2005)

Benign – Myoepithelioma
Sebaceous adenoma
Oncocytoma
Ontocytic hyperplasia

Malignant – Primary (a)Carcinoma not usually characterised by clear cells but with clear cell predominant areas eg. Mucoepidermoid carcinoma, Acinic cell carcinoma

b. Carcinoma usually characterised by clear cell – (i)Dimorphic- Epitheial Myoepithelial carcinoma
(ii)Monomorphic- Clear cell carcinoma
Myoepithelial carcinoma

Metastatic carcinoma- Carcinoma especially Kidney, Thyroid and Melanoma.

Classification of Odontogenic lesions with clear cells[10]

Odontogenic tumours- Clear cell odontogenic carcinoma
Clear cell calcifying epithelial odontogenic tumour
Clear cell Ameloblastoma

Odontogenic cyst – Clear cell variant of Lateral Periodontal cyst
Clear cell variant of Glandular cyst

Clear cell tumours of Salivary glands

Among all primary salivary gland tumours about 1% constitute the clear cell tumours. Major clear cell changes in salivary gland tumours are usually contributed by myoepithelial cells. Also except clear cell oncocytoma and Myoepithelioma mostly the clear cell tumours of salivary glands are malignant.[11] Clear cell salivary gland tumours with myoepithelial differentiation show positive reaction for Immunohistochemistry marker Calponineg. Clear myoepithelioma, Myoepithelial carcinoma and Epithelial-Myoepithelial carcinoma.[12] Salivary gland tumours such as clear cell variant of Mucoepidermoid carcinoma, Clear cell variant of Acinic cell carcinoma are positive for special stains for mucin(mucicarmine). Primary clear cell carcinoma, Epithelial-Myoepithelial carcinoma and clear cell myoepithelial tumours show positive for glycogen and on histochemical staining PTAH(Phosphotungstic acid hematoxylin) and PAS(Periodic Acid Schiff) show positive results. With aging the salivary glands show clear cells haphazardly and are referred to as Oncocytosis.

Clear cell Odontogenic lesions

Odontogenic neoplasms with clear cells are quite rare. Since the jaw bones show numerous benign and malignant tumours it is essential to diagnose rightly to provide appropriate treatment. Histopathological differentiation of various odontogenic tumours is required to obtain the diagnosis. Clear cell odontogenic carcinoma shows islands of epithelial tumour cells in three patterns namely biphasic, monophasic and ameloblastomatous. In biphasic

pattern along with polygonal hyperchromatic cells oval and liner cells are seen. In monophasic pattern islands of clear cells are seen and in ameloblastomatous pattern along with clear cells ameloblastoid palisading cells are seen in the periphery.Ameloblastoma too shows epithelial cells but with specific pattern such as follicular, plexiform. Calcifying epithelial odontogenic tumour show solid proliferation of large pleomorphic cells, spindle cells, clear cells, calcifications and amyloid deposits. Odontogenic cysts such as glandular odontogenic cyst and lateral periodontal cyst show clear cells. Glandular odontogenic cyst being a rare developmental odontogenic cyst. It shows nonkeratinized epithelial lining which is thin resembling reduced enamel epithelium. Also mucous cells, clear cells and epidermoid cells can be seen. The clear cells are positive for PAS without diastase as these cell contain glycogen. Lateral periodontal cyst is a developmental odontogenic cyst originating from cystic degeneration of clear cells of dental lamina. Multilocular variant of lateral periodontal cyst is botryoid odontogenic cyst. The multicystic cavity is lined by nonkeratinized epithelium with focal entangled thickenings and also clear cells are seen in the epithelium.[13]

Clear cells in osseous tumours

Chondrosarcoma is considered as malignant counterpart ofchondroma which is a benign tumour. Chondrosarcoma shows cartilage as its basic proliferating tissue. But it may also show myxomatous, calcified/ossified areas and also sometimes spindle tumour cells as seen in fibrosarcoma. Histopathologically chondrosarcoma has a clear cell variant which shows clear tumour cells and clusters of benign giant cells. Clear cell variant of chondrosarcoma has slow growth pattern and low metastatic potential and it may occur in jaws.[14] Osteosarcoma is malignant osseous tumour commonly seen in long bones. Its occurrence in skull and jaws account about 8%. Histopathologically osteosarcoma shows presence of osteoid with proliferation of atypical osteoblasts. The stroma shows spindle atypical cells with irregularly shaped nuclei.[14] The osteosarcoma shows clear cells as irregularly scattered small groups or large sharply demarcated clusters of clear cells with ovoid nucleus. These clear cells show glycogen and positive for PAS special stain.[15]

Clear cell variants of Epithelial tumours

Squamous cell carcinoma is malignant tumour of stratified squamous epithelium. Histopathology of squamous cell carcinoma shows dysplastic epithelial islands and clear cell variant of squamous cell carcinoma demonstrates sheets of clear cells within these islands. These clear cells may be round to polygonal with hyperchromatic centrally placed nucleus. The content of clear cells are water.[16]Basal cell carcinoma or Rodent ulcer is malignant tumour of basal cell origin. Clear cell variant of basal cell carcinoma shows lobules of clear cells from epidermis in the clusters of basaloid cells. Clear cells are round/polyhedral with peripheral condensed hyperchromatic nucleus. The cell contents of clear cells are glycogen/lysosomal degeneration and positive for Periodic acid Schiff stain.[17]

Clear cells in Metastatic tumours of oral cavity

Metastatic tumours of head and neck are usually of renal, bone, breast, lungs and thyroid. Malignant epithelial cells with clear cytoplasm in a compact alveolar growth pattern with branching vasculature is seen. The clear cells are large homogeneous with central or eccentric pyknotic hyperchromatic nuclei.[18]

CONCLUSION

The clear cells observed in the histopathology of a given specimen should be scrutinized. The awareness of the morphology and pattern of clear cells in various lesions is indispensable. Apart from actual clear cell lesions, knowledge about clear cell variants of certain lesions is also required to get into relevant diagnosis. In case of malignant tumours of different origin where clear cells are not indigenous shows the aggressiveness of the tumour. Thus as a pathologist, the differentiation, appropriate knowledge and awareness of clear cells in various tumours and cysts are imperative to render a precise diagnosis.

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