



HYALINIZING CLEAR CELL CARCINOMA OF PALATAL MINOR SALIVARY GLAND: A CASE REPORT

Pathology

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ABSTRACT

Hyalinizing Clear Cell Carcinoma is a rare malignant neoplasm of salivary gland origin and accounts for 0.5% of all head and neck malignancies. Histological diagnosis of the tumour is challenging and needs to be differentiated from other clear cell lesions of salivary gland. This case report enunciates a case of HCCC in a male patient of relatively younger age group and clearly elaborates on diagnosis, histopathology and immunohistochemical characteristics of this tumour.

KEYWORDS

Hyalinizing Clear Cell Carcinoma; Clear Cell Carcinoma; Salivary Gland.

Introduction

Hyalinizing Clear Cell Carcinoma (HCCC) is a rare malignant salivary gland neoplasm characterized by Milchrub et in 1994. It occurs most commonly in the minor salivary glands of females (72.7%) especially in the tongue and hard palate region and less frequently in the buccal mucosa(1). It commonly presents in the 6th decade of life as a small, painless mass that rarely ulcerates.

Microscopic diagnosis of this lesion is challenging as it demonstrates sheets, nests or islands of clear cells and eosinophilic cells in a hyalinized stroma(2). The stroma superficially resembles amyloid material but is positive for glycogen stains such as Periodic Acid Schiff instead of amyloid stains(3). This article presents a case report of HCCC of the palate in a male patient of relatively younger age group.

Case Report:

A 29 year old male patient reported to the dental out-patient department of SRM Dental College and Hospital, Ramapuram with the chief complaint of a slow growing painless swelling in the upper left back tooth region for the past 6 months. On intra oral examination a single well defined swelling measuring 2 X 1.5 cm was appreciated in the palate in relation to left first pre-molar region with apparently normal overlying oral mucosa (Figure 1). On palpation the swelling was smooth, firm in consistency and non-tender. The lesion was provisionally diagnosed as adenoma of minor salivary gland and was surgically excised and fixed in 10% formalin and sent for histopathological opinion (Figure 2).

Figure 1: Intra-oral view showing single well defined swelling in the palate



Figure 2: Surgical excision of the lesion



Figure 3: 4X View showing well-defined, non-capsulated tumour characterised by sheets, chords or trabeculae of monomorphic islands of clear cells in a hyalinized stroma.

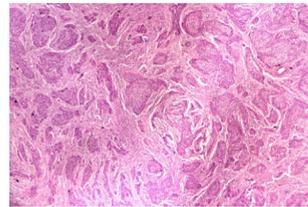


Figure 4: 10X View showing islands of clear cells in a background of hyalinized connective tissue stroma.

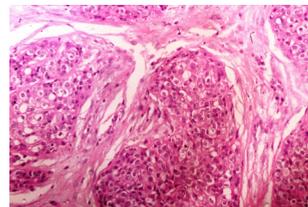


Figure 5: 40X View showing clear cells that were round to oval in shape with clear cytoplasm and pleomorphic nucleus with few cells showing vesiculated nucleus.

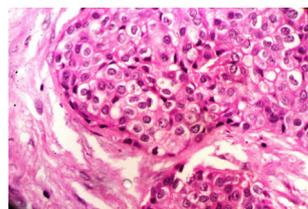
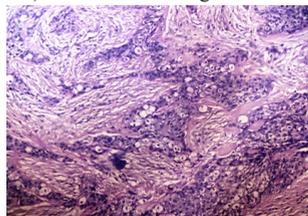


Figure 6: 10x view showing hyalinised stroma positive for Periodic Acid Schiff (PAS) without diastase digestion.



Microscopic examination revealed fibrous tissue demonstrating islands of clear cells in a background of hyalinized connective tissue stroma (Figure 3,4). The clear cells were round to oval in shape with clear cytoplasm and pleomorphic nucleus with few cells showing vesiculated nucleus. No evidence of mitosis was present (Figure 5). The stroma also showed few inflammatory cells. Further staining with special stains revealed staining of the hyalinized stroma for Periodic Acid Schiff (PAS) without diastase digestion and stained negative for Mucicarmine (Figure 6). These features were consistent with the diagnosis of Hyalinising Clear Cell Carcinoma of minor salivary glands of the soft palate.

Discussion

Neoplasm's of salivary gland origin are relatively rare and account for 0.5% of all head and neck malignancies of which 10-15% constitutes the malignant neoplasm⁽⁴⁾. Hyalinising clear cell carcinoma is one such malignant tumour that occurs almost exclusively in the minor salivary glands. In the previous WHO classification (2005) this tumour was classified under 'Not otherwise specified' category and diagnosis was by exclusion. With the latest advancement in gene mapping it was concluded that fusion of the EWSR1-ATF1 gene is responsible for 80-90% of these tumours and hence was upgraded as a distinct entity in the latest 2017 WHO classification of salivary gland neoplasm⁽⁵⁾.

Chen et al, classified Clear cell carcinoma of salivary gland into bimorphic (outer clear and inner eosinophilic cells) and monomorphic tumours⁽⁶⁾. HCCC is a monomorphic salivary gland neoplasm, whose histomorphogenesis is suggested to be from primary squamous differentiation due to the lack of myoepithelial cell differentiation. Glandular components were present only as a result of secondary differentiation of neoplastic squamous cells similar to that present in adenosquamous carcinoma⁽⁵⁾. The presence of surface epithelial dysplasia, uncharacteristic of salivary neoplasms further supports this hypothesis.

HCCC shows a female preponderance in older age but our case was reported in a male patient in a relatively younger age group. HCCC presents as a small, slow growing, dome shaped sessile painless mass intra-orally and seldom ulcerates⁽⁷⁾.

In Computed Tomography HCCC usually appears as a solid and poorly defined superficial mass, which is homogeneously and intensely enhanced with contrast⁽⁸⁾.

Fine needle aspiration and cytological smears reveal numerous sheets of cohesive epithelial cells of varying sizes with sharp cell outline and clear cytoplasm and round to oval granular nuclei with small nucleoli. Absence of myoepithelial cells and hyaline globules was characteristic of these tumours⁽⁹⁾.

Histopathologically the tumour is well-defined, non-capsulated with infiltrating areas characterised by sheets, chords or trabeculae of monomorphic optically clear oval to round cells with well defined cytoplasm and centrally placed nucleus in a typically hyalinised stroma which can sometimes be dense fibrous to myxoid or mucous in nature. The hyalinised stroma does not account for basement membrane material unlike tumours of myoepithelial origin⁽¹⁰⁾. The presence of clear cells in the tumour can be attributed to the high glycogen content of the cell cytoplasm which being water soluble and negatively charged does not take up the eosin stain and appears clear⁽¹¹⁾. In our case the sections revealed that the hyalinised stroma stained positive with PAS without diastase digestion which is indicative of glycogen and diagnostic of this tumour.

Histological diagnosis is challenging when clear cell lesions of salivary gland like epithelial-myoepithelial carcinoma, myoepithelial carcinoma, clear cell mucoepidermoid carcinoma, acinic cell carcinoma, clear cell oncocytoma, and metastatic renal cell carcinoma have to be ruled out (Table 1). In our case, the swelling was present in the premolar region close to the alveolar bone tempting to misdiagnose Odontogenic lesions like calcifying epithelial odontogenic tumour or a clear cell Odontogenic carcinoma but neither of them have a hyalinising component which is a distinctive feature of HCCC^(12,13).

Immuno-histochemical profiling of the tumour show positivity for CK A1/A3, p63 consistently and also for Epithelial membrane antigen and rarely carcinoembryonic antigen and negativity for Smooth muscle actin (SMA) and S100⁽¹²⁾.

Wide local excision is the treatment of choice and usually approached intra-orally. Based on the clinical, radiographic and histological features of cellular atypia and mitosis; lymph node metastasis has to be ruled out and partial or modified neck dissection considered⁽¹³⁾. Thus careful examination and neck dissection is warranted for HCCC treatment. Post-operative radiotherapy is usually recommended in such cases. Our patient was treated with wide localised excision and since the tumour margins were clear, the patient was kept under follow-up for past two years with no local recurrence and metastasis.

Conclusion:

HCCC is a low grade malignancy with infiltrative growth and evidence of recurrence and hence warrants regular follow up. The documentation of more such cases with follow up is necessary to understand the biological behaviour of this tumour.

REFERENCES

- O'Sullivan-Mejia ED, Massey HD, Faquin WC, Powers CN. Hyalinizing clear cell carcinoma: report of eight cases and a review of literature. *Head and neck pathology*. 2009 Sep 1;3(3):179-85.
- Milchgrub S, Gnepp DR, Vuitch F, Delgado R, Albores-Saavedra J. Hyalinizing clear cell carcinoma of salivary gland. *The American journal of surgical pathology*. 1994 Jan 1;18(1):74-82.
- Dardick I, Leong I. Clear cell carcinoma: review of its histomorphogenesis and classification as a squamous cell lesion. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*. 2009 Sep 30;108(3):399-405.
- Kauzman A, Tabet JC, Stiharu TI. Hyalinizing clear cell carcinoma: a case report and review of the literature. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*. 2011 Jul 31;112(1):e26-34.
- Seethala RR, Stenman G. Update from the 4th Edition of the World Health Organization Classification of Head and Neck Tumours: Tumors of the Salivary Gland. *Head and neck pathology*. 2017 Mar 1;11(1):55-67.
- Chen KT. Clear cell carcinoma of the salivary gland. *Human pathology*. 1983 Jan 1;14(1):91-3.
- Baghirath PV, Kumar JV, Vinay BH. Hyalinizing clear cell carcinoma: a rare entity. *Journal of oral and maxillofacial pathology: JOMFP*. 2011 Sep;15(3):335.
- Rodriguez MS, Reija MF, Rodilla IG. Primary clear cell carcinoma of parotid gland: Case report and review of literature. *Journal of oral and maxillofacial pathology: JOMFP*. 2013 Jan;17(1):101.
- Milchgrub S, Vuitch F, Hossein Saboorian M, Hameed A, Wu H, Albores-Saavedra J. Hyalinizing clear-cell carcinoma of salivary glands in fine-needle aspiration. *Diagnostic cytopathology*. 2000 Nov 1;23(5):333-7.
- Ponniah I, SureshKumar P, Karunakaran K. Clear cell carcinoma of minor salivary gland-case report. *ANNALS-ACADEMY OF MEDICINE SINGAPORE*. 2007 Oct 1;36(10):857.
- Nazir H, Salroo IN, Mahadesh J, Laxmidevi BL, Shafi M, Pillai A. Clear cell entities of the head and neck: A histopathological review. *IOSR Journal of Dental and Medical Sciences*. 2015;14(6):125-35.
- Solar AA, Schmidt BL, Jordan RC. Hyalinizing clear cell carcinoma. *Cancer*. 2009 Jan 1;115(1):75-83.
- O'Regan E, Shandilya M, Gnepp DR, Timon C, Toner M. Hyalinizing clear cell carcinoma of salivary gland: an aggressive variant. *Oral oncology*. 2004 Mar 31;40(3):348-52.