ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 8, Issue, 07, pp.34238-34240, July, 2016

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

IMMUNOPROFILING OF THE GRANULAR CELLS IN ODONTOGENIC TUMOURS

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ARTICLE INFO

Article History:
Received 15th April, 2016
Received in revised form
20th May, 2016
Accepted 23rd June, 2016
Published online 16th July, 2016

Key words:
Granular cells, Odontogenic tumour.

ABSTRACT

A wide variety of normal and neoplastic human tissues are characterized by granular cells. Granular cell lesions from many different sites share similar light and electron microscopic features. The striking histological feature is the morphological resemblance of the cells in these lesions which are characterized primarily by the presence of numerous cytoplasmic acidophilic granules. The entire tumor may be composed of these cells or the cells may be seen as focal aggregates. Odontogenic tumors of the jaws with a predominant component of granular cells are exceedingly rare. This presentation highlights the occurrence of granular cells of both epithelial and mesenchymal origin in odontogenic tumors of varying clinical behaviour, treatment and prognosis.

Citation: Dr. Jacob Prakash Animelli, Dr. Madhusudhan Reddy, Dr. Naveen, P., Dr. Mahesh, N. and Dr. Vijayalakshmi Mahanthi, 2016. "Immunoprofiling of the granular cells in Odontogenic tumours", *International Journal of Current Research*, 8, (07), 34238-34240.

INTRODUCTION

Because of their common but inexplicable morphological appearance and obscure origin, granular cell lesions continue to be a focus of laboratory investigation (Joseph *et al*., 1989). Of the odontogenic tumors, granular cells have been described in granular cell ameloblastoma and granular cell odontogenic tumor (Antonio *et al*., 1971). The granular cell ameloblastoma is an unusual variant showing marked transformation in the cytoplasm of tumor cells which are usually stellate reticulum like cells. The transformed cells possess very coarse granular eosinophilic cytoplasm. Because of invasiveness and tendency to recur the ameloblastoma is considered to be locally malignant (Harry F.Hoke, Jr and Austin B. Harrelson, 1967). Central granular cell odontogenic tumors (CGCOT) are very rare benign lesions. To date approximately 34 cases of this tumor have been reported (Carolina Cavalieri Gomes and Marcelo Drummand Naves, 2006). The CGCOT which is also known as Central granular cell odontogenic fibroma or Granular cell Ameloblastic fibroma is characterized by containing varying amounts of large eosinophilic granular cells and apparently inactive odontogenic epithelium (Robert R Brannon and Lewis D Eversole, 2002). The aim of this article is to elucidate and compare the Immunohistochemical findings of the granular cell ameloblastomas with the CGCOT that had been reported at The Department of Oral Pathology, Oxford Dental college, Hospital and Research centre, Bangalore (India).

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MATERIALS AND METHODS

Formalin fixed paraffin embedded granular cell lesions were retrieved from the files of Department of Oral Pathology, The Oxford Dental College, Hospital and Research centre. Clinical and historical information and haematoxylin and eosin stained sections were available for review in each of the cases. 3 cases of Granular cell ameloblastoma and 1 case of Central granular cell odontogenic tumor had been examined immunohist chemically. Antibodies used were Pan cytokeratin, Vimentin and CD68. All of these antibodies were obtained from BioGenex laboratories Inc. CA 94583 USA and were ready to

use, required no further dilution. The sections were taken on PLL coated slides with one positive control for each marker.
All sections were incubated at 60degrees overnight and treated with xylene, alcohol 100%, alcohol 96% and distilled water subsequently. Primary blocking with 3% H_2O_2 and incubation in a microwave at 800w was done. Secondary blocking with 3% BSA was done. Treated with primary antibody for 60mins, washed in TSBT I and II, secondary antibody washed in TSBT I and II, counterstained with Meyers haematoxylin. Sections from carcinoma of breast served as positive control.

RESULTS

The granular cells in granular cell ameloblastoma were reactive for keratin intermediate filaments and negative for vimentin. In contrast the granular cells in CGCOT had stained positively to vimentin and negatively to cytokeratin. The cells were positive for CD68 in both the lesions. (Table 1)

Table 1. Immunoreactivity of granular cell lesions

	No.	Keratins	Vimentin	CD 68
Central granular cell Odontogenic tumor	1	- ve	+ ve	+ ve
Granular cell Ameloblastoma	3	+ ve	- ve	+ ve

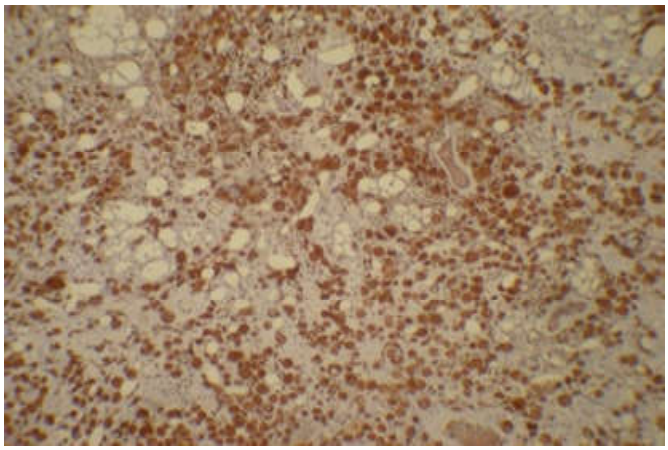

Fig. 1. Granular cell odontogenic tumor stained for Vimentin. Notice + ve staining of cells in the connective tissue

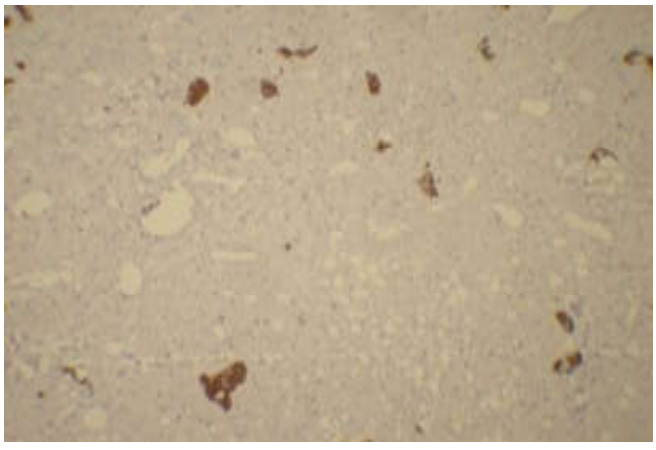

Fig. 2. Granular cell odontogenic tumor stained for cytokeratin. Odontogenic epithelial Islands were + ve while the granular cells are –vely stained

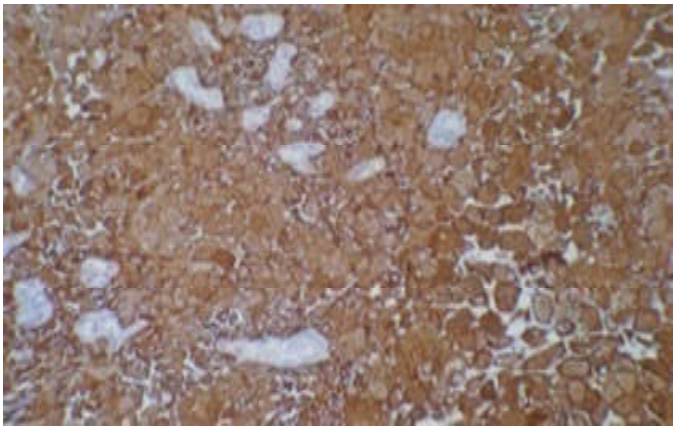

Fig. 3. Granular cell ameloblastoma stained for cytokeratin. Notice + ve staining of the Granular cells

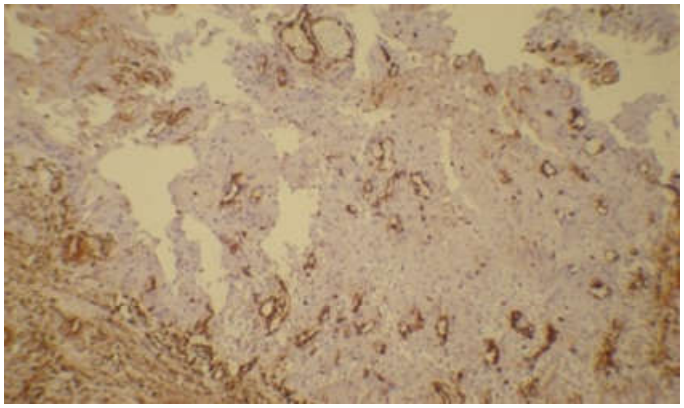

Fig. 4. Granular cell Ameloblastoma stained for vimentin. The granular cells are -vely stained while the connective tissue cells were + ve

DISCUSSION

Large eosinophilic granular cells present in normal and neoplastic human tissues have long been a matter of speculation among pathologists and histologists. These cells include the so called oxyphils (parathyroid), oncocytes (salivary glands), Hurthle or Askanazy cells (Thyroid) and granular cells of granular cell ameloblastoma, granular cell odontogenic tumor, congenital epulis of the new born (Antonio R. Navarrette and Marilyn Smith, 1971). The light microscopic changes noted in the granular cells from Odontogenic tumors are similar if not identical. The exact histogenesis of the granular cell change in these tumors is controversial and whether the granular cells with in these lesions are neoplastic, reactive, degenerative or metabolic in nature remains unclear (Shabnum Meer *et al*., 2004). Weithman is generally credited for reporting the 1st CGCOT in 1950 calling it "Spongiocytic Adamantinoma". Since then opinions have varied on its histogenesis resulting in its uncertain status nosologically. Accordingly over the years the judgement on the nature of the granular cells have varied with interpretations dependent in part on the diagnostic techniques available to the investigator. Conclusions of the investigators on the suggested origin of the granular cells were based at least in part on histochemical stains, Immunohistochemistry, Electron microscopy or a

combination there of (Robert R Brannon and Lewis D Eversole, 2002). In the current study Immunohistochemical staining was used in elucidating the possible origin and nature of the granular cells. In GCOT, vimentin positivity (Fig. 1) and Cytokeratin negativity (Fig. 2) confirms origin from mesenchyme while mitigating against the epithelial origin. The granular cells showed moderately intense positivity with CD68 supporting histiocytic differentiation. This study confirms various reports of numerous lysosomal granules within these lesions. Granular cell ameloblastoma showed positivity to cytokeratin (Fig. 3) and negativity to vimentin (Fig. 4) thereby establishing an epithelial origin. Positivity to CD68 reveals that the granules are lysosomal aggregates. Lysosomal aggregates with in the cytoplasm is caused by dysfunction of either a lysosomal enzyme or lysosome associated protein involved in enzyme activation, enzyme targeting or lysosomal biogenesis (Sathi Gul San Ara *et al*., 2007). However the contents of the lysosomal aggregates with in the granular cells are largely undefined which on further investigations might possibly explain the varied biological behaviour of these lesions.

Conclusion

The use of the above markers helped establish unequivocally the origin of the granular cells in the above tumours, however their biological behaviour cannot be explained.

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