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'Aging' Granular Cells in Ameloblastoma have a CD44+/Snail+ Phenotype

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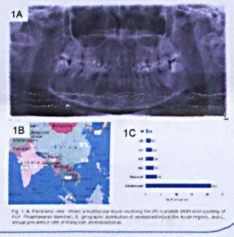
THE PROBLEM

Ameloblastoma, the most clinically significant odontogenic epithelial tumour, is benign but locally-infiltrative. It causes massive jawbone destruction, and local recurrences after treatment. The granular cell ameloblastoma is a rare variant of this neoplasm. The presence of these granular cells have been attributed to aging or degenerative changes.



THE RESEARCH QUESTIONS

- Do 'aging' granular cells in ameloblastoma express cytokines including cancer stem cell (CSC) proteins and epithelial-to-mesenchymal transition transcription factors?
- How important are these cytokines in terms of defining immunophenotypic characteristics and clarifying biological status of these granular cells?

THE CLINICAL CASES

Table 1. Patients' clinical parameters

Case No.	Age(yr)/sex/ethnic	Site*	Duration	Clinical presentation	Clin Dx	Xray	Rx	Hist Dx
1	15/Male/Chinese	41-47	6 mth	Expanding swelling, bony nodule	Amelob/ CEOT	NA	Excision	GCA
2	26/Male/Indian	33-35	1 yr	Swelling + pain	Lat perio cyst	ULRL	Enucleation	GCA
3	26/Female/Indon	R mand	6 mth	Mild swelling	Amelob	Large RL	Hemimand	GCA
4	29/Male/Malay	R maxilla	3 yr	Swelling w foul-smelling discharge & fungating growth	Follicular amelob	Large lesion	Hemimax	GCA

* FDI two-digit dental notation system; Amelob, ameloblastoma; CEOT, calcifying epithelial odontogenic tumour; Lat, lateral; perio, periodontal; ULRL, unilocular radiolucent lesion; RL, radiolucent lesion; mand, mandible; hemimand, hemimandibulectomy; hemimax, hemimaxillectomy; GCA, granular cell ameloblastoma

THE RESULTS and DISCUSSION

HISTOLOGY OF GRANULAR CELLS:

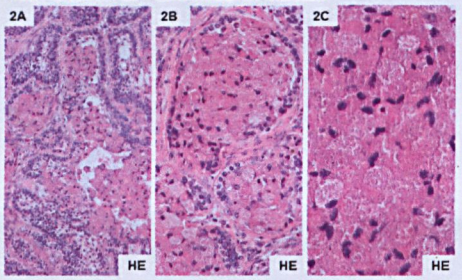


Fig. 2. Representative sections of a granular cell ameloblastoma showing granular cells identified as large polyhedral cells with abundant eosinophilic granules in their cytoplasm (2A-2C).(Original magnification 2A x40; 2B x100; 2C x400).

EMT EXPRESSIONS:

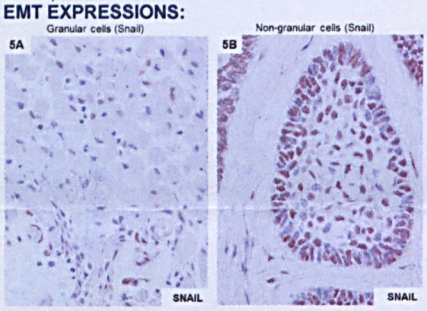
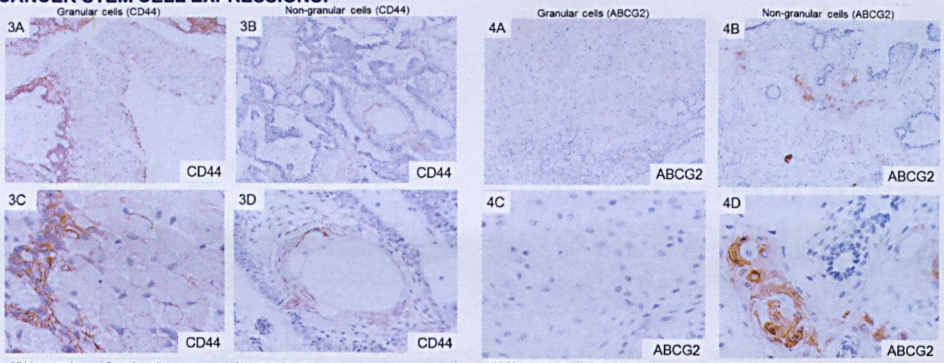


Fig. 5. Snail intranuclear expression in granular (5A) and non-granular cells (5B).(Original magnification 5A x200; 5B x100).

CANCER STEM CELL EXPRESSIONS:



CD44 expression	Granular cells	Non-granular cells
Membrane	-/++	-/+++
Cytoplasm	-/++	-/++
Nucleus	-	-

ABCG2 expression	Granular cells	Non-granular cells
Membrane	-	-/+++
Cytoplasm	-	-/+++
Nucleus	-	-/+

Figs. 3 and 4. Representative sections of ameloblastoma tumour epithelium showing differential immunoreactivity of granular (3A, 3C, 4A, 4C) and non-granular cells (3B, 3D, 4B, 4D) for two cancer stem cell proteins CD44 (3A-D) and ABCG2 (4A-D). (Original magnification 3A, 3B, 4A, 4B x40; 3D, 4D X100; 4C X200; 3C X400). Adjoining tables detail the subcellular localization and staining intensity levels of these proteins.

Granular cell metaplasia in ameloblastoma may involve the peripheral pre-ameloblast-like cells and/or stellate reticulum-like cells. Microscopically these cells are identified as large polyhedral cells with abundant eosinophilic granules in their cytoplasm(Fig. 2A-C).

CD44, a CSC marker and promoter of tumour invasion and metastasis, is detected in the membrane and cytoplasm of granular cells (Fig.3A), thus suggesting that these cells possess CSC characteristics and participate in tumur-induced biological activities. The other CSC markers (ABCG2, CD133 and Bmi-1) were not detected (Fig. 4A,C).

Snail, an EMT inducer and functionally active in its intranuclear position, is detected in the nucleus of the granular cells, thus providing evidence that Snail intranuclear accumulations in these cells support their active roles in EMT (Fig. 5A).

FUTURE WORK:

The next step would be to develop an *in vitro* model to study ameloblastoma granular cells in primary cultures.

ACKNOWLEDGMENTS AND REFERENCES:

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1. Masushita Y et al. Granular cell ameloblastoma: case report of a particular ameloblastoma histologically resembling oncocytoma. Path Int 2015;65:43-47.
2. Nikitakis NO et al. Granular cell ameloblastoma: An unusual histological subtype report and review of the literature. J Oral Maxillofac Res 2010;1:e3.
3.Lapthanasupkul P et al. Investigation of basement membrane proteins in a case of granular cell ameloblastoma. Int J Oral Sci 2012;4:45-49.