Nucleolar organizer regions in giant cell lesions of the jaws in relation to clinico-pathological parameters

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ABSTRACT

Background: It is to clarify the proliferatiove activity of the multinucleated giant cells and cellular component in giant cell lesions of the jaw in correlation to their clinico-pathological features.

Materials and methods: This study was carried on 23 cases diagnosed as GC lesion of the jaw. Patient's personal and clinical information were collected from their files. H&E and sliver nitrate stains were applied on their formalin fixed paraffin embedded tissue sections.

Results: the mean AgNOR count in MGC/cell was 49.83 and NORs/nucleus was 5.8, and 74% of them were grouped in large clusters and 26% were scattered. In PGCG the mean AgNOR count /MGC and /nucleus were significantly lower than that of CGCL (38.2 vs 59.5 and 4.6 vs 6.8 respectively, P<0.04). The mean AgNOR count of spindle and mononuclear cells were 4.7 in CGC lesions and 2.5 in peripheral lesions

Conclusion: evaluation of AgNORs showed that both MGC and fraction of mononuclear cells in CGCG were significantly higher than that in PGCG. (J Bagh Coll Dentistry 2009; 21(4): 59-62).

INTRODUCTION

Giant cell lesions (GCL) of the oral cavity and the jaws are benign, reparative metabolic lesions, that either presented as central giant cell granuloma (CGCG) (osteolytic type) or peripheral giant cell granuloma (PGCG) (epulis).

The giant cell granuloma located more frequently in mandible than maxilla, more commonly on right than left side. It is relatively uncommon lesion (3.5-0.1). It occurs in the 2nd and 3rd decades of life. And it is more frequent in females than males (3:1) [1,2,3].

Clinically CGCG appears as asymptomatic lesion that becomes evident on routine radiographic examination [4]. Nevertheless, it some times switches from relatively indolent growth pattern to become a rapidly enlarging and destructive one with recurrence tendency [5-7], then it associated with pain or parasthesia, facial deformity, displacement of the teeth, root resorption, and cortical bone perforation [3,8].

On the other hand, PGCG (epulis) is a slowly growing mass red-purple in color that may increase in size and interfere with eating [6,9]. One report indicates its predominance in males [10] unlike others that record more cases in females[11].

Radiographically CGCG of the jaws presents as well or ill defined uni- or multilocular radiolucent defect with trabiculations coursing through the lesion. While focal loss of alveolar crestal bone may associate with peripheral lesions. [2,6].

Histologically CGCG of the jaw is characterized by multi-nucleated giant cells (MGC) within fibro-vascular stroma beside foci of hemorrhage and osteoid tissue. These giant cells believed to be derived from macrophages. They have very large cytoplasm and contain multiple nuclei. Their role is still vague, they neither are able to phagocyte nor are efficient killer [12]. However, MGCs show characteristics of osteoclast phenotype and formed from mononucleal-stromal cells precursors, and differentiate into osteoclast under the influence of special mononuclear stromal cells found in the lesion [13,14].

Although GC lesion's cause and behavior are still obscure and matters for discussion, pathologists try to separate GCL of different behavior on histological basis. They could identify the significance of various distributions of mononuclear and multinuclear cells and the frequency of osteoid within the lesion of recurrence tendency [8].

Other observers attempt to understand the cell biology of these lesions in order to predict their behavior. Based on immunohistochemical findings, the results are controversy. In one study, mononuclear and multinucleated cells from PGCG of the jaws express vimentin, alfa-1 antichymotrypsine and CD68, but lacking CLA and lysozymes. While the dendritic cells were positive for S100 protein in 67% [8,15]. In other study, the multinucleated cells stained positively with MB1, the mononuclear round cells were positive to CLA and the spindle cells were uncreative to these markers, neither to S100 or actin [16]. While in a third study it remarked to the proliferation ability of the PGCG to be restricted to the mononuclear cells compartment, whereas, multinucleated giant cells lack mitotic activity,

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but it had high frequency of apoptotic nuclei than monocytes cells [17]. Beside that Gunhan et al [11] remarked that stromal cells and osteoclast-type giant cells in peripheral GCG express estrogen receptor (71% and 59% respectively).

On the other hand, the giant cell nuclear DNA content and DNA index seemed to be not useful in predicting the clinical behavior of GCG of the jaws [18].

Regarding the microvasculature within the GCG of the jaws, it seems that blood vessels were more prominent on the periphery of the lesion than on the deeper part of the lesion where the aggregation of giant cells [15].

Ultra-structural examination shows mono nuclear cells with sign of phagocytosis and some times inter-digitations with similar cells. Other represents non specific characters and third type exhibits cytoplasmic processes and occasional Birbeck granule. The giant cells show oval nuclei, abundant mitochondria and granular endoplasmic reticulum whereas other presented with irregular nuclei and giant number of cytoplasmic vacules [15].

Lastly GCL of the jaws could be treated by curettage, intra-lesional corticosteroid or calcitonin or even antiangiogenic therapy [5,19,20].

MATERIALS AND METHODS

This study was carried on 23 cases diagnosed as GCL of the jaws, including peripheral and central GCL. They were collected from the lab. of Oral Pathology in the College of Dentistry, University of Baghdad. Patient's age, sex, full clinical presentations were recorded from the files. Routine H&E and silver nitrate stains (one step technique, as described by Cromine et al [21]) were applied on formalin fixed paraffin embedded tissue sections. Ten high power fields were studied to evaluate the MGC density at the hot-spot lesion stroma, and not less than 20 MGC are analyzed for AgNOR at oil immersion X100 magnification under light microscope.

The differences in the mean values of the tested parameters were evaluated by t-test. The relationship among parameters was assessed by Pearson's correlation. P value <0.05 was considered statistically significant.

RESULTS

From the 23 specimens there were 12 males and 11 females, age ranging from 5-83 years. 11 were identified as PGCG and the remaining 12 were CGCG. The mandible was affected in 13 cases (9 posterior and 4 anterior) and the maxilla in 10 cases (7 anterior and 3 posterior) (Table 1)

The clinical appearance was an exophytic soft mass with or without bleeding surface in 10 PGCG cases, 6 cases were CGCG associated with teeth mobility and 4 CGCG cases appear as hard swelling, regrettably one case had no clinical description. The time duration of the lesion rang from 2 months to 7 years. One CGCG was recurrent case in 7 years male, and another case suspected to be chirubism in 5 years female.

It was determined that 43% of GCL occurred prior to the age 21 years. 60% of them were females, (Table-2). There was a correlation between age and sex (r =0.037). CGCG occurred in younger age-grouped patients than peripheral lesion (26 vs 34) (table 1).

Regarding the microscopical features and through the evaluation of the density of MGC, it seems that the mean number of MGC/ field and the number of nuclei/ MGC were nearly similar in central and PGCG (Table 3). However, the MGC/ field is correlated negatively with the age (r=-0.37) and upper or lower jaw (r = 0.3). i:e lesions in the maxilla had higher MGC/field and younger patients had both high MGC/ field and increase number of nuclei/ MGC (r = -0.55).

On the other hand, the mean AgNOR count /MGC was 49.83 and NORs/nucleus was 5.8 with a range of 19.5-138 and most of the AgNORs are grouped in large clusters 74%, other are scattered within cytoplasm 26%, in comparison with spindle cells and mononuclear cells which had 2-3 grouped NORs / cell.

In PGCG the mean AgNOR count /MGC and /nucleus were significantly lower than that of CGCL (38.2 vs 59.5 and 4.6 vs 6.8 respectively, P<0.04)(figure1-3). The mean AgNOR count of spindle and mononuclear cells were 4.7 in CGC lesion and 2.5 in peripheral lesion (Table 4).

There were stronge correlation among NORs in MGC(r =0.48) and number of nucleus /MGC (r= -0.55) (Table 5).

DISCUSSION

GCL in the oral cavity and jaws are non-neoplastic fibrous lesion. On the basis of our results and in comparison to previous studies [1-3] CGCG occurs more frequently in maxilla, while PGCG is seen more frequent in mandible.

There is no predominance to sex variation; but it is relatively more common at the 2nd decade of life, with a tendency toward female affection. In agreement with what is published in literatures [6, 9], most of PGCG were described as a mass red-purple in color with or without bleeding.

The case that suggested to be chirubism had very active spindle cells and monocytes (NOR count

was 14.6 and 13.6) and the mean NOR in the MGC was 138 with scattered distribution.

Although Whitaker and Waldron[8] reported that MGC distribution is significantly different between recurrent and non recurrent lesions, there was no previous study compare the density of MGC and the number of nucleus/MGC in such lesions. This study indicates that they had no value in differentiating lesion type or predicting cell behavior. However, this study offers new in sight about the correlation between MGC/ field and patient's age and site of MGL. i:e MGCs are more densely aggregated in maxillary lesions and in young patients, and in the later situation it is characterized by more nucleus / cell.

Whitaker et al[12] remarked to the significant difference between the mean number of AgNORs of recurrent and non recurrent/ non aggressive CGC lesion of the jaws in both the mononuclear and multinuclear population. Still, the importance outcome of the present study was the significant differences in NORs count /MGC, /single GC nucleus and in mononuclear cells between peripheral and CGCG. It is significantly higher in CGCG. Beside that, the statistical correlation leads us to speculate that younger patients had highest NORs/ MGC.

This demonstrates that CGL, mainly in young patients is mainly due to the activity of the spindle cells and monocytes within the lesion and consequently active cell fusion and nuclear aggregation within MGC. Nevertheless, most GC had large NORs clusters with separated NORs and only quarter of the cases show scattered NORs. This may reflect cell protein production. It is worth to mention that Pammer et al[17] indicated that the GC lack mitosis, however, Lim and Gibbins[16] express MB1(proliferating marker) staining in these cells. Still we can address that higher AgNORs count could be attributed to CGCG and low AgNORs count in PGCG. Anyhow, GCs are more active than monocytes in PGCG indicating certain functional issue of these cells. Kobayashi et al[22] indicated that AgNOR status could evaluate the over all metabolic activity in cells including proliferation, differentiation and protein synthesis. Therefore, the evident variation in AgNOR count of MGCs between central and peripheral GCG would be a sign of qualitative variation in protein production, since those in central lesions speculated to have osteolytic reaction in comparison to proteolytic nature of those in PGCG.

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Table 1: The clinical features of peripheral and central GCG

	Male	Female	Age		Mandible	Maxilla
			rang	mean		
Peripheral	6	5	7-83	34	8	3
Central	6	6	5-60	26	5	7
Total	12	11	5-83	30	13	10

Table 2: The age group distribution of 23 patients with GCG

	Male	Female	Total	%
5-20	4	6	10	43
21-40	3	3	6	26
41-60	4	1	5	22
160-83	2	0	2	9

Table 3: Multinucleated giant cell density in different lesions and their mean nuclear counts/ cell

	MGC/field	Nucleus/cell
Peripheral	9.06±3.9	9.89±2.12
Central	10.12±5.2	10.43±3.2
Total	9.6±4.6	10.2±2.7

Table 4: Mean values of AgNORs in different cells of giant cell lesions

	MGC*		Mononuclear or spindle cells
	NOR/cell	NOR/nucleus	
Peripheral	38.2±13.4	4.6±1.2	2.5±0.97
Central	59.5±29.3	6.8±2.3	4.7±3.79
Total	49.8±25.4	5.8±2.1	3.7±3

*** Significant difference in NOR/cell and NOR/nucleus between central and peripheral GCG**

Table 5: Pearson's correlation among different studied parameters

Sex	Type	MGC /field	Nucl /cell	NOR /Nucl	NOR /GC	
-0.37		-0.37	-0.55		-0.48	**Age**
	0.31	-0.3				**Site**
				-0.52	-0.43	**Type**
				0.33	0.71	**Nucl/cell**
					0.82	**NOR/nucl**

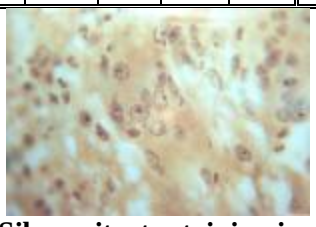
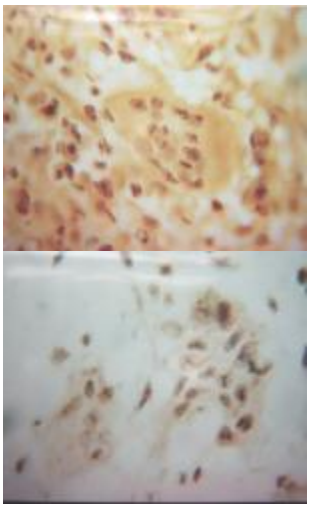


Figure 1: Silver nitrate staining in peripheral GCG is showing a MGC with few grouped NORs. The surrounding stromal cells are also in rest condition, every cell had no more than 1-2 NORs.



B

A

Figure 2 (A and B): Silver nitrate staining in central GCG is showing a MGC with numerous scattered NORs. Some of the surrounding stromal cells show more than 4 NORs.

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