The difference in proliferation assessed by AgNOR between giant cell lesions of the jaw and giant cell tumor of long bones

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Introduction

Central giant cell granuloma (CGCG) is a benign reparative metabolic bone lesion that occurs mainly in the jaws, either presented as central giant cell granuloma (CGCG) (osteolytic type) or peripheral giant cell granuloma (PGCG). They are of unknown origin and located more frequently in mandible than maxilla, in the 2nd and 3rd decades of life, and it is more frequent in females [1]. CGCG often exhibits an aggressive, though unpredictable, clinical course. They some times switches from relatively indolent growth pattern to become a rapidly enlarging and destructive one with recurrence tendency 10% [1,2], while PGCG is a slowly growing mass that may increase in size and interfere with eating [3]

In CGCGs, it has been believed that the mononuclear cells may to be responsible for the biologic behavior of these tumors, especially in young patients [4]. They consider CGCG primarily fibroblastic (and myofibroblastic) tumors in which macrophages appear to play a secondary role. Tumor cells show no differentiation toward endothelial cells or macrophage-related dendrocytes. However, cellular phenotypes and numbers of cells in cell cycle are similar in both aggressive and non-aggressive tumors [5].

On the other hand, the giant cell tumour (GCT) is a benign locally aggressive neoplasm located near the articular end of tubular bones, mainly seen in females. The mean ages of patients with GCT was 28 years [6] In contrast to CGCG, GCT rarely occurred in persons below the age of 10 years [7]. It is a very peculiar and interesting tumor due to of its biological behavior and the phenomenon of pulmonary metastases of a histological benign tumor. Literatures indicated that giant cell reparative granuloma only can be differentiated from giant cell tumor by younger age at diagnosis and the occurrence of giant cell clusters [8].

In a general population, large and aggressive GCT lesions are less common than suggested by the literature. Multiple lesions, however, occur more frequently than previously assumed. Local recurrence was observed in 12.6% [9]**.** Giant cell tumor GCT of bone remains a difficult and challenging management problem because there are no absolute clinical, radiographic, or histologic parameters that accurately predict the tendency of any single lesion to recur or metastasize. It is recommended to reduce the risk of local recurrence and pulmonary metastases by use an adjuvant therapy, carried out by individuals and institutions familiar with this entity. [9,10,11].

From histological point of view, the giant cells are 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

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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, The nature and the mechanism involved in the formation of the multinucleated giant cells (MGCs) in various giant cell-containing lesions of the jaws are not fully understood[13,14]. Whitaker et al [15] could identify the significance of various distributions of mononuclear and multinuclear cells and the frequency of osteoid within the lesion of recurrence tendency.

Stereological techniques have been used by some researchers to compare histological parameters of the giant cell component in giant cell tumors of; long bones, central and peripheral giant cell granulomas of the jaws. There was a significant difference, however, between the giant cells of central jaw lesions and long bone tumors in respect of both nuclear numerical density and mean absolute cell volume [16]. While local recurrence could not be predicted on the basis of histological grading (i:e) multinucleated giant cells in GCT bore no correlation to either recurrence or metastasis even when analysed objectively by IAS, despite the old suggestion to use a modified histological grading system based not on variations of the stroma and giant cells [17].

On the other hand, new quantitative approaches appeared to be more objective and more sensitive in evaluating the aggressiveness and predicting the prognosis of GCT than the subjective grading system used before. DNA parameters are useful in evaluating the aggressiveness of GCT for the selection of an adequate treatment [18]. Applying molecular analysis on GCT of bone displayed LOH in several microsatellite markers located on chromosomes and it exhibits frequently intratumoral heterogeneity. [19]. Finally, researchers suggested that in addition to the surgery factor, which no doubt had close relation with the prognosis, the most important risk factor in histological parameters determined cytometricaly is the percent of cells with nucleus larger than 40 square microns [18].

Aim:

The purpose of this study was to compare the proliferative features by AgNOR of giant cells in giant cell granuloma of the jaw, both central lesion and peripheral exofitic growth with giant cell tumor of long bones.

Materials and methods

The histological features of 10 giant cell tumors (GCT) of long bones, 11 with PGCG and 12 central giant cell granulomas (CGCG) of the jaws were compared.

Routine H&E and silver nitrate stains (one step technique, as described by Cromine et al [20] were applied on 4μm formalin fixed paraffin embedded tissue sections. 10 high power fields were studied to evaluate the MGC density at the hot-spot lesion stroma, and the number of nuclei in each case. 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. P value <0.05 was considered statistically significant.

Results

The number of nuclei in single giant cells in GCT of the long bone was 13.29, which was higher that that reported in CGCG (10.43) and PGCG

(9.98), still statistically not significant (P>0.05)

The proliferative value in giant cells expressed by the mean AgNOR count per multinucleated giant cell in GCT was 78.55 and the mean count of NORs dot per single nucleus was 11.28 (Table 1). Most of the AgNORs were grouped in large clusters 80%, other are scattered within cytoplasm 20% in comparison to the CGCG (74% and 26% respectively).

The GCT was significant differed from CGCG when we evaluated the mean count of NORs per/ nucleus P=0.00. While PGCG the mean AgNOR count per MGC and per single nucleus were significantly lower than that of GCT (38.2 vs 78.55and 4.6 vs 11.28 respectively, P<0.000) (figure1).

Disscussion

Some giant cell lesions of long bones are, however, morphologically indistinguishable from lesions of the jaws; and conversely giant cell lesions of the jaws are indistinguishable from some giant cell lesions of the long bones. Both lesions are characterized histologically by multinucleated giant cells in a background of ovoid to spindle-shaped mesenchymal cells, cortical erosion, high rate of recurrence, hemorrhage areas, predominant intercellular collagenous substance [8].Although previous findings suggested that the GCT and the CGCG represent a spectrum of a single disease process modified by the age of the patient and the site of occurrence, and possibly other factors that are not understood [1]. However data supported the view that giant cell tumor and giant cell granuloma are distinct entities. [6]. Moreover, it was found, unlike our results, that the giant cells of the jaw lesions contained significantly fewer nuclei than those of the lesions in other bones [21]and support the view that giant cell tumor and giant cell granuloma are distinct entities. [6]. It seems possible, that jaw lesions in our study were mainly of young patients that exhibit more active cells [4].

The study of cell proliferation may give insights into clarifying such aspect. Few studies were available concerning this point. De Souza [22] reported that CGCG has a higher proliferative activity compared with that of the GCT and also suggested that p53 inactivation by MDM2 expression may be involved in the pathogenesis of giant cell lesions of the jaws and long bones. This is unlike our result that declares GCT cells had higher AgNOR count. Nevertheless, in our study GC harvested from both lesions similar AgNORs morphological distribution (i: e clustered rather than scattered) [8]. Even more, Sulh et al [23] decumented that the degree of tumor cell proliferation and vascularity are not useful parameters to predict the recurrence of GCT of bone, and that there are no significant differences between the PI of mononuclear round-ovoid cells and mononuclear spindle cells.

Conclusion and suggestion:

CGT are more biologically active than CGCG, however, studying proliferative property alone may to be not enough in declaring a major differences between them. this may need to be correlate with the estimation of the rate of cell death that collectively give the end result of mass growth. So the behavior of these GC lesions are still obscure and matters for discussion, pathologists need to try more accurate means in order to separate giant cell lasions of different behavior on histological basis.

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Table (1) :Mean nuclear count/cell and mean AgNORs values of giant cells in the peripheral, central giant cell granuloma of the jaw and the giant cell tumor of long bones

Types of giant cell lesions	No.	Nucleus/cell	NORs/cell	NORs/ nucleus
Long bone	10	13.29±4.11	78.55±10.32	11.28±1.05
PGCG	11	9.89±2.72	38.28±13.39*	4.6±1.2*
CGCG	12	10.43±3.21	59.52±29.3	6.8±2.3*

* indicates statistical significant differences from CGCG (P<0.00)

Figure -1 Silver nitrate staining in (A): GCT of long bone showing a MGC with numerous scattered NORs. (B) Giant cell from CGCG.