Immunohistopathological Expression of (RANK), (TNF) & (ALP) Markers In Giant Cell Tumor of Bone and Central Giant Cell Granuloma of the Jaw

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Abstract

Background:

Central giant cell granuloma (CGCG) of the jaws and giant cell tumor of long bone (GCT) shares a number of similarities and dissimilarities in respect of their histopathological, cytometric and immunohistochemical features. What continues to be controversial and debatable is whether or not these two disease entities are the same disease biologically with selective site-specific morphologic and phenotypic characteristics. Despite the considerable number of literature reports on several aspects of the behavior and biology of the two diseases, the controversy remains. In the present study the histopathological, cytometric and immunohistochemical features of histologically diagnosed 20 giant cell reparative granulomas of the jaws and 20 giant cell tumors of long bones were compared to each other and with twenty samples of normal bone, breast carcinoma and lymphoma as control. This study investigated whether some components of the extracellular matrix and markers expression may drive the differences between the central giant cell granuloma (CGCG) of the jaws and giant cell tumor (GCT) of long bones, which present distinct evolution and clinical behavior.

Aim of the study:

To detect the presence of many markers like RANK (Receptor Activator of NF-Kb), TNF (Tumor Necrosis Factor) and ALP (Alkaline Phosphatase Enzyme), and their expression in these lesions; also to clarify the nature of bone osteolysis in CGCG & GCTB, to clarify the role of MGCs in the above lesions, finally to correlate the score and intensity of the expressed marker with tumor type, grade and stage.

Materials & Methods:

Twenty cases of central giant cell granuloma of the jaw (CGCG) obtained from the college of dentistry/ pathology department at Baghdad university, and other twenty cases of giant cell tumor of the long bone (GCT) obtained from the college of medicine/ pathology department at Baghdad university, were selected, : other twenty paraffin embedded sections including 5 cases of breast cancer, 5 cases of lymphoma, according to the patients' files and 10 cases of normal bone were taken as control.

All sections were immunohistochemically analyzed to verify the pattern of expression of RANK, TNF and ALP in them.

Clinical data were obtained on the age, gender, diagnosis, laboratory investigations. Selected histopatholgical features of mononuclear cells, stroma and giant cells were assessed.

Immunohistochemical analysis:

A formalin fixed, paraffin embedded block from a representative area of the two lesions were selected. Serial sections were cut at 5µm thickness and mounted. One slide of these was stained with Hematoxylin and Eosin (H & E), the others examined immunohistochemically by the avidin-biotin peroxidases complex method, using the following monoclonal primary antibodies: ***USBiological*** RANK (Receptor Activator of NF-Kb), ***USBiological*** Phosphate, Alkaline, Human, Bone (BAP) & ***USBiological*** Tumor Necrosis Factor alpha (TNFa).

Results:

There were no significant histological differences between the two lesions, with the exception of necrosis that was significantly higher in GCT. In addition, GCT showed higher mean number of giant cells per measurement field, higher number of nuclei per giant cell, greater fractional surface area and relative size index compared to CGCG. Both diseases showed similar cellular phenotype in nuclear factor kappa B (RANK), Tumor necrosis factor alpha (TNF a) and Alkaline phosphatase (ALP).

Immunohistochemistry of tumor necrosis factor (TNF), (RANK), (ALP) revealed nearly similar expression in giant cell tumor and in central giant cell granuloma of the jaw compared with the control group.

Central giant cell granuloma of the jaw showed an early age of presentation (35% <20 years) compared to giant cell tumor of long bone (all the cases ranged between 21-45 years). There was a female predilection in both lesions (60% of CGCG, 65% of GCT). The mandible was the more common anatomical allocation for CGCG (60%), while the femur was the more common anatomical allocation for GCT (45%). All the lesions were osteolytic in nature.

Conclusions:

At histologic analysis, CGCGand GCT are not readily distinguished ^{from} each other. They expressed many osteoblastic markers like RANK, TNF and ALP. Multinucleated giant cells components in these two lesions showed characteristics of osteoclasts phenotypes. The accumulation of osteoclast in these giant cell rich lesions occure by RANKL-dependent process.