A comparative study of clinicopathological and immunohistochemical expression of CD1a, RANK and RANKL in Langerhans cell histiocytosis of jaw and skull lesions

A Thesis

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By

Alya'a Kadhim Mohammad

B.D.S

Supervised by

Prof. Dr. Bashar Hamid Abdullah

PhD., Oral and Maxillofacial Pathologist

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Abstract

Background:

Langerhans cell histiocytosis (LCH) , is a rare disorder, clinically presents with heterogeneous manifestations ranging from an isolated to a multisystem disease. Commonly seen in infancy or early childhood, the disorder is characterized by clonal proliferation of Langerhans cells including bone, mucous membrane and viscera. The course of the disease varies from spontaneous resolution, unifocal (eosinophilic granuloma), or to a progressive multisystem disorder with organ dysfunction and potential life-threatening complications.

Aim of the study:

Histological comparision of jaw and skull lesions concerning the constituent cells confirmed by CD1a immunohistochemical marker, and assessment of osteoclastogenesis process by immunohistochemical expression of RANK (receptor activator of nuclear factor Kappa B) and RANKL (receptor activator of nuclear factor Kappa B ligand), to be compared in both sites.

Materials and methods:

Twenty five formalin fixed paraffin embedded tissue blocks of langerhans cell histiocytosis cases ,fourteen of which were located in the jaws; and the other eleven were located in the skull. That were collected from laboratories archives and included in the study. Diagnostic confirmation was performed through examination of hematoxylin and eosin (H&E) stained sections. Four micrometer thick sections were cut and mounted on positively charged slides and stained immunohistochemically with monoclonal antibodies to CD1a to confirm in the diagnosis as well as assessment of labelling index, RANK and RANKL to assess the osteoclastogenic mechanism. Comparison

regarding aformentioned markers' expressions was carried out between the two sites involved in the study.

Results:

The age range of the patients with langerhans cell histiocytosis of the jaws was between 2.5 and 50 years, with the mean (23.61±12.17), while for langerhans cell histiocytosis of the skull was between 2 and 35 years, with the mean (11.32±10.28). High significant difference between the two site according to age (p=0.009). The male/female ratio for jaws (LCH) was 12/2 (6:1), and it was 6/5 (1.2:1) for skull (LCH),with no significant difference. Regarding the locations, four cases of (LCH) of the jaws were located in the maxilla (28.57%) ,nine cases were located in the mandible (64.29%) and the remaining one case was located in both maxilla and mandible (7.14%).Where as skull (LCH) cases were distributed among skull(not specified location) (3cases) (27.27%) , base of skull (1case) (9.09%), frontal bone (2cases) (18.18%), orbital plate of frontal bone (2cases) (18.18%), parietal bone (2cases) (18.18%) and scalp (1case) (9.09%).

Histological examination showed variable numbers of Langerhans cell with grooved nuclei, lymphocyte, eosinophil and giant cells, variable number of mitotic figures were observed in 12 of total 25 cases of (LCH) based on the presence or absence of mitoses. Comparatively ,there was no significant difference in the expression values of CD1a, RANK and RANKL between the two groups.

CD1a immunoreactivity was recognized in all cases of either group. An average labeling index of (37.21±19.60) was calculated in the jaw cases, while the index for the skull was (38.64±17.33),with no significant difference. Collectively, 24of the 25 cases was positive for RANKL antibody with different

score value. Concerning the jaw bones, 1 of 14 cases was negative to RANKL antibody with the mean(51.79±21.45), whereas there was no RANKL negative skull cases with the mean(56.36±14.85). No statistically significant difference in the RANKL immunoexpression between jaws and skull bones (LCH) was found, also no statistically significant difference in the RANKL immunoexpression according to age, gender and site in each group.

Twenty cases of total twenty five samples were positive to RANK antibody. The cases with negative RANK expression (4 cases) were located in the jaws with the mean(60±16.98), whereas (1 case) were located in the skull with the mean(67.27±10.34). No statistically significant difference in the RANK immunoexpression between jaws and skull bones (LCH) was found, also no statistically significant difference in the RANK immunoexpression according to age, gender and site in each group.

Using Spearman's correlation among different immunehistochemical markers expression values employed in this study ,for the jaws, there was significant correlation between CD1a and RANK (P=0.016). In the skull, there was a high significant correlation between RANK and RANKL (p=0.001).

Among the sites, there was no statistically significant difference was found for each different immunehistochemical markers.

Conclusion:

Langerhans cell histiocytosis of jaws and skull bear similar osteoclastogenic mechanism when quantified with RANK and RANKL immunostaining respectively. There were high significant difference according to age between the two groups, being of wide range in the jaw than in the skull. Regarding the genders, there were no significant difference between the two groups. The immunoexpression of CD1a, RANK and RANKL in langerhans cell histiocytosis are not related to the age, gender and location. Regarding the jaw

lesions, labeling index (No. of positive cells), showed a positive correlation between CD1a and RANK. While in the skull lesions, there was a high significant correlation between RANK and RANKL.