ORIGINAL ARTICLE

HISTOMORPHOLOGICAL EVALUATION OF OSTEOCALCIN AND CYTOKERATIN IN FIBROUS DYSPLASIA AND OSSIFYING FIBROMA OF THE JAW

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ABSTRACT

Background: Fibrous dysplasia and ossifying fibroma are amongst maxillofacial fibro-osseous lesions and their incidence is reported to be approximately 37.1% and 22.9% respectively of all the jaw tumours. The present study was undertaken to analyze the expression of osteocalcin and cytokeratin in fibrous dysplasia and ossifying fibroma of the jaw. **Methods:** This descriptive case series of six months duration was conducted at Armed Forces Institute of Pathology Rawalpindi, Pakistan. Fifteen retrieved cases of fibrous dysplasia and ossifying fibroma, after preparation and re-diagnosis, were stained with immunohistochemical markers; Osteocalcin and Cytokeratin. The data were analyzed by using SPSS version 17. Descriptive statistics was used to describe the data and chi-square test was used to compare the intensity of expression of osteocalcin and cytokeratin in fibrous dysplasia and ossifying fibroma. **Results:** Osteocalcin showed positive result in cases of fibrous dysplasia while cytokeratin revealed the same in cases of ossifying fibroma. The expression of the two markers in these two pathologies statistically revealed highly significant results (p=0.000). **Conclusion:** Osteocalcin and cytokeratin can be used as a significant tool in differentiating between fibrous dysplasia and ossifying fibroma.

KEY WORDS: Osteocalcin, Cytokeratin, Fibrous Dysplasia, Ossifying Fibroma.

INTRODUCTION

Fibrous Dysplasia (FD) and Ossifying Fibroma (OF) are amongst the maxillofacial fibro-osseous lesions and their incidence is reported to be approximately 37.1% and 22.9% respectively of all the jaw tumours.[1,2] A Chinese study however, reports a considerably high incidence of OF; 33.9% versus 23% cases of FD.[3] These two lesions bear similar histopathologic features and cannot be clearly defined only on the basis of their clinical findings. These lesions should be distinguished from each other because of their distinct pattern of disease advancement and difference in management which varies from none to surgical re-contouring for fibrous dysplasia and complete resection for ossifying fibroma. Therefore, it becomes very essential to have a specific diagnosis.[4]

Osteocalcin is an immunohistochemical marker also known as bone gamma-carboxyglutamic acid-containing protein; secreted exclusively by osteoblasts and its high serum levels are correlated with increased bone mineral density. It is therefore, used as biomarker for bone formation process and also has a role in regulation of osteoblast function.[5-7] Cytokeratin is another immunohistochemical marker that is water-insoluble intracellular intermediate filament protein present in the intracytoplasmic cytoskeleton of all epithelial cells.[8]

The rationale for this study was to analyze the expression of Osteocalcin and Cytokeratin in FD and OF and determine their role in discerning these two entities. This will enable the treating surgeons in management of OF; using a more radical approach as it shows a significant growth potential, thus also decreasing the chances of associated recurrence.[4] It has also been observed that in many cases of FD, the disease tends to stabilize and the lesion essentially stops enlarging on skeletal maturation. Therefore, surgical intervention in children and adolescents should be delayed as long as possible.[4, 9]

The present study was undertaken to analyze the expression of osteocalcin and cytokeratin in fibrous dysplasia and ossifying fibroma of the jaw.

MATERIAL AND METHODS

This descriptive case series was conducted at Histopathology Department of the Armed Forces Institute of Pathology, Rawalpindi. 15 cases each of FD and OF alongwith their paraffin em-

bedded blocks were retrieved from the record of Histopathology Department. The slides after preparation were re-diagnosed on haematoxylin and eosin staining and later immunohistochemical markers; Osteocalcin and Cytokeratin were applied on them. The data collected was analyzed by using SPSS version 17. Descriptive statistics was used to describe the data and Chi-square test was used to compare the intensity of expression of osteocalcin and cytokeratin in FD and OF. A probability value of 0.05 or less was considered as significant.

RESULTS

The expression of osteocalcin in 15 cases of FD analysed in our study showed 10 cases (66.7%) with strong positive and remaining 5 (33.3%) with moderate positive results. None of these cases showed reactivity for cytokeratin. (Fig. 1-4)

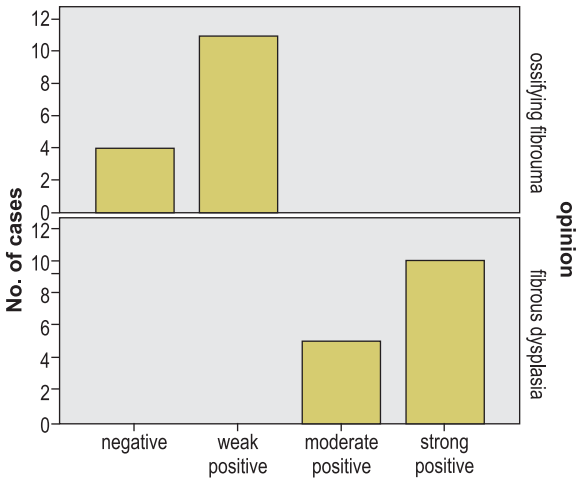

Fig. 1: Expression of osteocalcin in fibrous dysplasia and ossifying fibroma.

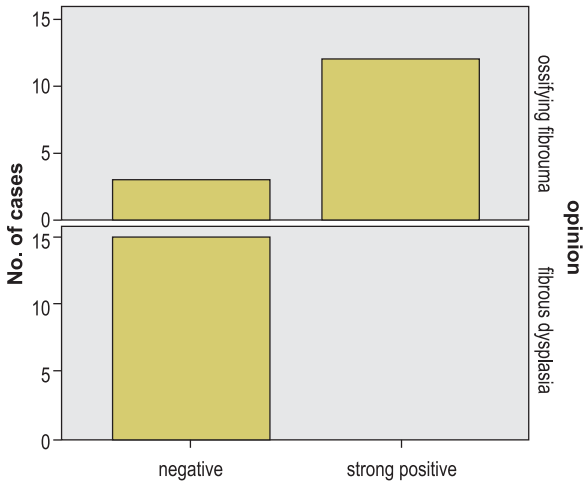

Fig. 2: Expression of cytokeratin in ossifying fibroma and fibrous dysplasia.

Out of 15 cases of OF the expression of osteocalcin showed weak positive in 11 (73.3%) and negative results in the rest of 4 (26.7%) cases. On the other hand, expression of cytokeratin showed strong positive reactivity in 12 (80%) and negative reactivity in the remaining 3 (20%) cases. (Figure 1, 2, 5 & 6).

The expression of the two markers in these two pathologies statistically revealed highly significant results ($p=0.000$), thus highlighting their importance as a significant tool to differentiate between FD and OF.

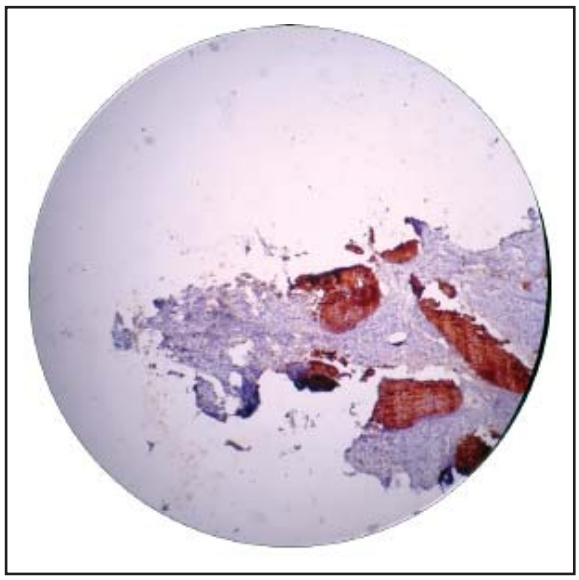

Fig. 3: Calcified regions of fibrous dysplasia showing strong positive reactivity for osteocalcin.

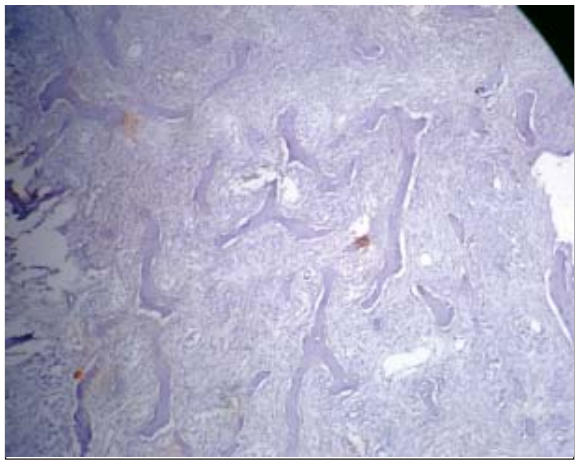

Fig. 4: Negative reactivity of connective tissue stroma of fibrous dysplasia for cytokeratin.

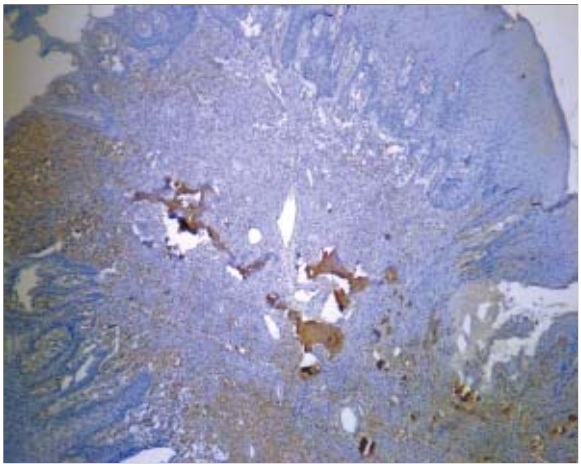

Fig. 5: Calcified regions of ossifying fibroma showing weak reactivity for osteocalcin.

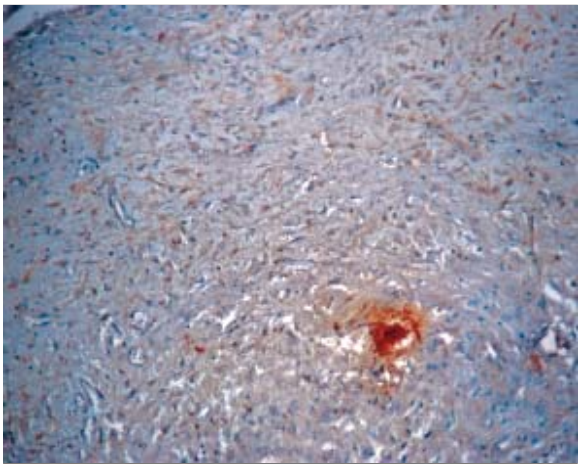

Fig. 6: Strong positive reactivity of spindle cells of ossifying fibroma for cytokeratin.

DISCUSSION

Fibro-osseous lesions are a diverse group of jaw lesions which include developmental (hamartomatous) diseases, reactive or dysplastic processes and neoplastic entities.[4,9] There is considerable overlap in their epidemiology, localization, clinical features, radiographic appearance and histopathologic examination. Hence, differentiation of these tumours on the basis of these said features is unreliable. Therefore, to have an accurate diagnosis specific clinico-pathological correlation is required.[10] This is also critical because of their distinct pattern of progression and vastly different management protocols.[4]

This study was planned with the objective to analyze the expression of Osteocalcin and Cytokeratin in fibrous dysplasia and ossifying fibroma, thus determining their role in differentiation of these two entities.

Our result of expression of Osteocalcin in FD as compared to OF is in accordance with many other studies conducted worldwide. In a Brazilian study conducted by Elias LSA *et al* in 2010, revealed that Osteocalcin has higher expression in FD as compared to that in OF.[11] Similarly, in a Japanese study by Toyosawa and his colleagues in 2007 demonstrated that the calcified regions of all of 9 cases of FD showed strong immunoreactivity for Osteocalcin but weak immunoreactivity in all of 5 cases of OF[12]. Similar results were shown by another Japanese study by Sakamoto A *et al* in 2001; showed higher immunoreactivity for osteocalcin in bone matrix of all of 20 cases of FD which were studied as compared to weak immunoreactivity in all of 17 cases of OF.[13]

Similarly the positive expression of Cytokeratin for OF as opposed to its negative immunoreactivity in FD seen in our study also matches with the results of other studies conducted time to time in other parts of the world. . In a study conducted by Genevieve Kuruvilla and German C. Steiner in New York in 1997 demonstrated cytokeratin reactivity in 5 out of 9 cases of OF.[14] Likewise**,** Park YK *et al* in 1993 demonstrated cytokeratin positive immunoreactivity in 2 of 6 cases of OF as compared to negative immunoreactivity in all of 5 cases of FD immunostained with a Cytokeratin antibody.[15] The same was reported by Sweet DE *et al* in their study conducted in 1992. They found Cytokeratin positive reactivity in 28 cases out of the total of 30 cases of OF studied.[16]

We have seen that the results of all the above mentioned studies collaborate with our results; thus validating the role of Osteocalcin and cytokeratin in differentiation of FD and OF.

The pattern of the bone marker (Osteocalcin) and epithelial marker (Cytokeratin) in FD and OF is studied for the first time in our setup, thus could be taken as pilot study and research area is open for future studies regarding the expression of other bone markers such as osteopontin and osteonectin and their role in differentiating between these two entities and other lesions which are included in the differential diagnosis.

CONCLUSION

The immunohistochemical markers osteocalcin and **c**ytokeratin can be used as a significant tool for differentiating fibrous dysplasia and ossifying fibroma, thus helping in the management of these pathologies.

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