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SCLEROSTIN EXPRESSION IN GIANT CELL TUMOR OF BONE AND CORRELATION TO PATIENT FACTORS

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INTRODUCTION: Giant cell tumor of bone (GCTB) is a destructive lesion with a high potential for recurrence. RANK-Ligand targeted therapy (denosumab) has provided promising, yet mixed results in GCTB. Unfortunately, cessation of therapy frequently results in a high rate of recurrence and/or disease progression. Sclerostin (SOST) has been purported to act as an osteoblast inhibitor and anti-SOST therapeutic agents have been FDA approved for the treatment of osteoporosis. In this study we sought to identify the presence of SOST in GCTB and identify correlative patient factors for potential future therapeutic and diagnostic uses.

METHODS: A tissue micro array (TMA) was used for all patients at a single institution undergoing surgery for primary GCTB of the extremity between 1993-2008 with a minimum of 6 months follow-up. SOST antibody staining was evaluated by a bone and soft tissue pathologist blinded to both diagnosis and patient demographics. Primary outcomes included the presence of staining of the stromal cells and giant cells from GCTB specimens. Secondary outcomes included correlation of patient and tumor specific predictor variables and correlation with SOST expression. Statistical analysis was performed using non-parametric tests of association.

RESULTS: SOST antibody staining of any type was present in 47 of 48 cases (97.9%). Positivity in the stromal cells was present in 39 of 48 cases (81.3%) and was associated with clinical/radiographic aggressiveness, symptomatic lesions, previous surgical treatment, and age at time of surgery. Positivity in giant cells was present in 41 of 48 cases (85.41%) and was associated with aggressiveness on histology only.

DISCUSSION/CONCLUSION: We found that, overall, GCTB demonstrates a high level of SOST staining. The expression of SOST in the mononuclear stromal cells is not unexpected given the proposed pathway of GCTB development and the role of SOST in bone remodeling. The unregulated expression of RANKL in GCTB stromal cells and its effect on bone metabolism could happen in isolation or, more likely, with additional factors such as SOST. Our correlation to clinical aggressiveness and presence of clinical symptoms with SOST staining in stromal cells could suggest a contribution of SOST to osteolysis in these tumors. The presence of giant cells staining for sclerostin and the correlation with histologic aggressiveness may suggest SOST as a marker of clinically aggressive GCTB. This would most likely represent an induction of the giant cells as opposed to a tumor driver given previous literature delineating the reactive nature of the giant cells. SOST has been expressed in both malignant and benign bone-forming tumors and cartilaginous tumors (enchondroma, osteochondroma, and chondrosarcoma). While the role of SOST in healthy bone metabolism has been well studied, SOST expression in tumorgenesis is less well known. Further research is warranted to define the role of sclerostin as both a prognostic factor and potential therapeutic target in GCTB