DIFFERENTIAL EFFECTS OF OVARIECTOMY AND ESTROGEN REPLACEMENT ON DBM-INDUCED BONE FORMATION IN IMMUNOCOMPROMIZED MICE AND RATS

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CLINICAL SIGNIFICANCE

The higher prevalence of osteoporosis and osteoarthritis in post-menopausal women results in a greater demand for bone grafts required for joint replacements, spinal fusions, and fracture repair. The diminished bone quality of this patient population makes obtaining autologous bone grafts difficult and therefore requires the use of allogeneic grafts, including demineralized bone matrix (DBM). It is unknown, however, how the post-menopausal environment may affect the osteoinductivity of the DBM. This study indicates that DBM-induced bone formation is reduced in estrogen (E2) deficient animals and can be restored by E2-replacement.

INTRODUCTION

DBM is a commonly used bone allograft in orthopaedics because of its osteoinductive properties. In vivo assays of effectiveness require the use of immunocompromised athymic animals, the observations are further complicated by their lack of functional T-cells. Little is known about DBM-induced bone formation in females and the role that E2 plays. Because in vivo assays of human DBM require the use of immunocompromised athymic animals, the observations are further complicated by their lack of functional T-cells. The complex biological relationship between estrogen, the immune system, and bone has been thoroughly studied in the athymic mouse. E2 has been shown to decrease osteoclast formation (1) and increase functional T-cells. Repletion in rats of estrogen levels. The whole of the calf muscles were covered with ossicles. Cartilage scores were derived as a variant of bone scoring, based on the number of sites and their area. Data were analyzed by ANOVA and significant differences between groups determined using Bonferroni’s modification of Student’s t-test.

RESULTS

OVX resulted in a 4-fold reduction in uterine weight at both day 35 and 56 in mice, and a 2-fold reduction in rats at 35 days and 3-fold at 56 days. E2 levels in rat blood were reduced 6-fold at day 35, and 9-fold at 56 days. E2 repletion in mice as determined by uterine weight was 2x the OVX values, but it did not reach the level of the sham-operated animals. Ovariectomy-induced bone formation in rats was complete, as judged by uterine weight and blood E2 values.

DISCUSSION

Ovariectomy reduced osteoinduction by DBM in both mice and rats, suggesting that E2 is necessary for bone formation regardless of origin. However, in no case was the process completely inhibited. While the QS indicated that the number of sites of new bone formation was not dramatically reduced, quantitative measures showed that the magnitude of the response at each site was reduced. The normal endochondral progression from cartilage to bone typically seen in DBM osteoinduction was delayed in rats, where cartilage was still evident at 56 days. In both animals, E2 repletion reversed the effects of OVX. Unlike mice, rats displayed cartilage in the implant sites, particularly at 56 days. In both mice and rats, the amount of residual DBM was lower at 35 days in the OVX animals.

REFERENCES


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