Alterations in osteoclast morphology following long-term 17beta-estradiol administration in the mouse

ABSTRACT

Findings extend our understanding of osteoclast structure and function in the mouse exposed in vivo to high doses of estrogen. Ultrastructural examination showed that osteoclasts from estrogen-treated mice were unable to seal against the bone surface and were unable to form ruffled borders.

INTRODUCTION

Background Although the role of the osteoclast in bone resorption is becoming better understood, much remains to be learned about osteoclastogenesis and the exact mechanism of action of anti-resorbing agents on the functional osteoclast. The anti-resorbing agent 17β-estradiol is especially noteworthy because of the association of its decline at menopause with the development of postmenopausal osteoporosis. As previously noted by Liu and Howard, the underlying cellular changes responsible the increased bone formation which follows estrogen administration are still not well characterized. In the present report we report findings on alterations in osteoclast morphology following long term administration of high doses of 17β-estradiol to B6D2F1 mice. Development of osteosclerosis and the disappearance of the marrow space in these estrogen-treated mice is an interesting and useful model since marrow stromal cells not only contain the precursors for osteogenic cell lineages, but they also exert important effects on osteoclastogenesis and lymphopoiesis, and modulate the effects of some systemic factors of bone turnover. Osteoclasts, as well as osteoblasts, possess estrogen receptors. Hematopoietic cells also influence osteogenic cell differentiation, and some evidence suggests that mature lymphocytes influence osteoclast and osteoblast function. In the estrogen-treated mouse model used in the studies reported here, natural killer (NK) cells, which rely upon an intact bone marrow for full marrow maturation, are arrested in a nonlytic state; since marrow space is lessened due to the osteosclerosis, the spleen provides the source for T and B cells and macrophages. The objective of the present study was to assess the functional state of osteoclasts in estrogen-treated mice by determining if osteoclasts retained tartrate-resistant acid phosphatase activity (TRAP) and normal ultrastructural features.

CONCLUSION

Conclusions Findings extend our understanding of osteoclast structure and function in the mouse exposed in vivo to high doses of estrogen. Ultrastructural examination showed that osteoclasts from estrogen-treated mice were unable to seal against the bone surface and were unable to form ruffled borders.