A Forum for Commentaries on Recent Publications

Aging and Kyphosis

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In the recent article by de Boer and colleagues, mice carrying a targeted mutation in the XPD gene, which is mutated in the human disorder trichothiodystrophy (TTD) and encodes a DNA helicase that is involved in DNA repair, were found to exhibit osteoporosis and kyphosis as symptoms of premature aging (1). Radiographs of 14-month-old TTD mice revealed prominent kyphosis (de Boer, Figure 4) and a generalized reduction in radiodensity of the skeleton except for the skull. As stated, “The osteoporosis and concomitant kyphosis exhibited by TTD mice are hallmarks of aging in humans.” TTD mice bred to be homozygous for a null mutation in the XPA gene, which further decreases DNA repair capacity, also developed “spinal kyphosis indicative of osteoporosis.” While both the kyphosis and osteoporosis were well documented, the linkage between the two was not referenced, nor discussed.

In humans, osteoporosis causes kyphosis through deformity of the vertebral bodies (2). Due to the loss of trabecular bone in vertebral bodies of the middorsal spine, anterior wedging, “codfish” deformity, and/or overt fracture lead to kyphosis, clinically known as dowager’s hump (3). While inspection of the radiographs of the TTD mice in de Boer’s Figure 4 reveals osteoporosis and increased kyphosis of the lower thoracic spinal column, no mention was made of the presence of compression deformities, wedging, or fractures. The radiographs of the TTD mice, though of excellent quality, are not of sufficient resolution to allow the reader to fully evaluate such changes, though none appear to be present. In several mouse knockouts, kyphosis unrelated to osteoporosis can be caused by growth plate abnormalities (4), osteosclerosis (5), and muscular dystrophy (6). In aging humans, annulus degeneration may also underlie kyphosis (7).

Age-related kyphosis or spinal curvature has also been reported in several small tropical fish species (8,9), whose life spans approximate the mouse, including aging zebrafish (10). In contrast to humans, osteoporosis does not appear to be involved in fish kyphosis, at least in these species. Other mechanisms, such as soft tissue changes, especially muscle degeneration, may be responsible for the spinal curvatures (10,11). These findings, coupled with several other possible mechanisms causing kyphosis in mice that are distinct from vertebral fractures, suggest that the osteoporosis and kyphosis in TTD mice may not necessarily be mechanistically linked as they are in human aging. Such morphological observations may superficially recapitulate the aging phenotype, but may not be causally similar.

If not a model for human aging, does the kyphosis of TTD mice resemble changes found in aged mice? de Boer and colleagues presented the radiograph of a single 14-month-old nonmutant wild-type mouse that did not manifest kyphosis, but this may be too young an age at which to detect age-related skeletal abnormalities. Analysis of strain-matched controls at older ages will be required to determine whether the kyphosis of TTD mice is a premature aging phenotype for its own species.

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REFERENCES


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