

NTP Nonneoplastic Lesion Atlas

Bone – Fibro-Osseous Lesion

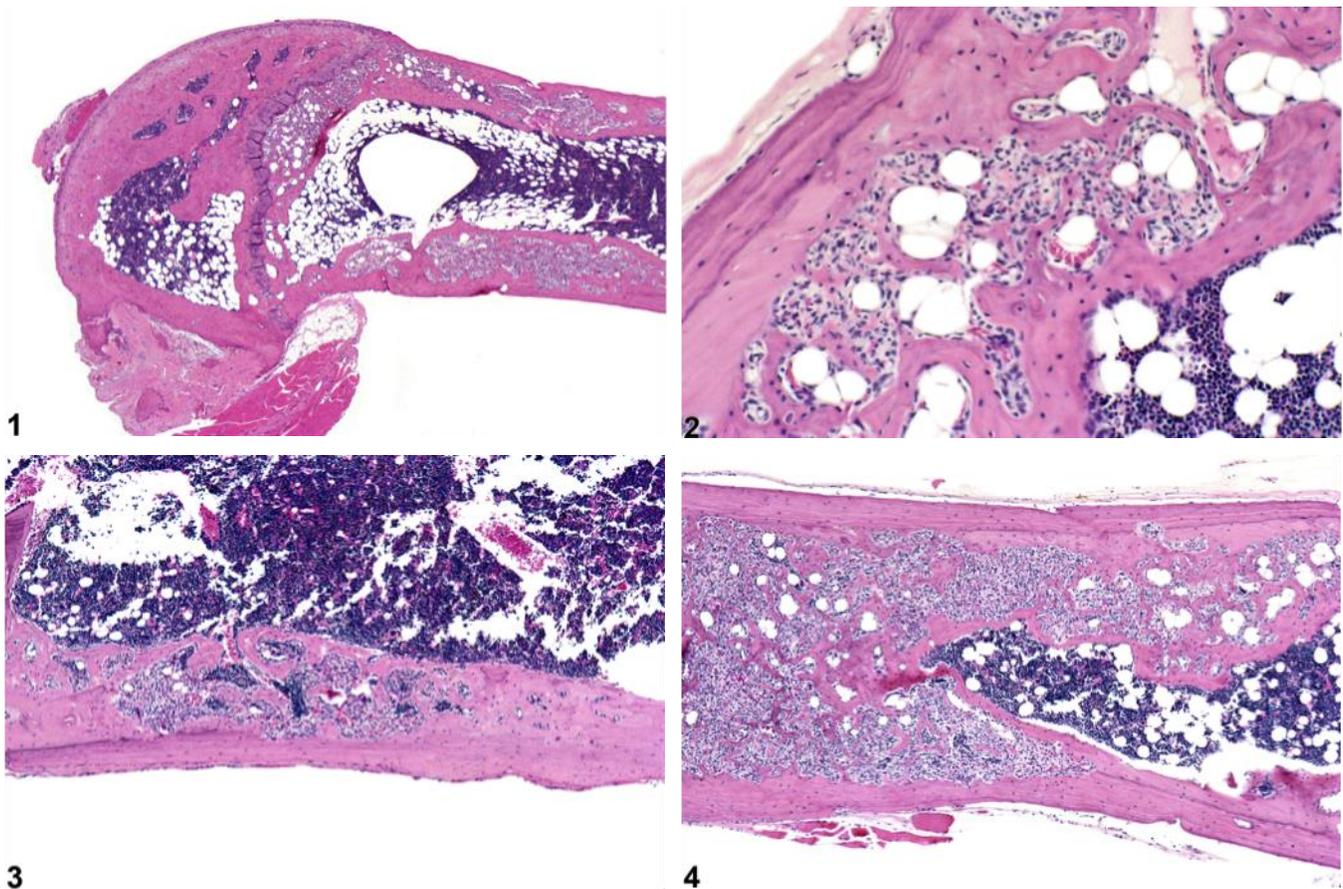
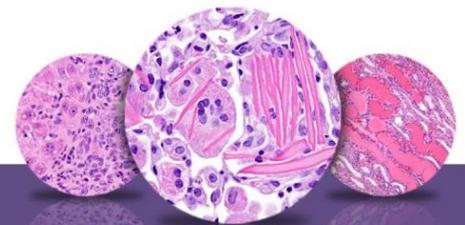


Figure Legend: **Figure 1** Bone - Fibro-osseous lesion in the femur of a female B6C3F1/N mouse from a chronic study. **Figure 2** Bone - Fibro-osseous lesion in a female B6C3F1/N mouse from a chronic study. This fibro-osseous lesion shows replacement of bone by fibrovascular tissue. **Figure 3** Bone - Fibro-osseous lesion in a female B6C3F1/N mouse from a chronic study. **Figure 4** Bone - Fibro-osseous lesion in a female B6C3F1/N mouse from a chronic study. There is replacement of bony trabeculae and the marrow cavity with fibrovascular stroma.

Comment: Fibro-osseous lesions (FOLs) arise commonly within the sternbrae, vertebrae, tibiae, femurs, and other bones in a variety of mouse strains. The incidence of FOL is higher in B6C3F1 mice than in other strains, and it is the most common primary bone lesion in B6C3F1 mice. This lesion has not been reported in the rat.



NTP Nonneoplastic Lesion Atlas

Bone – Fibro-Osseous Lesion

These lesions are characterized by partial or complete replacement of bony trabeculae and marrow cavity by fibrovascular stroma containing fibroblasts, osteoclasts, and osteoblasts embedded in eosinophilic matrix (Figure 1 and Figure 2). The histopathologic features are similar to fibrous osteodystrophy; however, FOLs occur in the absence of parathyroid or renal alterations, typically arise as focal lesions within the metaphyseal or endocortical regions (Figure 3), and may progress to involve larger areas of the bone (Figure 4).

FOL increases in incidence with age and arises most often in female mice (40–100% incidence in B6C3F1 females, <1% in males), suggesting involvement of estrogens. These lesions are often accompanied by alterations in the uterus or ovary consistent with hyperestrogenism (endometrial cystic hyperplasia, vaginal epithelial cell hyperplasia and hyperkeratosis, ovarian follicular development/atresia and cysts). However, these lesions also arise in ovariectomized female mice and castrated males.

Historically, FOL has been referred to by a variety of names, including fibro-osseous dysplasia, fibrous dysplasia, focal osteodystrophy, osteodysplasia, osteofibrosis, and osteodystrophy, but the preferred term for these lesions is “fibro-osseous lesion.”

Recommendation: Although this is a fairly common age-related background lesion in the B6C3F1 mouse, the incidence and severity of FOL may be influenced by treatment with compounds that possess estrogenic effects. Therefore, this lesion should be diagnosed, given a severity grade, and described in the narrative whenever present. Advanced FOL in mice is indistinguishable histologically from fibrous osteodystrophy. Therefore, when this lesion is observed in mice in an advanced state and in the absence of parathyroid or renal lesions, the diagnosis of FOL should be made. If the lesion occurs concurrently with chronic renal disease or proliferative parathyroid lesions, the diagnosis of fibrous osteodystrophy should be made (see Bone - Fibrous Osteodystrophy).

References:

Albassam MA, Courtney CL. 1996. Non-neoplastic and neoplastic lesions of the bone. In: Pathobiology of the Aging Mouse, Vol 2 (Mohr U, Dungworth DL, Capen CC, Carlton WW, Sundberg JP, Ward JM, eds). ILSI Press, Washington, DC, 425-437.



NTP Nonneoplastic Lesion Atlas

Bone – Fibro-Osseous Lesion

References:

Albassam MA, Wojcinski ZW, Barsoum NJ, Smith GS. 1991. Spontaneous fibro-osseous proliferative lesions in the sternums and femurs of B6C3F1 mice. *Vet Pathol* 28:381-388.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/1750163>

Dodd DC, Port CD. 1987. Hyperostosis of the marrow cavity caused by misoprostol in CD-1 strain mice. *Vet Pathol* 24:545-548.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/3137716>

Gervais F, Attia MA. 2005. Fibro-osseous proliferation in the sternums and femurs of female B6C3F1, C57black and CD-1 mice: A comparative study. *Dtsch Tierarztl Wochenschr* 112:323-326.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/16240910>

Greenman DL, DeLongchamp RR. 1986. Interactive response to diethylstilbestrol in C3H mice. *Food Chem Toxicol* 24:931-934.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/3781439>

Highman B, Roth SI, Greenman DL. 1981. Osseous changes and osteosarcomas in mice continuously fed diets containing diethylstilbestrol or 17 beta-estradiol. *J Natl Cancer Inst* 67:653-662.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/6944535>

McAnulty PA, Skydsgaard M. 2005. Diethylstilbestrol (DES): Carcinogenic potential in Xpa^{-/-}, Xpa^{-/-}/p53^{+/-}, and wild-type mice during 9 months' dietary exposure. *Toxicol Pathol* 33:609-620.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/16178126>

Sass B, Montali RJ. 1980. Spontaneous fibro-osseous lesions in aging female mice. *Lab Anim Sci* 30:907-909.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/7431877>

Travlos G. 2006. Histopathology of bone marrow. *Toxicol Pathol* 34:566-598.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/17067944>

Authors:

Mark J. Hoenerhoff, DVM, PhD, DACVP
Associate Professor
In Vivo Animal Core, Unit for Laboratory Animal Medicine
University of Michigan Medical School
Ann Arbor, MI

Amy Brix, DVM, PhD, DACVP
Senior Pathologist
Experimental Pathology Laboratories, Inc.
Research Triangle Park, NC