Osteosclerosis in Aged ICR Mice

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ABSTRACT. Osteosclerosis occurred in a high incidence in the sternum and tibia of 160 ICR mice examined histologically, at more than 300 days of age in the females and at more than 450 days of age in the males. It was initiated with a proliferation of osteogenous tissues at the metaphysis, resulting in replacement of the marrow cavity by a network of mature osseous trabeculae. There were osteochondrosis, osteoarthrosis and osteoporosis in mice affected with osteosclerosis. It was thought that osteosclerosis in the present mice might have occurred as one of the aging changes or a compensatory event for the weakened bone subsequent to the other bone changes.—KEY WORDS: aging change, bone disease, marrow cavity, mouse, osteosclerosis.

As to spontaneous bone disorders in mice, there are known degenerative osteoarthrosis [7, 9, 10], idiopathic necrosis of the bone [11], inherited abnormalities [1, 5] and fibrous osseous lesions [6]. The present authors encountered osteosclerotic lesions in aged ICR mice. This paper describes pathological findings and incidence aspects of the lesions.

MATERIALS AND METHODS

Materials used for this investigation were 160 (80 male and 80 female) specific-pathogen-free (SPF) mice of ICR strain. The animals were housed 4 mice to a wire mesh cage and kept in a barrier system room conditioned at a temperature of 24±1°C with relative humidity of 55±5%. They were fed a laboratory feed and fresh water ad libitum. Many died spontaneously; the rest were killed at 728 days of age in both sexes. The age at death for the males was from 227 to 728 days, average 567 days, and from 168 to 728 days for the females, average 546 days.

After postmortem examination, tissues were fixed in 10% formalin solution. Bony tissues were decalcified with 10% formic acid-formalin solution. Tissues were embedded in paraffin and sections stained with hematoxylin and eosin (HE). Bones examined were the sternum and tibia.

RESULTS

The affected bones were increased in hardness and had variable amounts of osseous trabeculae in the marrow cavity, and as a result, it was more difficult to cut them with a knife.

Sternum: The essential changes were abnormal endosteal osteogenesis, resulting in osteosclerosis. The lesions were initiated with a proliferation of osteogenous tissues consisting of osteoblasts, fibrous connective tissues, osteoid seams and a few osteoclasts on the marrow surface of the metaphyseal cortical bone and bone trabeculae. As the lesions progressed, slender or thick trabeculae of newly-formed immature or mature bone were formed in a network pattern at either one or both ends of each sternebra (Fig. 1). In the advanced lesions, the marrow cavity was completely occupied by thick trabeculae of newly-formed mature bone (Fig. 2).

Such osteosclerotic lesions were found at more than 450 days of age in the males and at
more than 300 days of age in the females, and the total incidence was 86% in the males and 90% in the females (Table 1). The lesions were more severe in degree in the females than in the males.

The mice affected with osteosclerosis were associated almost usually with osteochondrosis in the epiphyseal plate, osteoarthrosis in the sternal cartilage, and osteoporosis in all the bones. Osteochondrosis consisted of degeneration, focal colliquiative necrosis and focal ossification in the epiphyseal cartilage, some with cracking of the cartilage. Osteoarthrosis was composed of loosening of the matrix, focal narrowing or thickening, and chondrophytes in the articular cartilage. Oste-
osteoarthritis and osteoporosis were found in all the animals examined, namely, at more than 227 days of age in the males and at more than 168 days of age in the females (Table 2). Osteoporosis was observed at more than 400 days of age in the males and at more than 350 days of age in the females, and the total incidence was 68% in the males and 83% in the females (Table 2).

Tibia: There were osteosclerosis, osteochondrosis, osteoarthritis and osteoporosis in the tibia. These lesions were identical to those in the sternum, but they were milder in degree than those in the sternum. Osteosclerosis, which was associated almost usually with osteochondrosis, osteoarthritis and osteoporosis, was observed at more than 350 days of age in both sexes, and the total incidence was 82% in the males and 79% in the females (Table 1).

Other organs: No significant lesions related to the bone alterations were recognized in the other organs including the endocrine system.

DISCUSSION

Proliferative bone lesions seen in the sternum and tibia of the present mice are regarded as osteosclerosis which is initiated with a proliferation of osteogenous tissues. Osteosclerosis is found in the cancellous bone of the tubular bones of 4 aged rats [3]. Experimentally, osteosclerotic lesions are induced...
in mice [8, 15] and dogs [2, 13] by administration of estrogenic hormones, and in rats [12, 14] and rabbits [14] by calcitonin injection. Almost similar changes to the present cases, focal fibro-osseous lesions with occasional bone trabeculae, are observed in the sternum and long bone in 99 of 228 aged female mice and in only 1 of 226 males [6]. As the cause of these lesions, a hormonal disturbance is suggested because there is a relatively high incidence of ovarian cysts and cystic adenomatoid hyperplasia of the uterus. It should be noted for the lesions to have had the high incidence in both sexes in the present study.

Osteochondrosis, osteoarthrosis and osteoporosis were associated with the present condition. Osteoarthrosis is observed in laboratory animals including mice, and the aging or genetic factor is important for the pathogenesis [7, 9]. Osteoporosis is also one of aging changes [4]. Osteosclerosis in the present animals might have occurred as one of the aging changes or a compensatory event for the weakened bone resulting from osteochondrosis, osteoarthrosis and osteoporosis. Further investigation is needed for the pathogenesis.

REFERENCES


要 約

ICR 系老齢マウスに発生した骨硬化症: 山崎寛治、板倉智雄 (化学薬品検査協会、鳥取大学農学部家畜病理学教室) — ICR 系マウス160例の胸骨と脊骨を組織学的に検査した結果、骨硬化症が雄では300日齢以上に、雌では450日齢以上に高率に認められた。本病変は骨幹端における造骨細胞の増殖に始まり、最終的には骨皮質の成熟骨梁に転換している。ほとんどの本症例は骨髄腫症、骨髄腫症、骨髄腫症を合併していた。今回、骨硬化症は加齢性変化の一つとして、あるいは骨軟骨症、骨関節症、骨粗鬆症に後続した骨の細弱化に対する代償性変化として生じたと考えられた。