Fluoride exposure accelerates the development of postmenopausal osteoporosis: Animal model

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Introduction

From the viewpoint of the crystal formation mechanism (Fig. 1), we demonstrated recently that the combined effects of estrogen (Es) deficiency together with cadmium (Cd) exposure adversely affected the supply of carbonate ions during the crystal nucleation process, resulting in the increase of amorphous minerals in the bone associating with itai-itai disease, Cd-induced osteoporosis. We also reported that fluoride (F) exposure was much greater than that of Cd exposure in terms of the detrimental effect on the crystal nucleation process. This led to the assumption that F schemes such as water fluoridation for public health may accelerate the risk of developing postmenopausal osteoporosis. Therefore, the present study was conducted to raise awareness that water fluoridation for public health is the misconception. Furthermore, it is suggested that the primary cause of osteoporosis may result from the declining bone formation.

(No conflict of interest)

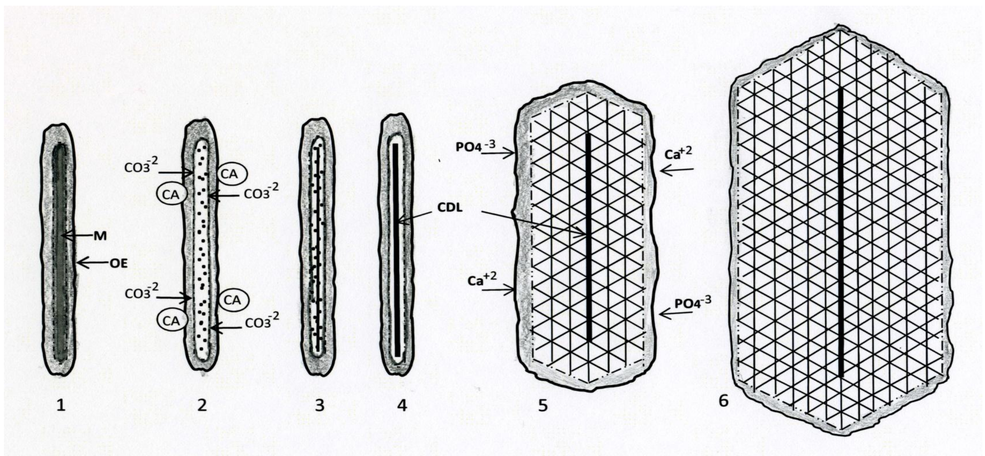

Fig. 1. The scheme of apatite formation process through central dark line (CDL) pathway.
1: Amorphous mineral, consisting Ca, PO4 and Mg ions within an organic envelope. Mg ions: an inhibitory effect on the mineralization process.
2: The carbonate ions supplied by CA generate huntite minerals (small dots), eliminating the inhibitory effect of Mg ions.
3: Creation of first apatite lattice line.
4: The first lattice line together with huntite minerals creates the CDL.
5 and 6: The crystal growth.

Materials and Methods

The overiectomized rats were divided into two groups: the Es deficient, and the combination of Es deficiency and F exposure groups. Also rats without ovariectomy were divided into two groups: the F exposure and the control groups. Rats of both the F exposure and combined groups were given free drinking water containing 1.0 mg/L F ions (NaF), while the control and Es deficient rats were given tap water. Three months later, the samples of calvaria were subjected to soft X-ray radiography and electron microscopy. The samples of tibia were examined under a light microscope. Rats were anaesthetized with ether, and the samples of calvaria and tibia were excised. The animal protocol was approved by the Animal Care and Use Committee of Meikai University.

Results

Soft X-ray radiographs showed that bone mineralization was significantly hampered by the combined effects (Fig. 2d).

A large number of minerals were observed in both the radiolucent and radiopaque (Fig. 3b) areas of the calvaria (Fig. 3b). Higher magnification showed that the minerals in the radiolucent area were amorphous due to the lack of lattice fringe (Fig. 3c), while crystals with lattice fringes were observed in the radiopaque area and control of the calvaria (Fig. 3e and f).

Toluidine blue stained sections showed that the combined effects caused to decrease the trabecular architecture of the tibia (Fig. 4d).

In this study, we could not confirm the increase of osteoclast number.

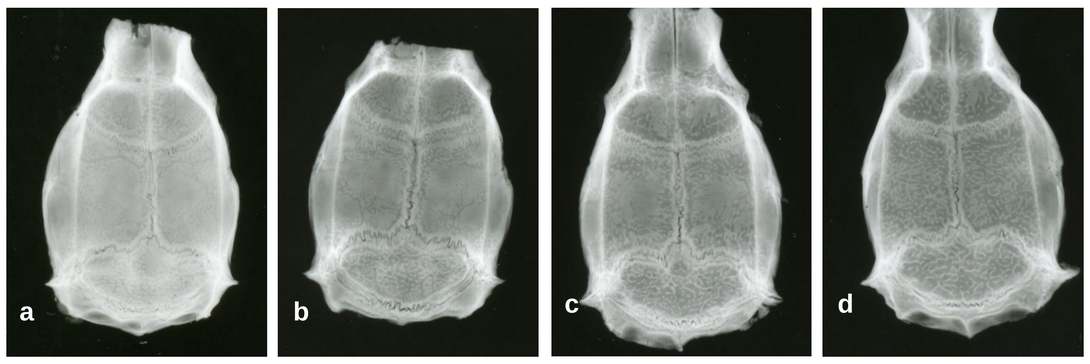

Fig. 2. Soft X-ray radiograph of the calvaria. The combined effects increase radiolucent areas in the calvaria. a:control, b: F 1.0 ppm exposure, c: Es deficiency, d: combined effects

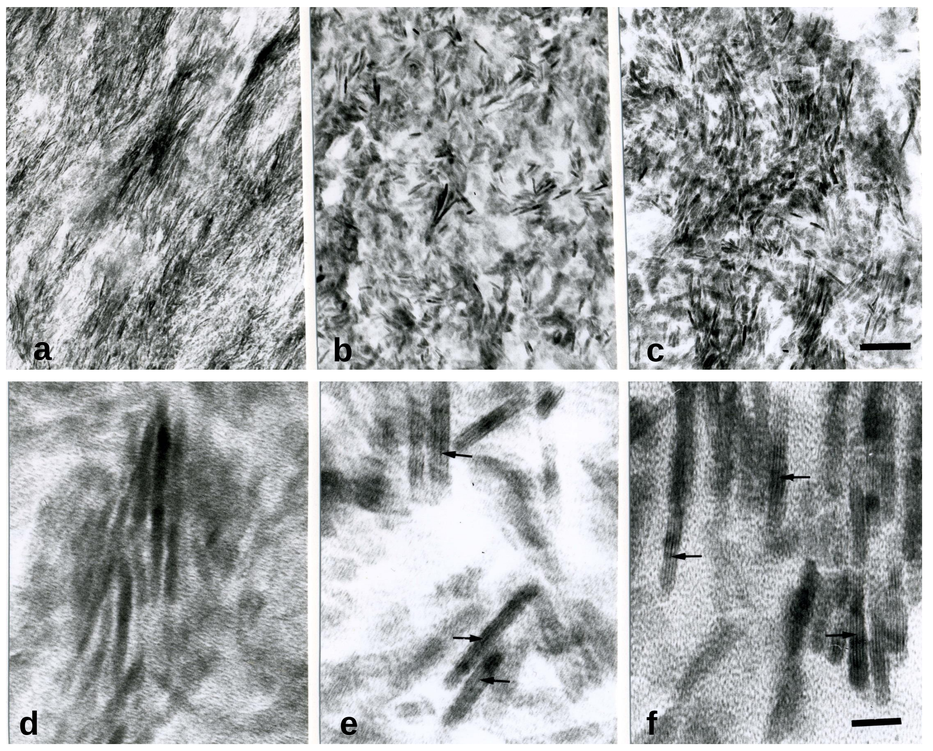

Fig. 3. Electron micrographs of minerals observed in the radiolucent (a), radiopaque areas (b), and the control (c) of the calvaria. Bar = 100 nm (a = b = c)
Needle-shaped minerals observed in the radiolucent area are amorphous.
e: Radiolucent area, e: Radiopaque area, f: Control. Bar =10 nm (d = e = f)
Crystals observed in the radiopaque area and control show lattice fringes.
Bar =10 nm, arrows are CDLs.

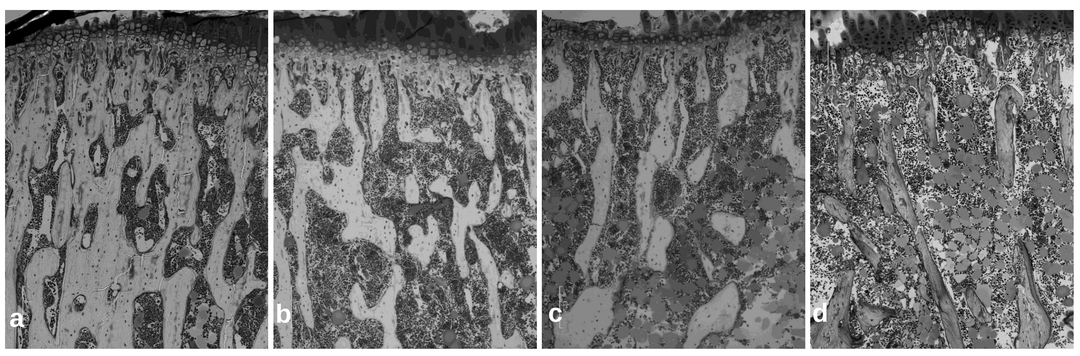

Fig. 4. Toluidine blue stained thick sections of the tibia of the control (a) and the experimental (b-d) groups. The combined effects accelerate the decline of trabecular architecture in the tibia (d). a:control, b: F 1.0 ppm exposure, c: Es deficiency, d: combined effects

Conclusions

From these findings, F exposure may accelerate the risk of developing postmenopausal osteoporosis even at a low dose of F ions.

And, it is suggested that the primary cause of osteoporosis may be resulting from a decline of the bone formation rather than excessive bone resorption.

Regarding not only the increase of bone mass without creating new trabecular but also the induction of abnormal bone mineralization caused by high dose of F treatment for osteoporosis, it is suggested that pathological calcification might occur.