

Case Report

Bone histomorphometric analysis in a patient with anorexia nervosa[☆]

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ABSTRACT

A 34-year-old Japanese woman with anorexia nervosa (AN) of a body mass index (BMI) of 11.0 kg/cm² was admitted to our hospital for assessment of renal dysfunction with a serum creatinine of 1.8 mg/dL and hypokalemia (3.0 mEq/L). Renal biopsy showed chronic interstitial fibrosis with hypertrophy of the juxtaglomerular apparatus. Iliac crest biopsy was performed because of a severe decrease in bone mineral density. It showed active resorption at the periosteal and endosteal surfaces of cortical bone by numerous osteoclasts, as well as bone island formation in cancellous bone due to marked decrease of trabecular connections. A dynamic study using double labeling showed that mineralization of cancellous bone adjacent to cortical bone occurred between the first and second labelings, but did not occur between the second labeling and osteoid formation during the 28-day period before biopsy, which implied that the mineralization was related to promotion of food intake after hospitalization, while the lack of mineralization was due to poor food intake outside hospital. Empty lacunae that indicated the death of osteocytes were seen. Because her bone mass and kidney injury improved after weight gain and normokalemia were achieved by a highly nutritious diet, malnutrition with hypokalemia may have a negative influence on bone formation due to impaired mineralization and may activate bone resorption by osteoclasts secondary to the formation of empty lacunae. This is the first report about the histological features of premenopausal osteoporosis in a patient with AN and kidney injury.

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Introduction

Anorexia nervosa (AN) is highly prevalent among women and is associated with bone loss that is multifactorial, although undernutrition and estrogen deficiency have been suggested to contribute to it [1]. Weight loss, the time since the last menstrual period, and the age at menarche have been shown to have a significant influence on bone mineral density (BMD), but estrogen use has not been shown to influence BMD [2]. This may indicate that the role of female sex hormones needs to be discussed in relation to nutrition.

Patients with AN are known to have a high prevalence of renal dysfunction and electrolyte abnormalities, such as hypokalemia, in association with use of diuretics and laxatives, vomiting, loss of intake, and hyperreninemia and hyperaldosteronism [3–5].

AN is one of the causes of premenopausal osteoporosis in women, but the bone histologic features of AN have not been evaluated, though

there have been reports that it resembles osteomalacia clinically [6,7]. Here we performed a histomorphometric analysis of bone in a 34-year-old Japanese woman with AN accompanied by severe bone loss and renal dysfunction, and evaluated development of the classical histological features of osteoporosis, including loss of trabecular bone, enlargement of the medullary spaces, cortical porosity, and reduction of cortical thickness [8].

Case report

In September 2005, a 34-year-old Japanese woman was admitted to our hospital for the evaluation of weight loss and renal dysfunction. When a nutritious diet was started because of love relations at the age of 20 years in 1990, her body weight was 43 kg, her height was 157 cm, and her body mass index (BMI) was 17.4 kg/cm² [by the formula of weight (kg) / height (m)²]. In 2000, anorexia nervosa was diagnosed according to the criteria of the International Classification of Diseases (ICD)-10 when her weight had decreased to 35 kg. Menstruation stopped in 2002. Her weight declined to 27 kg in 2005 with the onset of father's sickness and renal dysfunction became apparent. Use of diuretics or laxative abuse was not informed by hearing of her history.

On admission, the patient was 157.0 cm tall and weighed 27.0 kg, with a body mass index of 11.0 kg/cm². Her blood pressure was 80/

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48 mm Hg, her pulse rate was 96/min, and her temperature was 36.7 °C. Physical examination revealed severe malnutrition, but she had no bone pain.

Laboratory data were as follows: the white blood cell (WBC) count was 4900/ μ L, hemoglobin (Hb) was 10.0 g/dL, platelet count was 329×10^3 / μ L, total serum protein was 7.2 g/dL, and serum albumin was 3.2 g/dL. Sodium was 132 mmol/L, potassium was 3.0 mEq/L, chloride was 100 mmol/L, serum calcium was 9.2 mg/dL, phosphate was 3.8 mg/dL, pH was 7.38, $p\text{CO}_2$ was 33 Torr, $p\text{O}_2$ was 114 Torr, HCO_3^- was 19 mmol/L, base excess was -4.9 mmol/L, urea was 34 mg/dL, creatinine was 1.8 mg/dL, and uric acid was 12.3 mg/dL. In addition, total cholesterol was 170 mg/dL, triglycerides were 41 mg/dL, and glucose was 107 mg/dL. Furthermore, serum alkaline phosphatase (ALP) was 83 IU/L, parathyroid hormone (PTH) was 27.7 pg/mL, osteocalcin was 6.9 ng/mL, 1,25-dihydroxyvitamin D was 7.0 ng/mL (normal: 20 to 60), and 25-hydroxyvitamin D was 18.7 μ g/L (normal: 10 to 33). Serum renin was 87 pg/mL (normal: 10 to 20) and serum aldosterone was 136.0 ng/dL (normal: 3 to 15). Serum levels of adrenocorticotropic hormone, cortisol, and thyroid hormone were normal. Her 24-h urinary protein excretion was 0.17 g, N-acetyl- β -D-glucosaminidase (NAG) excretion was 54.0 IU (normal; less than 5.0), and β_2 -microglobulin excretion was 2828 μ g (normal; less than 400). Creatinine clearance was 36.5 mL/min and the estimated GFR was 36.5 mL/min. Urinary calcium excretion was low (55.5 mg/day). Sodium was 5.0 mmol/day, and potassium excretion was low (3.0 mmol/day). Radiographs showed severe generalized osteoporosis, but there were no pseudofractures (Fig. 1). Bone mineral

density (BMD) was measured by dual energy X-ray absorptiometry (DEXA), revealing T-scores of -4.8 SD and -2.9 SD for the lumbar spine (L2–L4) in the lateral and anterior–posterior views, respectively, as well as a T-score of -3.9 SD for the femoral neck. These findings were consistent with a diagnosis of osteoporosis (less than -2.5 SD) according to the WHO classification. After informed consent was given, renal biopsy was performed for the assessment of her kidney dysfunction, and right iliac crest bone biopsy was performed after double-tetracycline labeling (with a schedule of 3 days on-7 days off-3 days on-24 days off using doxycycline of 200 mg daily) for the examination of her bone disease. Histomorphometric analysis of bone was performed using undecalcified thin ($5 \mu\text{m}$) sections of the biopsy specimen stained by the Villanueva method. This analysis was done by Mrs. Akemi Ito of the Ito Bone Science Institute (Niigata, Japan). Sections were observed with an epifluorescence microscope under ultraviolet light at a magnification of $\times 160$, and histomorphometric parameters were measured directly by an image analysis system linked to a computer.

Renal biopsy findings

Light microscopic examination of the biopsy specimen containing 24 glomeruli revealed no evidence of global sclerosis. Glomeruli showed collapse, but immune complex deposits were not seen. There was diffuse atrophy with tubular epithelial flattening and vacuolation (cyst formation) with interstitial fibrosis (Fig. 2A), and hypertrophy of the juxtaglomerular apparatus was apparent (Fig. 2B).

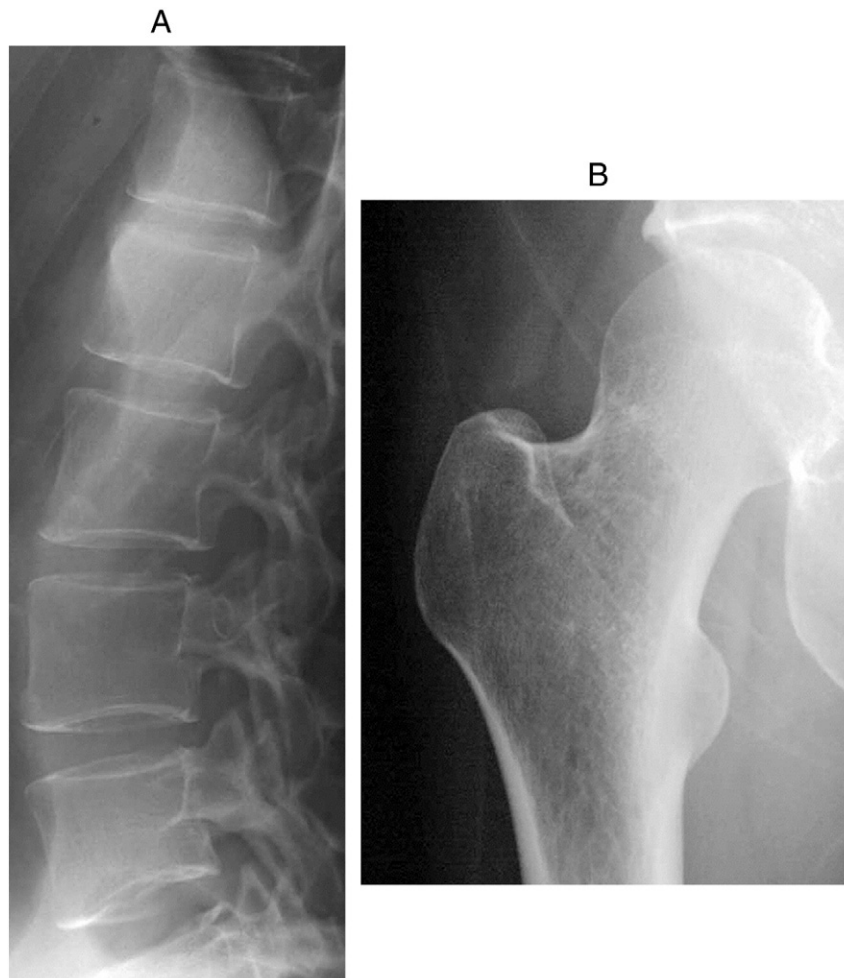


Fig. 1. Lateral radiograph of the lumbar vertebrae (A) and the right femoral neck (B) shows reduced bone density, cortical thinning and a reduced number of trabeculae.

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