Antacid-induced osteomalacia[1]

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Hypophosphatemic osteomalacia caused by antacid intake has been reported in nine cases. The authors report an additional case, which was cured by discontinuing antacids. A review of the literature is presented.

Index terms: Antacids • Osteomalacia

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Despite the widespread use of antacids, antacid-induced osteomalacia has been reported in only seven women[1–7] and two men.[8,9] This problem arises from the hypophosphatemia resulting from poor absorption of dietary phosphorus. We report an additional case in which chronic antacid therapy produced hypophosphatemic osteomalacia that was reversed after discontinuing antacids.

Case report

A 31-year-old woman was referred to our endocrinology department in July 1982 for evaluation of left lower extremity aches and weakness and suspected metabolic bone disease. For 13 years she had taken at least six tablets of Maalox TC daily (each tablet contains 600 mg of aluminum hydroxide and 300 mg of magnesium hydroxide) for acid peptic symptoms. In November 1981, muscle cramps, weakness, and pain in her left leg and ribs developed. In May 1982, she sustained an atraumatic rib fracture. The *Table* shows the results of laboratory studies. *Figure 1* is a bone scan. Hip and chest x-rays showed osteopenia. Vitamin D levels were normal. A tetracycline-labeled iliac crest bone biopsy was performed (*Fig. 2*). The results showed normal trabecular bone volume (24.0%) but a marked increase in the amount of unmineralized bone (osteoid). Osteoid was present over 60.7% of the trabecular surfaces (normal approximately 19%) and occupied 29% of the trabecular bone volume (normal approximately 2%). Mean osteoid seam width was 36 μm (normal, approximately 9.7 μm). The number of osteoclasts was not increased, and there was no peritrabecular fibrosis. These histologic features are consistent with osteomalacia. Aurine tricarboxylic acid stain for aluminum was negative. In addition, energy-dispersive x-ray analysis for aluminum as previously described[10] showed no increase in aluminum. Kidney function test results were normal.

Six months after stopping antacid intake, her bone pain diminished markedly and serum chemical values returned to normal (*Table*). In July 1984, a bone scan was completely normal.

Comments

In patients ingesting excessive oral aluminum hydroxide, a bone mineralization defect may develop because of accumulation of aluminum in bone[11,12] or because of chronic depletion of inorganic phosphorus secondary to its impaired absorption.[13] Aluminum, however, was not detected in our patient's bone biopsy specimen.

Features of the previously reported cases include normal serum calcium, increased urinary

Table. Laboratory values during antacid intake and recovery

Test	6/4/82*	11/2/82	7/84
Ca (mg/dL)	9.2	9.2	10.2
P (mg/dL)	2.4	4.2	4.4
Parathyroid hormone (pg Eq/mL)	215†	–	–
Alkaline phosphatase (pg Eq/mL)	231	57	42
Urine Ca (mg/24h)	542	43	–
Urine P (mg/24h)	1.2	221	–

* Date of initial admission to the hospital.
† Normal range = 163–347 (pg Eq/mL).

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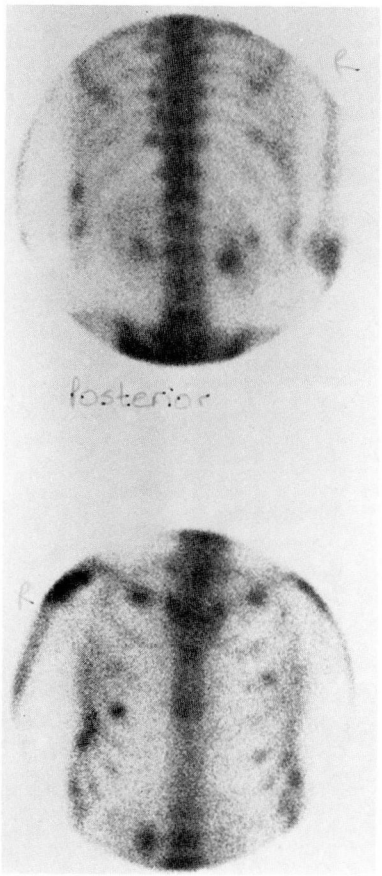

Fig. 1. Bone scan showing multiple areas of increased uptake in the ribs.

calcium, decreased serum phosphorus, and elevated alkaline phosphatase. Normal values of parathyroid hormone (PTH) were found in four of six reported cases, including our own. Similar results have been reported in normal and hypoparathyroid subjects during phosphorus depletion.[14] In patients ingesting excessive amounts of aluminum hydroxide (2.5 g daily or more), osteomalacia develops in the presence of normal serum PTH and 1,25 OH vitamin D levels.[15,16] Phosphate depletion leads to hypophosphatemia with increased intestinal absorption of calcium and increased renal excretion of calcium. Both these effects of calcium seem to be caused by changes in vitamin D metabolism.[17] Phosphate depletion causes an increase in renal 25-OH vitamin D-1 α hydroxylase that is independent of parathyroid function and an increased accumulation of 1,25 $(OH)_2$ vitamin D in intestinal target tissues. Even with high 1,25 $(OH)_2$ vitamin D, osteomalacia develops if insufficient phosphate is available in serum to support mineralization of osteoid. Withdrawing the aluminum hydroxide restores the serum phosphorus levels to normal and reverses all the skeletal manifestations of osteomalacia.

An interesting aspect of this condition is its predominance in women. Eight, including our case, of 10 reported cases were in women. This may be because phosphate losses in men are derived principally from soft tissues, whereas a significant fraction of phosphate losses in women comes from the skeleton.[17]

Since aluminum hydroxide antacids are commonly used and abused by patients, prospective studies are needed to better estimate the incidence of this serious problem.

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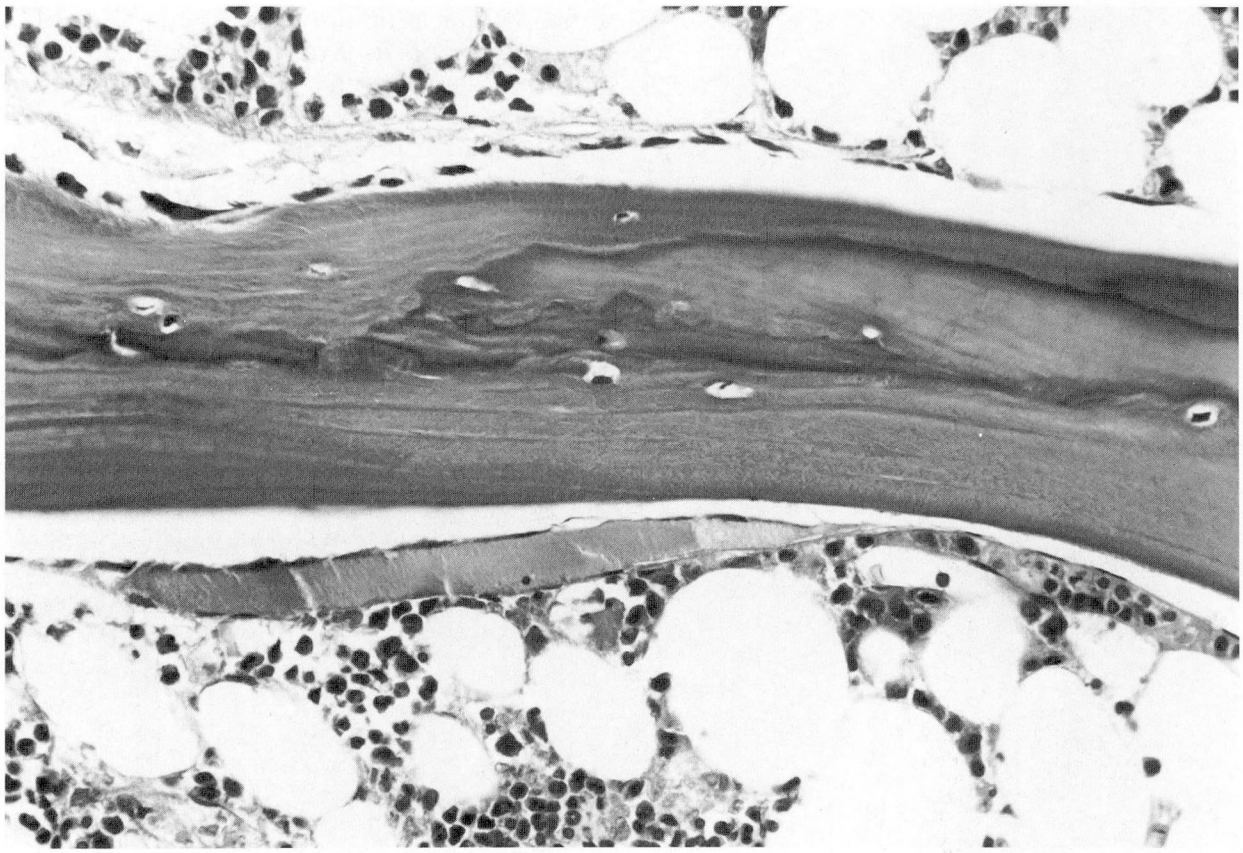

Fig. 2. Bone biopsy specimen showing osteomalacia. The histomorphometry measurements are shown in the text.

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