Bone biopsies and serum vitamin-D levels in patients with hip fracture

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To assess the correlation between osteoid and vitamin D in patients with a proximal femoral fracture, bone biopsies of the fracture site and the iliac crest were studied; and vitamin-D levels were measured in fasting blood taken on the day of admission. No osteomalacia was found at either site in any of the 95 patients investigated. In 65/95 patients, levels of 25-hydroxy-vitamin D (25-OHD) and 24, 25-dihydroxy-vitamin D (24, 25 -OH_2D) were within the normal range, whereas 30/95 patients were deficient. Because there was no correlation between the amount of osteoid and vitamin-D metabolites in our patients, we concluded that osteomalacia was not a contributory factor in the pathogenesis of the hip fracture.

It is now known 1) that vitamin-D metabolites perform specific regulatory functions in bone and bone-protein metabolism; 2) that many elderly people have impaired dermal production and/or intestinal absorption of vitamin D; and 3) that decreased conversion of vitamin D to its metabolites and thus reduction in levels of s-Ca and s-P (Exton Smith et al. 1966, Nordin et al. 1980, Finkelman and Butler 1985, MacLaughlin and Holick 1985) causes histologically demonstrable osteomalacia. This in turn has been implicated in the pathogenesis of hip fractures in 10–40 percent of patients over 65 years of age (Chalmers et al. 1967, Jenkins et al. 1973, Aaron et al. 1974, Boyce et al. 1982, Hoikka et al. 1982, Lund et al. 1982, Boyce et al. 1983). However, these histologic observations were made on iliac-crest biopsies and not on bone obtained from the femoral fracture site. In addition, there are conflicting reports concerning vitamin-D levels in patients with hip fracture; not all patients with low levels have fractures and not all patients with fractures have low levels of vitamin D (Baker et al. 1979, Nordin et al. 1980, Lips et al. 1982).

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We have addressed the following questions:

1. Do patients with a femoral hip fracture have histologic osteomalacia?

2. Is there a correlation between histologic osteomalacia and vitamin-D metabolities in peripheral blood?

Patients and methods

Totally, 136 patients admitted to our hospital for a hip fracture were operated on within 3 days. During surgery, open biopsies were taken from the fracture site and Jamshidi needle biopsies (Jamshidi and Swaim 1971) were obtained from the ipsilateral iliac crest. All the biopsies were immediately fixed, dehydrated, and embedded in methacrylate without decalcification (Frisch et al. 1985). Sections were cut at 4 μand stained with Giemsa toluidine blue and Ladewig's stain for demonstration and quantitative assessment of mineralized bone and osteoid, the latter considered specific for demonstrating osteoid.

Serum 25-hydroxy-vitamin D (25-OHD) and 24, 25-dihydroxy-vitamin D (24, 25-OH_2D) concentrations were measured in fasting blood taken on the day of admission. Totally, 97 healthy young adults (43 women and 54 men) served as the control group for the measurement of vitamin levels and the normal range in our laboratory. Briefly, levels of 25-OHD and 24, 25-OH_2D were measured by competitive protein-binding radioassay: viz., 25-OHD after preparative Sephadex

LH.20 column chromatography and 24, 25-OH_2D after successive Sephadex LH.20 and high-pressure liquid chromatography (Weisman et al. 1981).

In 25 of the 136 fracture cases, one or both of the bone biopsies were not histologically evaluable: iliac crest biopsies because they were taken tangentially and therefore contained mainly cortical bone, and femoral biopsies due to crushing artefacts. Results of the vitamin D determinations were not available for 16 cases. Therefore, these two groups were excluded. The remaining 95 patients consisted of 74 females and 21 males, with a mean age of 75 (58–89) years. There were 71 intracapsular fractures (58 females and 13 males) and 24 extracapsular (16 females and 8 males). None of the patients had fractures due to malignancy or to Paget's disease; none had chronic renal or hepatic diseases, gastric surgery, or had been taking anticonvulsant drugs or barbiturates.

This study was carried out over a period of 2 years, thereby eliminating any possible bias in results due to seasonal variations. All the bone biopsies were initially examined by two of the authors (IE and BF) without knowledge of the patients' vitamin-D status.

Results

Histology

Not a single biopsy, either of femoral neck or of iliac crest, showed trabecular osteomalacia. In all the biopsies the amounts of osteoid present—both in extent of trabecular surface covered and in osteoid seam width—were within the accepted normal values of < 25 percent and < 5 μ, respectively (Jenkins et al. 1973). In biopsies containing cortical bone, some streches of osteoid were generally present on the subcortical endosteal surface.

Vitamin-D metabolites

Sixty-five of our 95 patients had serum concentrations within the normal range: 5–50 ng/mL 25-OHD and 0.7–4 ng/mL 24, 25-OH_2D, mean 19.7 ±8.87 and 1.74 ±0.79, respectively. There was no difference between these values and those of the control group (mean 24.7 ±6.1 and 1.9 ±0.3, respectively).

Twenty-seven patients were vitamin-D deficient: 3.09 ± 2.42 ng/mL 25-OHD. Three patients had low levels of 24, 25-OH_2D; 0.38 ±0.34 ng/mL though their values of 25-OHD were within the normal range with a mean of 13.3 ±4.30 ng/mL.

Because osteomalacia was not found in any of the femoral-neck or iliac-crest biopsies, no correlation with levels of the vitamin-D metabolites could be made.

Discussion

A number of factors, singly or in combination, may contribute to low levels of vitamin D in the elderly: 1) inadequate exposure to sunlight, 2) reduced capacity of the skin to produce vitamin D, 3) reduced intestinal absorption and reabsorption of vitamin-D metabolites, 4) impaired renal and hepatic conversion of precursors to active metabolites of vitamin D, 5) dietary deficiency (Exton-Smith et al. 1966, Weisman et al. 1978, Nordin et al. 1980, Hoikka et al. 1982, Lund et al. 1982, Finkelman and Bulter 1985, MacLaughlin and Holick 1985). It is difficult to determine to what extent any or all of these factors were operative in the individual patient or in the group as a whole. However, as far as could be ascertained, our 95 patients did not suffer from dietary deficiency or lack of exposure to sunlight in contrast to patients in countries such as the U.K., in which the incidence of histologic osteomalacia is higher and has been attributed in part to insufficient sunshine (Aaron et al. 1974). Thus, there is no obvious explanation for the patients' differences in levels of vitamin-D metabolites, nor for the lack of their manifestation in the histologic bone structure. Other authors have also noted low vitamin-D levels in the elderly in the absence of known predisposing factors (Daw et al. 1979), as well as a lack of correlation between levels of vitamin-D metabolites and bone structure in fracture patients (Baker et al. 1979, Daw et al. 1979, Lips et al. 1982). It appears that osseous manifestations of vitamin-D deficiency in the elderly are different from those in younger individuals.

Osteomalacia and pathogenesis of femoral neck fractures

There is no agreement on the possible contribution of histologic osteomalacia to the pathogenesis of femoral neck fractures in the elderly. Earlier investigators found increased osteoid in 10–40 percent of their patients (Chalmers et al. 1967, Jenkins et al. 1973, Aaron et al. 1974, Boyce et al. 1982, Hoikka et al. 1982, Lund et al. 1982, Boyce et al. 1983), though more recent studies (Wilton et al. 1987) in larger series of patients documented osteomalacia in only 2 percent. Campbell (1984) calculated a prevalence of 3.7 percent in a large

population of patients over 65 years of age, none of whom had femoral neck fractures. Moreover, a disadvantage of the histologic results, cited above, is that the observations were made only on iliac-crest biopsies. Jenkins et al. (1973) took femoral biopsies in 15 of 74 patients, but these proved to be unsuitable for assessing trabecular structure.

The absence of osteomalacia in our femoral biopsies confirms and extends our previous observations on bone biopsies from this site (Frisch et al. 1982), as well as those of Hodkinson (1971) on 35 femoral heads of patients with a hip fracture. Further, the fact that osteomalacia was not found in the iliac-crest biopsies of our 95 patients corresponds well with the low incidence found by Wilton et al. (1987). Thus, it appears that osteomalacia need not be a contributory factors in the pathogenesis of hip fracture—at least not in our population at our latitude.

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