Bone Metabolism in Idiopathic Juvenile Osteoporosis: A Case Report

Richard A. Evans, Colin R. Dunstan, and Ellen Hills

Metabolic Unit, Repatriation General Hospital, Concord, New South Wales 2139, Australia

Summary. A previously healthy 12-year-old boy developed pain on walking and x-rays showed osteoporosis. Over the next 2 years deterioration occurred, the condition became extremely severe, and he was confined to a wheelchair. After 5 years, marked kyphoscoliosis and pigeon chest deformity were present and little increase in height occurred. A wheelchair accident at the age of 17 resulted in several major long bone fractures. Iliac crest biopsies were taken at ages 15 and 17, and subjected to quantitative histology. A histochemical technique for osteoclast recognition by acid phosphatase activity showed resorption parameters to be normal. Double tetracycline labeling and histochemical identification of osteoblasts showed no abnormality of endosteal bone formation. Because of coupling of endosteal formation and resorption, these measurements might primarily reflect bone turnover. Failure of periosteal bone formation as shown by failure of radial growth of long bones and of epiphyseal growth was clearly evident. It is likely that osteoporosis developed in this patient due to a reduction in bone formation of unknown etiology rather than by increased bone resorption.

Key words: Osteoporosis — Quantitative bone histology — Bone metabolism — Developmental bone disease — Growth disorder.

Bone Metabolism in Idiopathic Juvenile Osteoporosis is a rare condition, with less than 45 patients having been reported [1]. The typical pattern, as described by Dent [2] and his colleagues, is the development, in a previously normal subject, of osteoporosis with bone pain shortly before puberty, failure to respond to therapy, and usually spontaneous improvement 2–4 years later. In this form it differs from classic osteogenesis imperfecta, which frequently has a familial history, is associated with blue sclerae, is present from birth, and does not improve [3]. The patterns are, however, not always typical in that idiopathic juvenile osteoporosis can present in younger patients [4], and osteogenesis imperfecta can present with white sclerae and no family history [3].

Quantitative histological studies of idiopathic juvenile osteoporosis are few [1, 5]. One study of 7 patients employed microradiography [5] and found a large resorbing surface. The abnormality was therefore considered to be increased bone resorption. Another study of 4 patients [1] found a normal osteoclast count but increased crenated surface and reduced osteoblast surface. In those patients the abnormality was considered to be reduced formation. Neither study employed tetracycline labeling or specific staining methods for identification of osteoclasts and osteoblasts.

In this report we describe a youth with severe idiopathic juvenile osteoporosis in whom quantitative bone histology was carried out at two widely separated intervals.

Case Report

At age 12½ years a previously healthy youth, active in contact sports such as football, developed foot pain on walking. This gradually increased in severity over succeeding months and he became unable to walk. One year after the onset of symptoms idiopathic juvenile osteoporosis was diagnosed, and he received three courses of intravenous infusions of calcium gluconate [6], each consisting of 10 g of elemental calcium. Clinical and radiologic deterioration occurred during this period, the x-ray pattern changing from cortical striation to gross cortical thinning. Puberty occurred at age 13 years.

He was first seen at the Metabolic Unit 2 years after the onset of symptoms. He was confined to a wheelchair but was cheerful and intelligent. The sclerae were white. He had a mild pigeon-chest deformity and kyphoscoliosis. The crown-pubis length was 68 cm, pubis-heel 80 cm, and span 162 cm, suggesting an upper segment loss (or failure of growth) of at least 12 cm. There were no other abnormalities on physical examination, and primary and secondary sexual characteristics were normal. Plasma calcium...
was 2.50 mmol/l (normal, 2.20–2.65), inorganic phosphorus 1.61 mmol/l (normal for this age, 0.60–1.65), and alkaline phos- 
phatase 178 IU/l (normal for this age, 30–300). Parathyroid hor- 
mone was not detectable in the serum, and 24-h urinary calcium 
was 2.25 mmol. X-rays showed thin cortices, biconcave verte-
brae (Fig. 1), and a triradiate pelvis. It was initially intended to 
not attempt treatment, and to await the usual spontaneous im-
provement. However, during normal activities over subsequent 
months he had several episodes of pain in hands, spine, or ster-
num, which resulted in repeated hospital admissions.

An iliac crest wedge bone biopsy was taken, and he was begun 
on a regimen of oral calcium 1 g twice daily alternating at 3-h 
intervals with phosphate Sandoz 1 g daily, methyclothiazide 5 
mg/day, and dihydrotachysterol 0.25 mg/day. With this therapy 
plasma biochemistry was unchanged, urinary calcium was 1.50 
mmol/24 h, and phosphorus 34.6 mmol/24 h. There was no im-
provement in pain, and his height increased only 2 cm from when 
he was first seen at the age of nearly 15 years until his epiphyses 
fused 2½ years later; of this 1 cm was lower limb growth. X-rays 
showed, in addition to bone deformity, a failure of radial growth 
of the diaphyses of long bones (Fig. 2). The osteoporosis was 
most marked in the metaphyses, a phenomenon described by 

Five years after the onset of the illness, he fell from his wheel-
chair to the ground and fractured his left femur, left tibia, and 
right tibia and fibula. In the ensuing week, despite cessation of 
oral therapy, his plasma calcium rose to 2.81 mmol/l and 24-h 
urinary calcium to 7.01 mmol; these returned to normal spon-
aneously after 3 weeks. The fractures healed normally. He re-
ceived no therapy for the 6 months following this injury, and, 
becoming depressed by his pain and deformity, he unsuccess-
fully attempted suicide with barbiturates. He then agreed to try 
the alternating intravenous calcium and phosphorus infusions, 
which have been reported as effective therapy for osteoporosis 
[7]. A supraclavicular vein cannula required surgical insertion 
because of the thoracic deformities, and during the period of 
anesthesia a transileal bone biopsy was taken. The central can-
nula did not function satisfactorily, so peripheral veins were 
used. However, the solutions produced painful thrombophlebitis 
and were discontinued.

Six years after the beginning of symptoms there has been no 
detectable improvement in the osteoporosis, and he remains 
short, deformed, confined to a wheelchair, and in constant pain.

**Bone Biopsy**

Two tetracycline markers were given prior to each biopsy. The 
first biopsy was a large wedge, the second a 7-mm diameter core. 
They were fixed in formalin, dehydrated in ethanol, and embed-
ed in a methylmethacrylate-hydroxyethylmethacrylate mixture 
suitable for histochemistry [8]. Quantitation was performed by 
superimposing 3 adjacent sections: a 7 μm unstained section for 
tetracycline fluorescence, a 5 μm section stained for acid phos-
phatase activity to demonstrate osteoclasts [8], and a 5 μm sec-
tion stained with pyronin to identify osteoblasts. The sections 
were traced by means of a camera lucida attachment to the mi-
roscope and the tracings quantitated using an electronic digi-
tizer interfaced to a desk-top computer.

Because living rather than cadaver bone is required for this 
technique, the controls were adults [9]. They were 6 healthy 
hospital employees, 5 men and 1 woman, aged from 23 to 43 
years.

Additional parameters measured in the biopsies of the patient 
and the controls for this study were mean trabecular thickness,