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Original Article

The Radiology of Vertebral Fractures in Childhood Osteoporosis Related to Glucocorticoid Administration

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Abstract

A number of unusual conditions cause decreased bone mass and density in children and these may be associated with low-trauma fractures. However, a series of reports have more recently identified that children with chronic disease sustain vertebral fractures (VFs) much more often than had been suspected. The common denominator involved is glucocorticoid (GC) administration, although other factors such as disease activity come into play. This review will focus on the imaging findings in this form of secondary osteoporosis. Spinal fractures in children have been found to correlate with back pain. At the same time, up to 2/3 of children with VFs in the GC-treated setting are asymptomatic, underscoring the importance of routine surveillance in at-risk children. Other predictors of prevalent and incident VFs include GC exposure (average daily and cumulative dose), declines in lumbar spine bone mineral density Z-scores and increases in body mass index Z-scores, as well as increases in disease activity scores. The imaging diagnosis of osteoporotic VFs in children is made differently from that in adults because immature vertebral bodies continue to ossify during growth. Thus, it is not possible to assess the vertebral end plates or periphery until late, as enchondral ossification extends centripetally within the centrum. Diagnosis, therefore, is much more dependent upon changes in shape than on loss of structural integrity, which may have a more prominent diagnostic role in adults. However, children have a unique ability to model (a growth-dependent process) and thereby reshape previously fractured vertebral bodies. If the underlying disease is successfully treated and the child has sufficient residual growth potential, this means that, on one hand, treatment of the bone disease may be of more limited duration, and, as a last recourse, the diagnosis may be apparent retrospectively.

Key Words: Children; glucocorticoids; osteoporosis; vertebral fracture reshaping; vertebral fractures.

Introduction

There are a number of causes of low bone mineral density (BMD) in children and adolescents that have the potential to result in low-trauma fractures (Table 1) *(1)*. Recently it has become increasingly apparent that childhood osteoporotic spinal fractures are common in chronic disease. Implicated in particular have been leukemia *(2–4)*, rheumatological disease *(5,6)*, nephrotic syndrome *(7,8)*,

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Table 1
Some Disorders, Medications, and Behaviors That May Cause Secondary Osteoporosis or Reduced Bone Mass in Childhood and Adolescence (After Reference *1*)

Primary disorders	Medications	Behaviors
• Idiopathic osteoporosis • Juvenile rheumatoid arthritis • Diabetes • Osteogenesis imperfecta • Hyperthyroidism • Hyperparathyroidism • Cushing's syndrome • Malabsorption syndromes (e.g., coeliac disease) • Anorexia nervosa • Kidney disease	• Anticonvulsants • Glucocorticoids • Immunosuppressive agents (e.g., for cancer)	• Prolonged inactivity or immobility • Inadequate nutrition (especially lack of calcium and vitamin D) • Compulsive exercise leading to amenorrhea

and Duchenne-type muscular dystrophy *(9)*. The common denominator involved in causing osteoporosis and fracturing is glucocorticoid (GC) administration, although other factors may well come into play. We here describe this form of secondary osteoporosis to illustrate some of the distinctive characteristics of vertebral fractures (VFs) in children. Our goal here is to highlight fracture patterns in children treated with protracted GCs. We use data, principally from a cohort of GC-treated children with leukemia, and combine these with a literature review to illustrate fracture patterns and how these differ from those in adults.

Patients and Methods

The patients we describe were enrolled into a multicenter Canadian study under the umbrella of the Steroid-Associated Osteoporosis in a Pediatric Population consortium administered at the Children's Hospital of Eastern Ontario, wherein one of us (LW) is the principal investigator *(3–8)*. Patients from 11 children's hospitals across Canada were enrolled with the particular entry criterion being the treatment of leukemia, rheumatological disease, and nephrotic syndrome with medication, including GCs, in each case.

Conforming to the *image gently* paradigm by which to minimize radiation exposure of children, radiographs were generally intended to be limited to lateral images of the spine from T4 to L4 inclusively *(10)*.

All the studies were approved by the ethics board in each institution and informed consent/assent was obtained, as appropriate.

Fracture Diagnosis

The diagnosis of fractures by imaging in children is different from that in adults *(11,12)* because immature vertebral bodies are not completely ossified until after growth ceases. Thus, it is not possible to assess the vertebral end plates until late in this process as enchondral ossification extends centripetally within the centrum from a primary ossification center and concludes locally with fusion of the "ring" apophysis to complete formation of the end plate. Fracture diagnosis, therefore, is much more dependent upon changes in shape than on loss of structural integrity with or without changes in shape *(3,5–7,9,10)*. This situation may differ from that in adults *(11)*. However, the unique ability of vertebral bodies of children to reshape themselves, if the underlying disease is successfully treated, means that (1) the observation of postfracture modeling on follow-up provides validation of the fracture, which is often lacking in the various diagnostic strategies proposed for use in adults *(12)*; and (2) as a last recourse, the radiological diagnosis of fracturing may be apparent retrospectively.

We have, therefore, adopted the Genant method for classifying VFs *(11)* as it has been widely used in osteoporosis. Moreover, it is subject to good interobserver performance comparable to that seen in a similar context in adults *(13,14)*. All of the radiographs were scored by 2 radiologists (MAM and NS) with discrepancies resolved by referral to a third (BL).

To quote 1 particular context, children with acute lymphatic leukemia (ALL) were enrolled in a prospective, observational study through a national bone health research program during the first 12 mo of chemotherapy *(3)*. VF assessment was carried out by the Genant semiquantitative method on lateral thoracolumbar spine radiographs around the time of diagnosis and at 12 mo, with the sum of the Genant grades from T4 to L4 in each patient expressed as the Spinal Deformity Index (SDI) at both time points. Clinical features including VF at diagnosis, lumbar spine areal BMD Z-score, back pain, and cumulative GC and methotrexate doses were analyzed for association with incident vertebral fracture (IVF) as were calcium intake and serum vitamin D concentrations.