

Approach to the Child with Fractures

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- Recognize the numerous primary and secondary causes of childhood osteoporosis
- Perform a complete evaluation of a child with fractures, including the importance of a thorough history and physical exam
- Consider confounding variables in the interpretation of DXA scans in pediatric patients, including body size, bone age and pubertal status
- Select the most appropriate pharmacologic and non-pharmacologic therapies for the management of low bone density in children

Target Audience

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Activity release date: July 2011

Activity expiration date: July 2012

Evaluation of the child with fractures is challenging, as no clear guidelines exist to distinguish traumatic from pathological fractures. Although most fractures in childhood are benign, recurrent fractures may be associated with a wide variety of primary skeletal diseases as well as secondary causes, necessitating a careful history and physical exam to guide the evaluation. There is no "gold standard" for the evaluation and treatment of children with fractures and low bone mineral density (BMD); therefore, the diagnosis of osteoporosis in a pediatric patient should be made using a combination of clinical and radiographic features. Interpretation of bone densitometry in growing patients presents a unique set of challenges because areal BMD measured by dual-energy x-ray absorptiometry depends on multiple dynamic variables. Interpretation of pediatric dual-energy x-ray absorptiometry should be based on Z-scores (SD scores compared to age, sex, and ethnicity-matched controls), using normative databases specific to the brand of densitometer and the patient population. Given the skeleton's ability to recover from low BMD through modeling and remodeling, optimizing management of underlying conditions leading to bone fragility is the initial step. Conservative measures including calcium and vitamin D supplementation and weight-bearing physical activity are important interventions that should not be overlooked. The use of bisphosphonates in children and adolescents is controversial due to lack of long-term efficacy and safety data and should be limited to clinical trials and compassionate therapy in children with significantly compromised quality of life. Close monitoring is required, and further study is necessary to assess their long-term safety and efficacy in children. (*J Clin Endocrinol Metab* 96: 1943–1952, 2011)

Case

A 12-yr-old girl presents with a history of multiple vertebral compression fractures. At age 10, she fractured T6 while riding a roller coaster. She was evaluated by an orthopedist who instructed her to resume her regular activities, including lacrosse and basketball. At age 10 $\frac{3}{4}$, she fractured T3 playing sports, and at age 11 $\frac{1}{2}$, she fractured T5 playing laser tag. Two additional thoracic vertebral fractures soon followed. She was seen by a hematologist who performed a bone marrow biopsy of T6, which was normal. She is an otherwise healthy girl, previously very athletic, with normal puberty. Her only complaint is back pain, treated

Abbreviations: BMD, Bone mineral density; DXA, dual-energy x-ray absorptiometry; IJO, idiopathic juvenile osteoporosis; LRP5, low-density lipoprotein receptor-related protein 5; OI, osteogenesis imperfecta; QCT, quantitative computed tomography.

mineral density (BMD) in children with fractures. Although standards for diagnosis and treatment of osteoporosis exist in adults, differences in the etiology and clinical significance of bone fragility in children make extrapolation of adult data inappropriate. Lack of data in children and adolescents has prevented the development of a “gold-standard” when approaching the child with fractures.

Fractures in Childhood

Fractures are common in the pediatric population, with an incidence of approximately 50% in boys and 40% in girls (1–3). Fracture rate appears to be increasing over time (1–5), particularly at the distal radius, which remains the most common site of fracture in children and adolescents. Fracture rate peaks between ages 11 and 15 yr (2, 4–7), corresponding to the period of maximum postnatal growth velocity. There is relative undermineralization of the adolescent skeleton, due to a delay of approximately 8 months between the period of peak growth velocity and peak bone mineral accrual (8, 9). This leads to transient cortical weakness, particularly of the distal radius in adolescent boys (10), which may contribute to the increased incidence of metaphyseal forearm fractures. Increased participation in competitive youth sports has also led to a concurrent rise in pediatric overuse injuries, such as stress fractures (11).

Distinguishing a traumatic from pathological fracture is often difficult because the literature has not clearly defined what constitutes a fragility fracture. Vertebral compression fractures and femur fractures in the absence of a significant trauma, such as a motor vehicle accident or fall from a great height, are rare in childhood and should be considered pathological fractures. In some cases a child may present with a more minor fracture and no reported history of trauma. In such situations, it can be difficult to determine whether this is a true atraumatic fracture or a case of an inaccurate history. Parents may report a history of multiple fractures treated with short-term immobilization; however, review of the radiographs may reveal that some of these injuries were sprains treated with splinting. One must always consider the possibility of physical abuse in a child who presents with repeated injuries, fractures in infants, and fractures that appear inconsistent with the reported history.

Differential Diagnosis

The list of conditions associated with an increased risk of fragility fractures in childhood is long (Table 1). However, many of these conditions are quickly diagnosed or ex-

TABLE 1. Disorders associated with fragility fractures in children (not all-inclusive)

Primary conditions
Genetic disorders (selected)
Osteogenesis imperfecta
Osteoporosis pseudoglioma syndrome
Ehlers-Danlos syndrome
Marfan syndrome
Homocystinuria
Hajdu-Cheney Syndrome
Pycnodysostosis
Osteopetrosis
Hypophosphatasia
Polyostotic fibrous dysplasia
Rickets (genetic forms)
Idiopathic juvenile osteoporosis
Secondary conditions
Chronic inflammatory conditions
Systemic lupus erythematosus
Inflammatory bowel disease
Nephrotic syndrome
Reduced mobility
Cerebral palsy
Duchenne muscular dystrophy
Posttraumatic
Infiltrative
Leukemia
Thalassemia
Mastocytosis
Endocrine
Hypogonadism
GH deficiency
Cushing syndrome
Hyperthyroidism
Diabetes mellitus
Female athlete triad
Nutritional/malabsorptive
Vitamin D deficiency
Celiac disease
Biliary atresia
Cystic fibrosis
Anorexia nervosa
Renal
Chronic kidney disease
Secondary hyperparathyroidism
Iatrogenic
Glucocorticoids
Anticonvulsants
Methotrexate
Radiation therapy
Antiretrovirals

cluded with a thorough history and physical exam along with selected diagnostic tests. Primary bone disorders leading to juvenile osteoporosis are relatively rare (Table 1). The most common cause of primary osteoporosis is osteogenesis imperfecta (OI), a syndrome of increased bone fragility due to defects in the quality or quantity of collagen I. There are several subtypes, ranging from mild to perinatal lethal. Type I OI is the most common and mildest form, typically presenting in early adolescence with clinical improvement after puberty. On examination, these children are often of normal stature before fracture and may have blue-tinted sclerae, dental involvement (dentinogenesis imperfecta), and an affected parent; hearing loss develops in approximately 50% of affected indi-

viduals by adulthood (12). Genetic testing for abnormalities in the genes encoding collagen I (COL1A1/COL1A2) is commercially available and identifies over 90% of patients with OI (13). Analysis of type I collagen synthesized *in vitro* by culturing dermal fibroblasts from skin biopsy has an estimated sensitivity of 87% in nonlethal OI and 98% in the lethal form (14). Because negative testing cannot definitively exclude OI, practitioners must rely on clinical characteristics to determine diagnosis and treatment. In patients with negative genetic testing, normal sclerae and hearing, and absent family history, one must consider idiopathic juvenile osteoporosis (IJO), a rare condition characterized by multiple fragility fractures, which also typically arises in the school-age child and spontaneously remits after puberty. Similar to type I OI, the overall prognosis for IJO is favorable, although some patients with severe disease may have permanent disabling deformities of the spine and long bones (15). The diagnosis of IJO can be made only after likely secondary causes have been excluded. Primary juvenile osteoporosis can also be seen in connective tissue disorders and other rare genetic conditions associated with intrinsic skeletal defects, including the osteoporosis pseudoglioma syndrome, an autosomal recessive disorder due to inactivating mutations in low-density lipoprotein receptor-related protein 5 (LRP5). This diagnosis should be considered in any patient with visual impairment. Heterozygous mutations in LRP5 have also been reported in autosomal dominant forms of juvenile osteoporosis (16). Fragility fractures can also occur despite high BMD in sclerosing bone disorders due to impaired osteoclast function, such as pycnodysostosis and osteopetrosis.

Secondary osteoporosis is observed as a complication of many chronic conditions, particularly those associated with inflammatory disease, malabsorption, endocrine/metabolic disturbances, decreased mobility or prolonged glucocorticoid therapy (Table 1). In these conditions, low BMD may be a sequela of the primary disorder, a complication of treatment, or a combination. Vitamin D deficiency and decreased dietary calcium intake can contribute to low BMD, in addition to causing rickets. Decreased BMD has also been reported in children with idiopathic hypercalciuria (17).

Evaluation

Bone densitometry

Any child with a history of fragility fractures should be assessed with bone densitometry. A significant family history of recurrent fractures is suggestive of an underlying inherited condition, and in these cases it is often helpful to

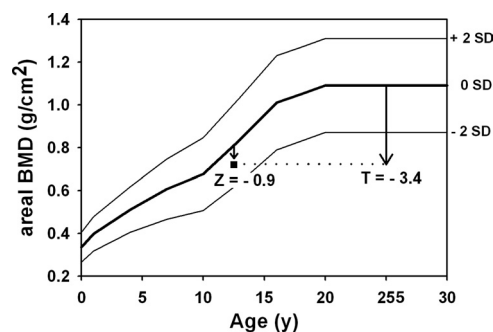


FIG. 2. BMD Z-score and T-score for a 12-yr-old child (23). The curves demarcate the normal (mean \pm 2 SD) areal BMD of the lumbar spine, which depends on skeletal size and thus increases with age. The square symbol represents a patient who received an erroneous diagnosis of osteoporosis based on a low T-score. The Z-score of this patient is well within the normal range for age.

study first-degree family members. An expert panel has recently recommended densitometry for children with a history of clinically significant fractures, defined as a long bone fracture of the lower extremities, a vertebral compression fracture, or two or more long-bone fractures of the upper extremities (18). The decision to screen becomes less clear when evaluating children with multiple trauma-related fractures. For most patients, assessment is made on an individual basis, taking into consideration severity and number of fractures, along with other risk factors.

Multiple methods are available for assessing bone density including DXA, quantitative computed tomography (QCT), and quantitative ultrasound. Plain radiographs are not recommended for quantification of BMD but are useful for identifying fractures, deformity, skeletal dysplasias, rickets, and sclerosing bone disorders. DXA is currently the preferred method, given its wide availability, rapid scanning time, and low radiation. The sites typically studied are the postero-anterior lumbar spine, proximal femur, distal radius, and total body. The postero-anterior spine and TBLH (total body without the head) for evaluation and monitoring because they are the most reproducible and accurate sites measured by DXA (19, 20). In children with impaired mobility, scans of the distal femur may be more informative (21). A comprehensive pediatric reference database for Hologic densitometers is available (22); it is important that only normative databases specific to the brand of densitometer be used for interpretation. Z-scores should be calculated as SD scores compared with age-, sex-, and ethnicity-matched controls. The diagnosis of low BMD in a child should never be made on the basis of T-score (SD score compared with young adults at peak bone mass) (Fig. 2). This error has led to the overdiagnosis of low BMD in children (23).

DXA is a two-dimensional technology measuring areal BMD, calculated as the bone mineral content divided by the area of interest, reported in grams per square centi-

meter. The inability of DXA to measure the true three-dimensional volume of the bone has important implications because areal BMD will be decreased in smaller bones and increased in larger bones. A patient with short stature may therefore have abnormally low areal BMD compared with the average population despite normal true volumetric BMD (24). There are several methods that may be applied to correct areal BMD for body size, using mathematical models (25, 26) and adjusting TBLH or body composition (27). Interpretation of DXA scans should include consideration of not only height but also bone age and pubertal status. Lean body mass has been shown to correlate with BMD (28–30), which may have particular significance in patients with complications of chronic disease leading to relative sarcopenia. Methods have been developed to estimate the effects of lean body mass on BMD (29, 30); however, these adjustments may be problematic in children with fluctuating body composition, acute exacerbations of underlying disease, and/or their treatment. In addition, local structural changes such as vertebral fractures, osteophytes, and arterial calcifications can lead to spuriously elevated BMD measurements (31).

Quantitative ultrasound can be used to assess BMD; however, diagnostic significance has not been well-established, and it is not recommended. QCT of the spine has the advantage over DXA in that it can distinguish between trabecular and cortical bone and can determine true three-dimensional volumetric BMD (32). Unfortunately, expense, availability, and high radiation exposure makes axial QCT impractical for routine clinical use. QCT can be performed on the peripheral skeleton using much less radiation; however, this technique is confounded by the continually changing size and shape of the growing skeleton (33). There are multiple emerging modalities, used primarily in research, such as high-resolution peripheral QCT, high-resolution magnetic resonance imaging, and micro-computed tomography, which surmount many of the limitations of DXA and have the potential for future clinical use.

The clinical definition of osteoporosis includes low BMD, increased bone fragility with associated changes in bony microarchitecture, and an increased risk of fracture (34). There is evidence in adults that low BMD is predictive of increased fracture risk, and a BMD T-score less than -2.5 SD is suggestive of osteoporosis in adults (35). The clinical relevance of low BMD in children has not been well-established, although there are retrospective data that suggest an increased fracture risk when the Z-score is less than -2 (36) and one prospective study reporting an 89% increase in fracture risk for every SD decrease in size-adjusted BMD (27). However, spine BMD by DXA may

overlook clinically apparent osteoporosis, as was recently described in a child with multiple thoracic compression fractures despite a normal lumbar spine Z-score (37). Concurrent vertebral fracture assessment done by DXA has lower radiation than plain radiographs and is useful in adults; unfortunately, the current software is inadequate for pediatric use (38). The diagnosis and management of osteoporosis in the pediatric patient must therefore be based on a combination of clinical and radiographic findings, rather than relying upon bone densitometry alone. The International Society for Clinical Densitometry recently updated its official position on DXA evaluation in children and adolescents, recommending that the “diagnosis of osteoporosis requires the presence of both a clinically significant fracture history and low bone mineral content or bone mineral density” (20, 39).

Conventional densitometry methods provide information about bone mass. However, bone strength is dependent not only on bone mass and density but also the structural properties that resist bending and fracture. Mathematical models exist that use DXA and QCT to estimate measurements of bone strength (40, 41). Further research into this area may yield applications in the clinical setting.

Identification of underlying etiology

Given the extensive list of possible causes for fracture with low bone density, testing must be guided by the history and physical exam. At a minimum, we recommend evaluation of routine hematologic and biochemical indices, erythrocyte sedimentation rate, intact PTH, serum calcium and phosphorus, urinary calcium excretion, and screening for celiac disease. Patients should be screened for vitamin D deficiency using a serum 25-hydroxyvitamin D level. Bone marrow aspirates, endoscopy/colonoscopy, liver biopsy, and genetic tests may be performed where indicated but are not done routinely in an otherwise healthy, asymptomatic child. Given the clinical similarities between type I OI and IJO, we recommend genetic testing of COL1A1/COL1A2 for all children before assigning a diagnosis of IJO. In IJO, additional search for mutations in genes related to osteoblast and osteoclast recruitment and differentiation, as well as mutations in LRP5 may lead to a better understanding of the genetic determinants of bone density. Finally, measurement of bone turnover markers such as bone-specific alkaline phosphatase, osteocalcin, collagen cross-linked N-telopeptide, *etc.*, may suggest a “low-turnover” or “high-turnover” state that can help guide therapy. Results must be interpreted with caution because these markers vary relative to age and skeletal maturation, and pediatric nor-

mative data are limited (42). Additionally, elevated markers in the setting of acute fracture may be misleading.

Bone biopsy

When a diagnosis is unclear, the definitive method for assessment of bone density, turnover, and microarchitecture is the bicortical transiliac bone biopsy. Administration of tetracycline before biopsy, which is incorporated into areas of active bone turnover, allows for measurement of dynamic indices such as bone formation rate and mineral apposition rate. This procedure is particularly helpful for distinguishing low-turnover from high-turnover osteoporosis and identifying osteomalacia. Thus, this procedure is most often considered in a child with severe osteoporosis of unknown etiology because it may provide diagnostic clues and direct therapeutic intervention. For example, a biopsy demonstrating a paucity of osteoclasts suggests that bisphosphonate therapy may be ineffective. However, given its invasiveness, bone biopsy is rarely performed in children.

Treatment

The first step is to identify and treat underlying causes of low BMD and use bone-sparing therapies whenever possible. Studies in juvenile animals and children have demonstrated that decreased BMD during childhood is largely reversible with remission or optimized management of the underlying disease process (43–45).

In healthy children with multiple traumatic fractures and normal densitometry, observation is usually the best course, with repeat densitometry performed on an as-needed basis. Adequate rest and rehabilitation are essential in patients with stress fractures to prevent recurrence and complications (46). Ensuring adequate calcium intake and vitamin D stores is important for all patients, recognizing that the recommended daily intakes may not be sufficient for patients with primary bone disorders, malabsorption, or other chronic conditions. The Institute of Medicine recently released recommendations stating that serum 25-hydroxyvitamin D levels should be maintained above 20 ng/ml (50 nmol/liter) to optimize bone health (47). Weight-bearing physical activity is critical for bone health, and children with reduced mobility have been shown to gain bone mass with physical therapy (48) and standing on vibrating platforms (49). It is important to counsel the family and the school regarding activities that may predispose a child with osteoporosis to further fractures. Typical restrictions include the avoidance of jarring activities (*e.g.* horseback riding, roller coasters), contact sports, forward flexion exercises, and heavy backpacks.

Children often require a separate set of schoolbooks at home to avoid excessive carrying.

In addition to calcium and vitamin D, there are several Food and Drug Administration (FDA)-approved therapies to treat osteoporosis in adults but no FDA-approved therapies for children. Calcitonin has not demonstrated significant decreases in adult fractures and is rarely used. Teriparatide (PTH 1–34) is a very effective anabolic agent; however, its black box warning regarding the risk of osteosarcoma precludes its use in children except in perhaps extreme circumstances. Denosumab, a recently approved RANKL (receptor activator of nuclear factor- κ B ligand inhibitor), is a potent antiresorptive agent; pediatric trials have yet to be conducted. Bisphosphonates are approved for adults with osteoporosis, Paget's disease, and hypercalcemia. They are not indicated in sclerosing bone diseases (*e.g.* osteopetrosis) or primary mineralization disorders (*e.g.* hypophosphatasia or rickets). Although there are numerous publications reporting bisphosphonate use in pediatric populations, few have adequate controls or long-term safety data. The greatest experience comes from use in patients with OI, where bisphosphonates have been found to improve BMD, reduce functional impairment, and relieve pain (50–52). Bisphosphonates are now widely used for treatment of this disorder, although uncertainty remains regarding appropriate regimen, method, and dose. Bisphosphonates also may be effective in other forms of primary osteoporosis including IJO (53) and the osteoporosis pseudoglioma syndrome (54), although definitive recommendations cannot be made due to the lack of controlled data (55).

The use of bisphosphonates for treatment of secondary osteoporosis in children is also unclear. Gains in BMD have been demonstrated in several pediatric populations, including children with cerebral palsy (56), postrenal transplant (57), and rheumatologic conditions (58). A recent Cochrane review examining bisphosphonate use in children with secondary osteoporosis concluded that data are not currently sufficient to support use of bisphosphonates as standard therapy (59). Short-term data over a 3-yr period found the medications to be well-tolerated, and preliminary positive effects on BMD and pain were sufficient to justify compassionate use for patients with significantly impacted quality of life.

Pediatric dosing of bisphosphonates has not been established, as evidenced by the wide variability of dosing regimens of the published studies (60). Practitioners may be inclined to treat all causes of juvenile osteoporosis with the OI pamidronate protocols of 0.5–1 mg/kg dose on 3 consecutive days every 2–4 months. However, small studies suggest that improvements in BMD can be achieved with a single infusion every 3–6 months (61–63). Newer

bisphosphonates have been approved for use in postmenopausal osteoporosis as an iv push given every 3 months (ibandronate) and a once-yearly infusion (zoledronate). Although administration of these drugs is much easier than pamidronate and could be considered for older adolescents, there are no pediatric data supporting efficacy and safety of these regimens. For oral agents, there is even less consensus as to the correct dose; some studies use an individualized milligrams per kilogram dose, whereas others use a weight cutoff to divide subjects into two dosing groups (60). Whatever dose is ultimately chosen, monitoring for efficacy and side effects is important.

Side Effects and Monitoring of Bisphosphonates

Bisphosphonates act through inhibition of osteoclastic bone resorption, placing patients at risk for hypocalcemia. Vitamin D stores must be adequate before initiating treatment, and calcium and vitamin D intake should be optimized for the duration of therapy. Many children experience an acute phase reaction with the initial dose of oral or iv bisphosphonate, which can include fever, malaise, diarrhea, nausea, and bone or muscle pain. Symptoms typically begin within the first 24 h of treatment and last 1–3 d. Starting with a lower initial dose and premedicating with nonsteroidal antiinflammatory medications can potentially decrease the severity of these symptoms.

In adults, bisphosphonates have been associated, often without direct evidence of causality, with a number of side effects including musculoskeletal pain, irritant esophagitis and esophageal cancer, atrial fibrillation, and iritis (64). Given the risk of gastrointestinal ulcerations associated with the oral forms, administration instructions should be reviewed at every visit, and the patients should be questioned for any gastrointestinal complaints. We do not recommend the use of oral bisphosphonates in patients with gastroesophageal disease, significant neuromuscular disease, or impaired cognition because they may be unable to report epigastric pain. Osteonecrosis of the jaw has been linked to use of bisphosphonates; however, this complication is typically seen in the setting of multiple high-dose iv infusions in adult cancer patients, and there have been no reported cases in children or adolescents (65). Nonetheless, we recommend a full dental exam and the completion of any required dental work before initiating treatment, along with maintenance of good oral hygiene. Bisphosphonates may negatively affect orthodontic treatment in adults (66); the effects in children are unknown.

Bisphosphonates have a long skeletal half-life and can be detected in the urine of children years after discontin-

uation (67), raising concerns surrounding release from bone during pregnancy. Bisphosphonates cross the placenta easily, and administration of high doses in pregnant rats was found to be associated with fetal skeletal anomalies (68). A recent prospective study of 21 women exposed to bisphosphonates during or within the first 3 months before pregnancy found no difference in major birth defects compared with controls (69). Although preliminary data in humans are encouraging, families must be informed that the risk to the fetus is unknown. Practitioners should screen for pregnancy before initiating therapy and should counsel sexually active girls on effective birth control for the duration of treatment.

Long-term suppression of bone modeling and remodeling may have important repercussions in a growing skeleton. Reports suggest that linear growth continues normally with bisphosphonate therapy in IJO (53); however, abnormalities in modeling at the distal femur and radius have been demonstrated in OI even after discontinuation of bisphosphonate therapy (70). A child treated with excessive doses of pamidronate developed osteopetrosis with persistent remodeling defects more than 6 yr after discontinuation (71, 72). The long-term effects on fracture healing and bone strength have yet to be elucidated. One study in patients with OI reported delayed fracture healing despite gains in BMD (73). Another study found no effect on healing of spontaneous fractures, but delayed healing after osteotomies (74); thus, we often recommend discontinuation of bisphosphonates several months before scheduled orthopedic procedures. Reports of atypical fractures in adults treated with long-term bisphosphonates further raises questions regarding the safety of continuous suppression of bone remodeling (75). These concerns have led to the suggestion that bisphosphonate therapy be interrupted every few years, depending upon the severity of the bone disease (64, 75).

Patients on bisphosphonate therapy should undergo follow-up densitometry to monitor treatment; the interval between studies depends upon the severity of disease, but most agree that studies should not be done more frequently than every 6 months (39). Ideally, these studies should be performed at the same center to facilitate comparison with previous exams. Discontinuation of bisphosphonates should be considered when the Z-score is greater than -2 and/or the patient is no longer fracturing. Children with open epiphyses should have periodic radiographs of long bones to monitor for modeling defects. Typical changes include hyperdense, sclerotic bands representing areas of decreased bone turnover and slight widening of distal metaphyses resulting from mild undertubulation (76, 77) (Fig. 3). These findings tend to resolve after discontinuation of therapy and closure of epiphyses.



FIG. 3. Hyperdense sclerotic bands in the epiphyses of a child treated with serial infusions of pamidronate. [Reproduced with permission from M. Al Muderis et al.: *J Bone Joint Surg Am* 89:1511–1516, 2007 (76).]

Intermittent measurements of bone turnover markers are a noninvasive measure of bone activity and may provide additional information regarding response to therapy.

Case Follow-up

Our 12-yr-old patient underwent a battery of tests including screening for rheumatologic disease, celiac disease, thyroid dysfunction, hypercalciuria, and vitamin D deficiency, all of which were normal. Markers of bone turnover were unremarkable, and no mutations in COL1A1/COL1A2 were detected. The patient was given a presumptive diagnosis of IJO and started on vitamin D supplementation, physical therapy, weight-bearing exercise, and pamidronate infusions every 3 months. She was restricted from playing contact sports. Over the course of 18 months, she experienced a decrease in back pain, and an increase in height achieving the 50th percentile for age (Fig 1). She did not experience any fractures during that time. A DXA scan after 12 months of therapy revealed an improved spine Z-score of -2.5 .

Conclusion

Fragility fractures in children may be due to a wide variety of genetic, medical, or nutritional disorders. The decision to perform screening densitometry in a child or adolescent must be made on an individual basis, taking into account fracture history and risk factors. The clinical implications of low BMD in the pediatric population have not been well-established, and the diagnosis of osteoporosis must be made in association with clinical history rather than relying upon bone densitometry alone. The primary step in treatment should include management of underlying conditions as well as conservative measures including vitamin D and calcium supplementation and weight-bearing physical activity. The use of bisphosphonates in children and adolescents is controversial due to lack of long-term efficacy and safety data and should be limited to clinical trials and as compassionate therapy in children with significantly compromised quality of life.

Acknowledgments

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This manuscript reflects the opinions of the authors and not those of the National Institutes of Health or the U.S. Federal Government.

Disclosure Summary: The authors have nothing to declare.

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