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Multiple Vertebral Fractures in a Young Girl: A Question of Treatment

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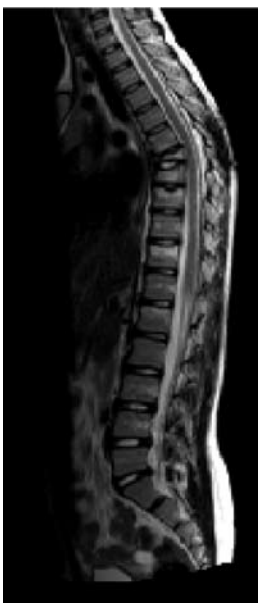
Osteoporosis, the most common metabolic bone disease in adults, is rare in children. In the pediatric population, the diagnosis of osteoporosis requires both a history of pathologic fractures and low bone mineral content or density [1]. The differential diagnosis of osteoporosis in childhood is large and often requires extensive testing to determine a definitive cause of the disease. Idiopathic juvenile osteoporosis is a very rare condition of bone demineralization that presents in childhood [2]. Diagnosis is reached by excluding other causes of osteoporosis in this age group. Only a very small case series of this disorder in children has been reported. We present an interesting case of IJO and discuss the main diagnostic and treatment options currently available for this disease.



Spine MRI revealing multiple new condensed vertebral fractures at T8, T9, T10, and T11, in addition to the old fracture at T7. Note the significant kyphosis of 29^0 from T6 to T9 of the spine.

PATIENT DESCRIPTION

An 11 year old, otherwise healthy, young girl of Ashkenazi-Jewish descent presented with severe back pain. The patient was an active child who danced regularly but not intensively. There was no history of trauma, eating disorder or systemic complaints, and no family history of pain or bone disease. Other than local tenderness of her back, the physical examination was normal. Plain X-ray and further magnetic resonance imaging revealed T7 compression fracture. Laboratory inflammatory markers were normal. An open biopsy of the T7 vertebra ruled out infection or tumor such as eosinophilic granuloma. The patient was put on a TLSO (thoraco-lumbo-sacral orthosis) brace and was free of pain after 1 month. While still asymptomatic, repeat MRI 10 months later revealed multiple new compressed fractures [Figure]. Bone scan revealed the same findings. A second open biopsy of the T8 vertebra demonstrated acute and chronic inflammatory infiltrate with no granuloma or eosinophils.

Further investigations were within normal limits. These included complete blood count with differential, erythrocyte sedimentation rate, C-reactive protein; liver, kidney and endocrinological studies; acid phosphatase, alkaline phosphatase, calcium, and phosphate. Autoimmune serology of antinuclear antibody, DNA, complement, immunoglobulins, and angiotensin-converting enzyme, and serology for celiac disease were negative.

No further therapy was suggested at this point, and the girl was kept in the TLSO brace and without sport activities. Nine months later she was referred to our department, while asymptomatic, and physical examination showed kyphosis but no tenderness to palpation of the vertebrae. An updated third MRI showed no new fractures and the kyphosis angle was 29^0. Since bone marrow was preserved and non-edematous, with no enhancement with gadolinium, malignancy was ruled out. The intervertebral disks were preserved, ruling out osteomyelitis or infection. DXA (dual X-ray absorptiometry) hologic measurement adjusted for children by using the Stanford pediatric software normative data (http://www.stat-class.stanford.edu/pediatric-bones/) showed a low bone mineral density at the lumbar spine of 0.503 g/cm, bone mineral content of 15.98 g, a lumbar spine Z score of -3.03, and hip- Z score of -2.245. Laboratory investigation showed normal calcium, phosphate, ALP, vitamin D and parathyroid hormone levels, and a low 24 hour urinary calcium and phosphate. Adrenocorticotropic hormone and cortisol levels, and thyroid function were

IJO = idiopathic juvenile osteoporosis

ALP = alkaline phosphatase

normal, and no inflammatory markers were present. Metabolic evaluation of bone revealed high bone turnover; serum P1NP (propeptide of type 1 procollagen), a bone formation marker, and CTX (cross-links of collagen), a bone resorption marker, were elevated at 815 (normal for premenopausal women < 59) and 1.9 (normal for premenopausal women < 0.6), respectively. In adolescents the usual values are about three times the upper limit of normal for the premenopausal range.

At this stage, after excluding other causes of osteoporosis, we reached the diagnosis of IJO. Since the patient was asymptomatic and there were no new fractures and no increase in the kyphosis angle, we decided, after consulting with an orthopedic surgeon, to put her on calcium and vitamin D supplementation, and an enriched diet high in calories and protein. The patient returned to low intensity/low impact sports activity and the TLSO brace was removed. After 4 months of therapy, repeat bone turnover studies had improved. At her last follow-up, at age 14, she had started puberty and was asymptomatic with no new fractures. There was clear improvement in her bone metabolism, and repeat adjusted DXA also demonstrated improvement.

COMMENT

The differential diagnosis of a child who presents with osteoporosis is wide ranging and often requires extensive workup to identify a definitive origin. Common causes of osteoporosis in children include osteogenesis imperfecta, leukemia, homocystinuria, inflammatory diseases, corticosteroid use, immobilization, celiac disease, malignancy, and osteomyelitis of bacterial and non-bacterial causes.

Clinical symptoms on initial presentation include musculoskeletal pain, most likely due to fractures of the vertebra and long bones. These fractures may occur after minor trauma or spontaneously. Metaphyseal fractures in the bones of the lower extremities may cause gait disturbances and may be accompanied by muscle weakness. Physical malformations may also be present, which include kyphosis, as seen in our patient, loss of height, or a sunken chest.

The next step in diagnosis is to perform blood tests to rule out infectious, metabolic, autoimmune, or endocrinological causes of the condition. Plain X-rays are a pertinent test to perform as an initial evaluation for osteoporosis, together with newer, non-invasive testing methods such as DXA and quantitative computed tomography. The problem with DXA studies is the over-diagnosis of osteoporosis in children due to misinterpretation of data based on adult reference data. To help correct this misinterpretation, the Stanford graph is used for children (http://www.statclass.stanford.edu/pediatric-bones). Histomorphometry may reveal markedly decreased cancellous bone volume with a low bone turnover (decreased bone formation), resulting in load failure at sites where cancellous bone is essential for stability [3].

In the differential diagnosis for idiopathic juvenile osteoporosis, one must also include chronic recurrent multifocal osteomyelitis, a relapsing sterile inflammatory disease that affects 2–5% of all patients with osteomyelitis [4]. This disease involves multiple sites on plain X-rays and bone scans, including the pelvis, sternum, clavicle, mandible, spine and long bones. It presents more often in girls, with pain, limited activity, possible periarticular swelling, fever, and elevated ESR. Adjacent joint arthritis may precede the bone lesion, and non-specific histological features include acute and chronic inflammatory changes. There is no abscess, fistula, or sequestra formation. Since our patient had only vertebral involvement, and no fever, pain, or elevated inflammatory markers, we ruled out this option. A congenital cause, osteogenesis imperfecta, must be ruled out before a diagnosis of IJO can be reached. OI is a structural genetic defect in the quantity or quality of bone collagen production. Presentation of OI may be similar to that of IJO, but the family history, together with the blue, purple or gray sclera commonly found in OI, radiographic findings and, in some cases bone biopsy, help to distinguish between the two.

There is no established medical or surgical therapy for IJO, and often the condition remits spontaneously, so no treatment is necessary. However, it is important to detect IJO early, to protect the child's spine and other bones until remission occurs, or to relieve severe pain. These protective measures include a back brace and/or crutches (especially if severe kyphosis is present), physical therapy, and the avoidance of unsafe weight-bearing activities. A well-balanced diet rich in calcium and vitamin D is important. Another treatment option is bisphosphonates, which have been approved for the treatment of osteoporosis in adults. Bisphosphonate [4,5], specifically intravenous pamidronate, has been effective in conditions such as chronic recurrent multifocal osteomyelitis and OI. Its use in IJO, usually for cases of severe pain, has also been proposed, with promising results, but is still regarded as experimental and should therefore be closely monitored. The follow-up of IJO consists mainly of monitoring bone metabolites and DXA.

In conclusion, this case illustrates the challenges in diagnosing and treating IJO, a diagnosis of exclusion following the use of various modalities to rule out other causes with similar presentations. IJO patients usually recover spontaneously following puberty. However, in some cases the sequelae can lead to disability. In our patient, supportive measures, only, were provided when multiple vertebral fractures were found.

DXA = dual-energy X-ray absorptiometry
ESR = erythrocyte sedimentation rate

OI = osteogenesis imperfecta

If prevention of new fractures was considered the main therapeutic goal, the outcome was excellent since there was no disease progression. Hence, the question – whether or not to treat with bisphosphonates at that stage in order to protect the spine until remission, and with which modality – requires clinical skill and judgment. Because our team evaluation and diagnosis was done 10 months after onset of the initial symptoms, it was easier to decide on a conservative approach and not to use bisphosphonates.

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