CME

Case Report: Osteogenesis imperfecta

Elusive cause of fractures

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Osteogenesis imperfecta (OI), a secondary cause of osteoporosis, principally manifests as bone fragility. It is an inherited disorder of connective tissue integrity; it affects up to one in 10 000 persons.[1,2] Diagnosis of mild OI is challenging due to its variable phenotypic expression and inconstant course. Family physicians must maintain a high index of suspicion, as diagnosis, along with proper follow up and counseling, can prevent many complications of this disorder.

Case description

A 24-year-old woman presented with low back pain after water-tubing. Her medical history included a Colles fracture at age 9 and several digital fractures in childhood. She denied smoking or consuming alcohol, she had adequate calcium intake, and her menstrual history was non-contributory. Her father, who had been diagnosed with osteoporosis, had had more than a dozen fractures, including a hip fracture at age 54. Her sister, age 35, also had osteoporosis.

On examination, the patient was 167 cm tall and weighed 52 kg. She had blue-gray sclera and normal dentition. A mid-peak ejection murmur was heard over the left sternal border. Musculoskeletal examination demonstrated scoliosis and paralumbar tenderness. Other systems were intact.

Lumbar radiographs confirmed an L1 compression fracture, and computed tomography demonstrated fracture stability without cord impingement. Osteoporosis was suspected, and dual-energy x-ray absorptiometry assessment of bone mineral density confirmed severe disease in the lumbar spine and femoral neck. Secondary causes of osteoporosis were ruled out. Owing to her physician's high index of suspicion, a diagnosis of OI was pursued. Because the patient presented as an adult with relatively minor symptoms, Type IA OI (the mildest form) was established. Systemic screening for disease complications included an echocardiogram, pulmonary function tests, an audiogram, and consultation with a geneticist. Therapy with calcium and vitamin D was initiated, and an in-depth discussion regarding bisphosphonates was pursued. Close follow up and screening of family members were arranged.

Discussion

MEDLINE was searched using the key words osteogenesis imperfecta, osteoporosis, fractures,

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and diagnosis. Articles on OI and its epidemiology, natural history, and management were reviewed.

Osteogenesis imperfecta results from mutations in genes encoding for type I collagen. Collagen is the major structural protein in bone, ligaments, tendons, skin, sclera, and dentin.[3] Mutant expression produces non-functional collagen (severe OI) or insufficient quantities of collagen (mild OI). There are seven subtypes of OI varying in severity, age of presentation, and clinical features.[4-7]

Type IA OI is the most prevalent and mildest form and is genetically transmitted in an autosomal-dominant or sporadic-mutation fashion.[2] Children with Type IA OI are five to 15 times more likely to fracture than unaffected children, and parents are often accused of abuse.[8] Fracture frequency declines after puberty but increases again with inactivity, childbirth, and aging. In women with OI, the third trimester of pregnancy and the postnatal period, particularly when breast feeding, are periods of high fracture risk.[9] Type IA OI does not affect longevity but influences morbidity due to recurrent fractures and related complications.

Other clinical characteristics of Type IA OI can include blue-gray sclera and sensorineural hearing loss beginning in early adulthood. Neurologic sequelae result from basilar invagination and cervical spinal cord compression syndromes presenting as paresthesias, peripheral weakness, incontinence, central sleep apnea, and upper motor neuron signs.[10] Cardiac complications include aortic and mitral valve insufficiency as well as increased aortic root diameter predisposing to dissection.[11,12] Restrictive lung disease secondary to spinal deformity and rib fractures can occur.[13] Hypermetabolism with nephrolithiasis and vascular fragility can also occur.

In practice, diagnosis of OI is by exclusion, fortified by consistent clinical presentation, family history, and low bone mineral density scores. Specialized investigations, although rarely warranted, include serum quantification of low levels of type I procollagen peptide, bone biopsy demonstrating high osteocyte levels with low bone turnover, direct collagen analysis from fibroblast culture through skin biopsy, and confirmation of mutation by DNA extraction from white blood cells.[3,14]

EDITOR'S KEY POINTS

- Osteogenesis imperfecta is a rare but striking cause of bone fragility and fractures. It usually presents in children or young adults.
- Consider it in the differential diagnosis when a young person presents with a history of recurrent fractures. Early detection can improve morbidity.

POINTS DE REPÈRE DU RÉDACTEUR

- L'ostéogenèse imparfaite est une cause rare mais impressionnante de fragilité et de fractures osseuses. Elle se manifeste habituellement chez l'enfant ou le jeune adulte.
- Pensez à ce diagnostic en présence d'une jeune personne qui a des antécédents de fractures à répétition. Un diagnostic précoce peut réduire la morbidité.

Prenatal diagnosis is possible as well through isolation of mutation-specific DNA polymorphisms.

Recent developments in OI therapy are promising. Lifestyle modifications, such as use of orthotics and physiotherapy, should be considered.[15] Medical management of OI, with the exception of bisphosphonates, has been largely unsuccessful. Bisphosphonates (antiresoptive agents that inhibit osteoclasts) have been shown to increase bone mass, decrease fracture rates, and relieve symptoms of OI patients.[16-18] The long-term safety of bisphosphonates in mild OI has not been determined, particularly for women of child-bearing age, because the drug is thought to remain in the system for many years after treatment is stopped. More invasive surgical interventions include intramedullary rod insertion, surgery for basilar invagination, and correction of scoliosis.[19]

Conclusion

Fractures, particularly in adults older than 45, are associated with osteoporosis.[20] This case illustrates the importance of family history, fracture history, and clinical correlation when assessing patients with osteoporosis. Mild OI most often presents after infancy and should be considered whenever children or adults have recurrent fractures. Early diagnosis of this disease by family physicians will enable initiation of therapy as well as patient education regarding management of modifiable risk factors linked with osteoporosis (eg, diet, smoking, alcohol). For

many, disease detection can prevent the trauma of separation of parents and children when OI is misdiagnosed as child abuse. Genetic counseling and family screening could also be offered.

Competing interests

None declared

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