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Case Report

Brittle bone disease: a case report

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We report a case of a female patient, 27 years old, with several episodes of fractures after low energy trauma and the first documented episode only to 18 years of age. Extensive research has not found the exact etiology of the disease. The orthopedic monitoring has targeted prevention and treatment of fractures.

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Introduction

Osteogenesis imperfecta (OI) is a hereditary disorder of connective tissue that is characterized by bone fragility with clinical manifestations that vary widely, and OI is caused by a defect in type 1 collagen.¹ The number of individuals with the disorder and its incidence are unknown in Brazil, while in the United States, the estimated incidence is 1 in 15,000-25,000 live births.²

OI encompasses a group of mostly autosomal dominant hereditary alterations that are caused by several mutations in one of the two genes encoding the alpha chains, i.e., COL1A1 and COL1A2, of type 1 collagen.¹⁻² However, in approximately 10-20% of patients, it is not possible to identify the mutation site.³

Bone fragility is conditioned by the quantity and quality of abnormal structural collagen protein. Therefore, bone deformities or fractures at minimal trauma are expected in patients with the disease. OI presentation varies from the lethal forms of intrauterine fractures to late cases in which fractures start in adolescence or even adulthood.⁴

Due to collagen modifications, other alterations may be observed in addition to fractures, such as ligamentous laxity, cutis laxa, short stature, dentinogenesis imperfecta, blue or gray sclera and, more rarely, alterations in the mitral valve and aortic dilation.^{4,5}

Among the differential diagnoses one should exclude maltreatment, hypophosphatemia, Paget's disease, idiopathic juvenile osteoporosis, Cushing's disease, calcium deficiency or malabsorption, defects in vitamin D metabolism and Ehlers-Danlos syndrome types VIIA and VIIB, which are characterized by ligamentous laxity and may predispose patients to fractures.⁶

In 1979, Sillence et al.⁷ proposed the current classification of types I to IV based on clinical findings. Although more comprehensive than the classification previously proposed by Looser and Seedorf in 1906, as cited in Kim and Gonzales⁴, it does not include the entire spectrum of cases described. Recently, types V, VI, VII and VIII^{2,8} have been included, and although they exhibit bone fragility, the defect is not located in the collagen gene.

Case report

The patient was a 27-year-old female pharmacist of Italian descent, 162 cm in height and 57 kg in weight, who had been undergoing orthopedic monitoring since the age of 18 due to episodes of fracture after low-impact events.

The patient had been previously healthy, delivered by caesarean section at term due to fetal-pelvic disproportion (SIC), with uneventful pre, peri or postpartum. During childhood, the patient had no significant morbidities, with a report of inguinal hernia repair at 12 months.

She had normal psychomotor development, started walking at 1 year of age, micrognathia with orthodontic correction, and

menarche at 15 years with regular cycles. The family reported low-energy traumas characteristic of each age range, without the need for medical evaluation. Orthopedic examination showed the presence of ligamentous laxity and grayish sclera.

The patient reported that at age 18, during recreational activity, there was sudden pain onset in the right foot and difficulty walking, and a fracture of the fifth right metatarsal was identified. She was treated in the city of Ouro Preto (state of Minas Gerais), where treatment by immobilization with plaster cast was chosen, which progressed into full consolidation of the fracture. At age 22, she had a new episode of sudden pain in the same right foot when getting out of bed and was treated in the city of Goiania (state of Goias), when a fracture of the fourth right metatarsal was identified. She was again treated by immobilization with a plaster cast.

At this time, the patient and family returned to Belo Horizonte (MG) and sought evaluation at the Department of Orthopedics and Traumatology, Hospital Universitario Sao Jose at the Faculdade de Ciências Médicas de Minas Gerais, where a contralateral foot x-ray was requested and showed bone callus formation in contralateral metatarsals, which was not associated with trauma or pain (Fig. 1). The immobilization treatment was maintained until consolidation and was followed by the prescription of custom-made orthopedic insoles because the foot scans showed pes cavus varus with bilateral adduction of the forefoot, which caused 4th and 5th metatarsal overloading. Since then, she has had no complaints of pain in the feet and has not had new fractures.

At age 25, four years after the last visit to the orthopedist, she claimed that while dancing, she started with severe pain in the anterior right thigh, which continued for 30 days, after which she sought orthopedic care in the city of Vicosa (MG). She reported that was instructed to rest and return the following week. The patient again sought treatment at the Department of Orthopedics of HUSJ/FCMMG, where a stress fracture was found in the right femur neck (Fullerton and Snowdy types A and B in the contralateral neck) (Fig. 2). DHS plate and screw fixation



Fig. 1 - Oblique view x-rays of the left foot; AP and oblique view of the right foot showing fractures in different stages of consolidation, with no history of major trauma or previous complaint of pain.

was performed to the right, and two large-fragment cannulated screws were used in the left neck, anticipating the possibility of progression of fracture trace. Investigative workup was started to screen for inborn errors of metabolism or osteogenesis imperfecta (OI), which was performed via endocrinological, cardiology and genetics investigation.

In November 2011, at age 27, she started having pain in the anterior aspect of the left thigh, similar to the contralateral side three years before. She came to the department, and diastasis in the neck of the left femur was identified, with a type A trace of Fullerton and Snowdy for stress fractures of the neck of the femur, which had been preventively fixed two years previously, when she had a type B trace of Fullerton and Snowdy (Fig. 3). Due to the patient's good sociocultural level and emotional fragility to undergo a new surgical procedure, it was decided to postpone operative treatment and remove the load from the left leg.

The patient has shown good evolution towards consolidation without pain, as reported in March 2012 (Fig. 4). She has



Fig. 2 - AP view x-ray of coxofemoral joint; the arrows show signs of stress fractures of the femoral neck.



Fig. 3 - Sign of new stress fracture in the left femur neck, despite preventive fixation two years prior to the complaint of hip pain.



Fig. 4 - AP view x-ray of the left coxofemoral joint showing fracture healing after conservative treatment.

maintained a strict multidisciplinary follow-up; however, the underlying pathology has yet to be definitively established.

Extensive laboratory investigations showed very low TSH (0.01 μ UI/mL) and normal T4 in December 2009. Endocrinological follow-up was maintained, and the patient underwent FNA in August 2010 with a diagnosis of toxic nodular goiter. She underwent surgical treatment in 2011 and receives sodium levothyroxine 88 mcg daily. Other laboratory assessments, such as alkaline phosphatase, PTH, vitamin D (25-OHD), C-telopeptide, ionic calcium, phosphorus, potassium, magnesium, antistreptolysin-O, FAN, and 24-hour calciuria, have all been repeated annually from 2009 until 2011 and have always been within normal limits.

Bone densitometry on 9/16/2010 showed a T-score of -2.7 and Z-score of -2.7, indicating decreased bone mass, with 73% of the expected mass for her current age range and weight.

An echocardiogram on 12/4/2008 showed mitral valve prolapse associated with mild mitral regurgitation, left-to-right interatrial shunt (patent foramen ovale) and mild aortic dilation.

An ECG performed in 2009 at the time of surgical risk showed atrial arrhythmia. The patient uses metoprolol daily, with rhythm normalization since then.

A genetic study performed on 12/15/2010 did not demonstrate consanguinity between parents and a healthy 10-year younger brother, who were negative for OI or other genetic more common disorders. It was suggested by clinical examination that the patient might have Ehlers-Danlos syndrome, one possible case of mutation due to autosomal dominant inheritance, though the parents do not have the same characteristics. It is important to note that there is no confirmatory test of diagnostic proof.

Discussion

This is an atypical case in the daily practice of an orthopedic consultation office. Despite the suggestion made by the

geneticist that the patient might have Ehlers-Danlos syndrome, which cannot be ruled out, the patient meets the epistemological criteria for OI classification, although laboratory confirmation is not possible. Genetically, one cannot attest to the case. This case may resemble the new types described by Glorieux et al. in Canada. The patient currently maintains the regular use of metoprolol, injectable teriparatide and risedronate, in addition to calcium and vitamin D supplementation. Until a new treatment is available, a regular multidisciplinary follow-up will be maintained. It is the orthopedic team's objective to prevent further fractures or manage them so the patient has quality of life and a daily routine as close to normal as possible.

Conflicts of interest

The authors declare no conflicts of interest.

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