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Case Study

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Difficulties in Managing Multifactorial Osteoporosis in an Adolescent with Demyelinating Neuropathy

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ABSTRACT

Introduction: Secondary osteoporosis is rare in children/adolescents. Delays in the specific management of risk factors for bone fragility can lead to a silent loss of bone mass and an increased risk of early osteoporosis. We reported a case of a teenage girl with multifactorial bone fragility complicating a chronic neuropathy treated between 2021 and 2024.

Case Report: A 15-year-old girl patient has been under observation for demyelinating sensorimotor neuropathy since the neonatal period. The condition was complicated by multiple skeletal deformities that have required surgical treatment. Bone fragility was noted intraoperatively. The etiologic diagnosis favored a multifactorial origin, including neurological, endocrine, nutritional, and mechanical factors. Treatment of the offending factors was inadequate. Osteoporosis was diagnosed in the presence of a z-score for bone densitometry below -2 standard deviation and multiple long bone fractures. The specific treatment of osteoporosis was limited by the lack of pediatric approval for most molecules. After a two-year course of symptomatic then specific treatment, there was a favorable clinical response and partial improvement in osteodensitometry.

Conclusion: This clinical case illustrates the difficulty of managing multifactorial bone fragility leading to osteoporosis in a girl with chronic neuropathy, in terms of managing the incriminating factors and prescribing bisphosphonates.

Key Words: Bone fragility, Child, Multifactorial causality, Osteoporosis, Fracture, Treatment

INTRODUCTION

Osteoporosis is a generalized disease of the skeleton characterized by a reduction in bone mass and/or changes in bone microarchitecture, leading to a reduction in bone strength.[1] The presence of fractures and low bone mass are strongly correlated.[1] Bone damage is often asymptomatic in the early stages, delaying diagnosis and treatment.[2] In advanced stages, it manifests as functional symptoms and fractures of the long bones and/or vertebrae, affecting quality of life.[2] We reported the case of an adolescent girl with multifactorial bone fragility complicating a chronic neuropathy treated between 2021 and 2024 in the Department of Infant Medicine A in Children's Hospital Bechir Hamza (Tunis, Tunisia).

Clinical Observation

Patient information

A 15-year-old girl with a demyelinating sensorimotor neuropathy that manifested as generalized hypotonia and arthrogryposis in the neonatal period. The patient come from a second-degree consanguineous marriage. She had undergone orthopedic treatment for several bone deformities, including scoliosis, genu varum, and hallux valgus. She had intermittent mild mechanical spinal pain at rest, sometimes moderate when walking. These conditions led to a gradual reduction in physical activity, limited to the journey to and from school and lack of sun exposure. The patient suffered from two toe fractures and a femoral condyle fracture caused by minor trauma between the ages of 12 and 14 years. At the age of 15, when she underwent genu varum surgery, the orthopedic surgeon noted bone fragility. The bone was friable and prevented fixation of the metaphyseal-metaphyseal plate, which was postponed.

Clinical findings

Pediatric examination revealed the above-mentioned bone deformities, as well as thinness with a low body mass index of 15.14 g/m^2 secondary to a diet low in protein and vitamins, muscle weakness and slowness of movement.

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Diagnostic Assessment

Bone densitometry revealed a z-score of -3.9 standard deviation (SD) for the whole body and -4.5 SD for the spine column. Etiologic assessment of the bone demineralization revealed a state of chronic hypothyroidism (Thyroxin = 16.97 pmol/L and Tyrostimulin = 7.82 mU/L) and vitamin D deficiency (25 Hydroxy-vitamin D = 10.67 ng/mL).

Diagnostic and Therapeutic Intervention

At this stage, the diagnosis of multifactorial bone fragility was retained. The incriminating factors were chronic neuropathy, hypothyroidism, vitamin deficiency, hypotrophy, and lack of physical activity and sun exposure.

The management plan was based on the correction of these incriminating factors, which included a balanced, high-protein diet, motor kinesitherapy, offering physical activities of progressive duration, the administration of levothyroxine at a dose of 25 µg/day, the provision of calcium supplementation at a dose of 500 mg/day, and the administration of vitamin D supplementation at a dose of 100,000 IU every 15 days for a period of three months, followed by monthly administration until vitamin D levels were normalized.

Euthyroidism was reached after one month. Dietary rules were not followed, and physical activity improved only slightly by adding a walk of about an hour on weekend days. There has been improvement in the patient's weight 40 kg versus 40 kg. Vitamin D levels normalized (36.42 ng/mL versus 10.67 ng/mL) after six months. The subsequent bone densitometry examination showed stable z-score values of -3.8 for the whole body and -4.1 for the spinal column.

Over the next six months, the patient experienced two additional pathologic fractures: one of the right femora and one of the coccyx. Osteoporosis was diagnosed in the presence of a z-score below -2 DS and multiple long bone fractures. The decision was made to continue Vitamin D supplementation at a dose of 100,000 IU every two months because of persistent risk factors and to start treatment with bisphosphonates. The specific treatment of osteoporosis was limited by the lack of pediatric approval for most molecules.

The patient received an intravenous dose of pamidronic acid at a rate of 3 mg/kg over a three-day period, followed by a subsequent administration every three months for one year. Due to the absence of pathological fracture recurrence during treatment, the decision was made to continue the treatment for an additional year. However, the pamidronic acid was no longer available, and the only alternative was to administer two courses of zolidronic acid, with a six-month interval between each course, at a dose of 0.025 mg/kg. The treatment was clinically and biologically well tolerated.

Outcomes

Bone densitometry performed six months after completion of treatment showed a z-score of -3.4 for the whole body and -3.0 for the spine column. Given the absence of pathologic fracture recurrence during treatment and the observed improvement in bone density, the patient underwent reoperation of her genu varum without complications.

Despite the persistence of risk factors for bone fragility that we could not address, namely chronic neuropathy, lack of physical activity and low weight, it was decided to settle for two years of treatment with bisphosphonates, as these treatments are not without risk.

DISCUSSION

Bone fragility in children is often a secondary, multifactorial phenomenon.[1,2] This patient's sensorimotor neuropathy and reduced joint mobility had favored the onset of other factors implicated in bone fragility. The first goal of management is to address the underlying risk factors.[3,4] We have been able to address medically treatable factors such as hypothyroidism and vitamin D deficiency. However, these interventions were not enough. Factors that depend primarily on the patient's will to change are more difficult to manage, and our interventions has failed. The lack of specific treatment for the known chronic neuropathy and its orthopedic sequelae has perpetuates the other factors.

Despite the existence of all these bone fragility factors, the treatment of osteoporosis could not be instituted earlier because of the definition of osteoporosis in children/adolescents itself. Bone fragility in pediatrics is defined primarily by its clinical consequences (long bone and/or vertebral fractures).[5] The diagnosis of osteoporosis had to await the occurrence of two long bone fractures were not included in the diagnostic criteria. Curative measures for osteoporosis are aimed at children/adolescents with symptomatic bone fragility in conjunction with appropriate orthopedic treatment. However, pharmacological options are limited by the lack of pediatric approval for most molecules.[6]

The rationale for prescribing pamidronate and zoledronic acid was based on their efficacy in increasing bone mineral density and reducing fracture rates.[7] The intravenous route was recommended for this patient. It was found to be more effective than the oral route in treating severe forms of the disease.[8] The duration of treatment was arbitrary in the absence of clear recommendations regarding the duration of treatment.

CONCLUSION

This clinical case illustrates the difficulty of managing multifactorial bone fragility leading to osteoporosis in a girl with

chronic neuropathy, in terms of managing the incriminating factors and prescribing bisphosphonates.

In children/adolescents at risk for fractures due to osteoporosis, identification of the factors involved in bone fragility and early intervention are crucial. Management strategies should prioritize hormone replacement, adequate nutrition, and sufficient physical activity.

Ethics: The consent of the institutional ethics committee was obtained prior to publication of this case (3/2024 obtained on March 18, 2024), as was the authorization of the patient's parents.

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