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Case Study

Osteogenesis Imperfect Type 5 and Fibular Tumor in 2 Brothers: A Case Report

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Abstract

Osteogenesis Imperfecta is a hereditary disease, in which there is an abnormality in the bone structure, resulting from changes in the collagen type 1 chain: thus, increasing the risk of fractures in children and adults with it.

The objective is to report two brothers with osteogenesis imperfecta type V, who presented identical images of bone fibrous dysplasia in the distal region of the fibula bone. Both underwent resection of the bone tumor, and dynamic stabilization of the ankle, in an interval of 8 years.

Keywords: Osteogenesis Imperfecta Type 5; Fibrous Dysplasia; Bone Tumor

Introduction

This case report was approved by the institutional ethics committee (No. 139/IEC/PGM/2021), and the patients and their respective supervisor signed the term of free and informed consent to participate in the study.

Osteogenesis imperfect (OI) is the most prevalent genetic disease causing bone fragility, in which there is abnormality in the bone structure, due to alteration of the pathway of collagen type-1 [1,2]. The prevalence described in China in 2016 is 11.3/100.000 people [3]. It has as main characteristics the increased risk of partial and complete fractures in children and adults, having a variable degree of compromise and set of signs and symptoms, where the types of OI are differentiated [4]. Currently OI is classified into 15 subtypes [5].

In 1979 Sillence and colleagues initially classified the OI into four types, and in 2000 Glorieux and colleague added a fifth group. In which OI type 5 has different clinical and radiological characteristics to type 4; such as: restriction in prone-supination by calcification in the interossei membrane, anterior luxation of the head of the radio, hypertrophic Callus after fractures and increased metaphysical density and absence of mutation in genes COL1A1 or Col1A2 [6].

We analyzed that the most characteristic phenotypes of OI type 5 were: Radio head luxation and mineralization of the interossei membrane, phenotypical diversity is clearly present [7]. In a group study in the Netherlands conducted in 2018 with 216 patients with OI, the incidence of type 5 was 0.9% [8].

Although Osteogenesis imperfecta affects the formation of bone and various other tissues through a type 1 collagen defect, it is not known whether it predisposes to any type of skeletal tumor.

Ionizing radiation is also among the risk factors for inducing primary and secondary bone tumors. Usually, patients with OI are routinely exposed to radiological imaging throughout their life, but this dosage could rarely lead to the development of cancer, unlike therapeutic irradiation [2].

Among other considerable risk factors for malignant transformation are also metal implants, due to their routine use in correctional surgical procedures in the OI. It is known that, osteosarcoma in patients with OI is extremely rare, where until 2004, only 9 cases were in the English-language literature in our research [9].

Only 36 publications were raised in the medical literature, in the English language, through the PubMed Platform with the associa-

tion of Osteogenesis imperfecta and benign or malignant tumors, of which 20 were bone tumors. Being Twelwe, corresponding to the locomotor apparatus and the remainder of skull-maxillo-facial location or that was not possible to an analysis after review of these articles.

We managed to find described in the literature the association of OI with bone tumors in locomotor apparatus in the following quantitative: 02 cases with multiple myeloma [10,11,07] cases with osteosarcomas [12] to [18, 01] case with osteochondromas [19, 01] cases with chondrosarcoma20 and a cystic bone formation [21].

No cases of tumors have been in patients specifically with type 5 IO. No case of tumor was recorded at the same site between brothers with OI. In this way, we made the first tumor registration in brothers with type 5 OI [10].

In conclusion, we will describe two male brothers with type 5 Osteogenesis imperfecta (OI-5), of different ages and of the same parents, who presented fibrous fibular dysplasia in an 8-year interval between their discovery. Both were subjected to complete resection of the distal fibula associated with the dynamic reconstruction of the ankle.

Clinical Case

Patient 1

Case 1, male, 25 years old, born from normal birth on 11.01.1998, without bone complications between the pre- and postnatal periods. No auditory, ocular, dental and low-stature changes were observed, such changes were common in other subtypes of imperfect osteogenesis.

He presented his first episode of fracture at the age of three, occurred by a low-energy accident, a fracture that at the level of the right forearm. Accumulating during its growth fractures due to minimal trauma to the skull, forearm and left clavicula, having undergone surgical treatment only of the ante arm fracture (Figure 1). In this surgical event, in the postoperative, clearly evidenced the ossification of the interossei membrane. It was on this occasion, in the year of 2006, confirmed the diagnosis of imperfect osteogenesis type 5, as well as that of his other two brothers, through the evaluation of a group of geneticists in a Reference Center for the treatment of Osteogenesis imperfecta (CROI) located at the Fernandes Figueiras Institute.

He used oral bisphosphonates, started around the age of 4 and continued to use them for approximately 2 years. It was discontinued on the guidance of the CROI medical team.

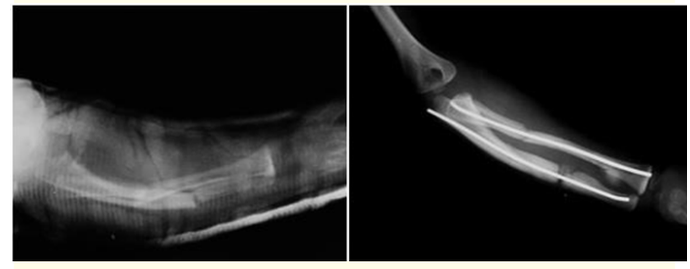

Figure 1: Radiography of the forearm showing diaphyseal fractures of radio and ulna and subsequent osteosynthesis with flexible intramodular nail. Visualize the formation of ossification of the interossei membrane in the postoperative.

In 2007, at the age of 8, he returned with increased volume in the distal and lateral region of his right leg, with associated picture of local pain, of insidious characteristics. Initially requested radiological examination, which demonstrated: presence of a benign tumor lesion, inflatable, compatible with fibrous dysplasia in the region of the distal third of the right fibula. After an inconclusive needle biopsy, he underwent complete resection of this lesion (Figure 2).

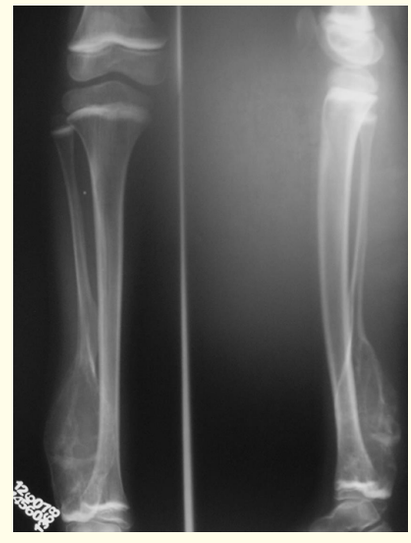

Figure 2: Inflatable lesion in the distal region of the right fibula of the patient 1.

The surgical procedure was performed at the National Institute of Traumatology and Orthopedics (INTO) in the year 2009, by the chief assistant physician, evolved without interference, and the material was duly sent for anatomopathological study. After analysis, the diagnosis of fibrous dysplasia and OI was confirmed.

In the initial post-operative, he was immobilized with a sural-type cast device for 60 days, followed by ankle/foot orthosis until

completing the six months. Since then, it has been monitored annually.

He returned to his physical activities, proper to his pathology, without showing signs of ligamental instability at the level of the ankle. In its last assessment in January 2023, despite showing slight ankle valgus deviation, it no complaints of local instability (Figure 3).

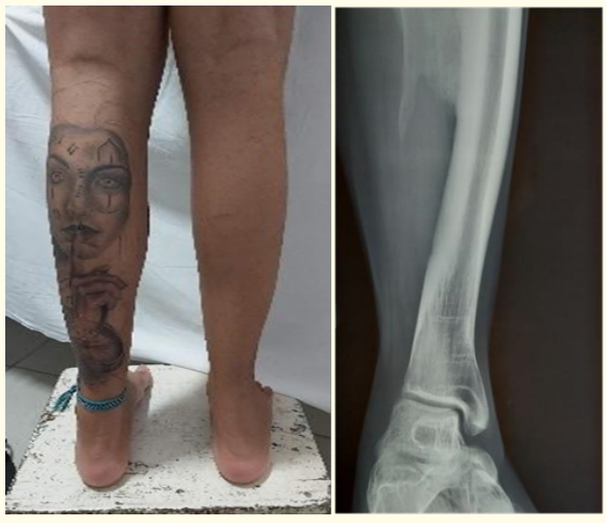

Figure 3: Clinical and Radiological evaluation (AP with 15o of internal rotation) of the right ankle of Patient 1, after 12 years of resection of the tumor lesion in the distal third of the fibula.

Patient 2

Case 2, male sex, 19 years old, born of normal birth on 20.04.2004, without complications at birth and in the postnatal period. No hearing, eye and dental changes were.

His first fracture was at the age of two, occurring in both forearms. He subsequently suffered a fracture in the right thigh, all due to low-energy trauma. Submitted to surgical treatment and intra medular osteosynthesis of the femur on the occasion.

The diagnosis of Osteogenesis imperfecta of type 5 was given at the age of two, together with her brothers, and at this time began the use of oral bisphosphonates. It was in use for 2 years, being monitored by the CROI.

Diagnosed in 2014, after a radiological examination, of the presence of an inflatable lesion in the distal third of the left fibula, due to complaints of increased local volume, without associated pain. As he presented benign characteristics and few symptoms at the time of the diagnosis, nothing was done by the medical institute that accompanied him (Figure 4).

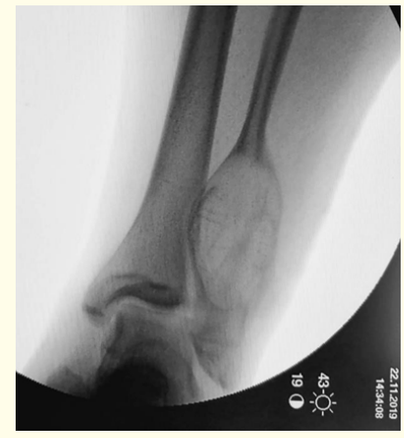

Figure 4: Inflatable lesion to the left fibula of the patient 2.

In 2019, due to the emergence of constant pains at the site of the tumor, he again sought help, and was indicated surgery for the resection of his distal fibula. It was held in November 2019, at the Federal Hospital of State Servants by the same assistant physician of case 01. The dried piece was sent for histopathological analysis, examination carried out by the same physician pathologist of the previous case, which confirmed the diagnosis of fibrous dysplasia.

Like his brother, he was submitted to the same post-surgical protocol, and continues in annual follow-up in the pediatric orthopedic sector of the Federal Hospital of Servidores. So far, with 04 years of postoperative, does not show signs of ligamental instability in the ankle treated or local painful complaints (Figure 5).

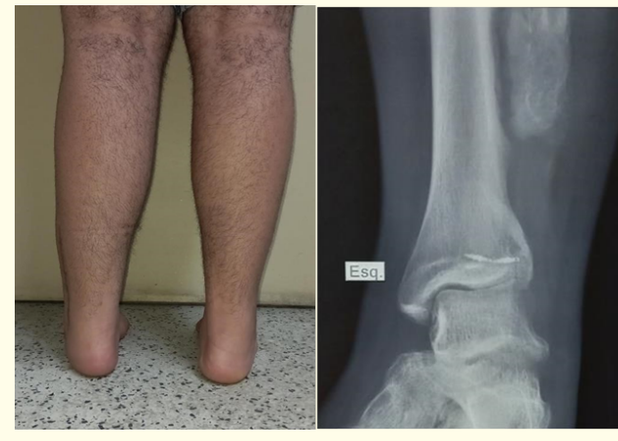

Figure 5: Clinical and Radiological Appearance (AP with 15° of internal rotation) of the right ankle of patient 2, after 2 years of resection of the tumor lesion in the distal tertiary of the fibula.

Pathological anatomy

The histopathological findings of the two cases are similar and characterized by the presence of trabecula's of immature and poorly structured bone in the middle of the fibrous stroma.

Patient 1 A.K.S.C.

Figure 6: Fibula distal segment, measuring 18x5.5 cm on the larger axes. After section, shows tumor meta diaphysis of white color with brown spotted and firm consistency, distancing 1.5cm from the proximal surgical limit.

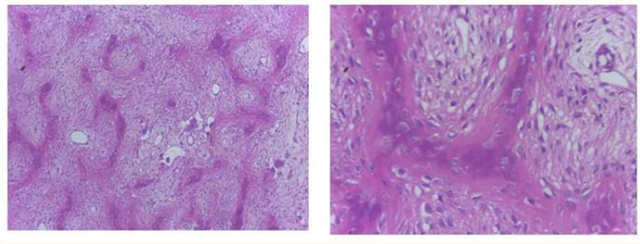

Figure 7: A and B - (H.E, A 10X and B 40X): Fibrous dysplasia: Lesion characterized by the proliferation of fusiform cells related to the formation of immature bone trabecula's.

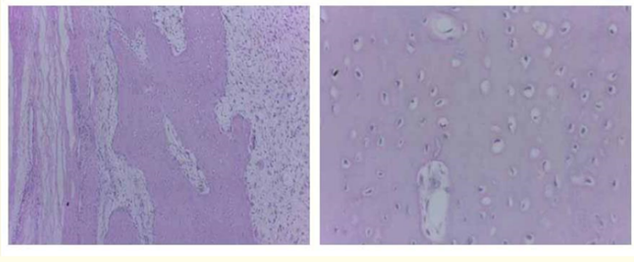

Figure 8: A and B- (H.E, A 10X and B 40X): Osteogenesis imperfecta Changes: Hypercellular cortical (Hyper osteocytes) dissociated by fibrous connective tissue.

Patient 2 V.K.S.C.

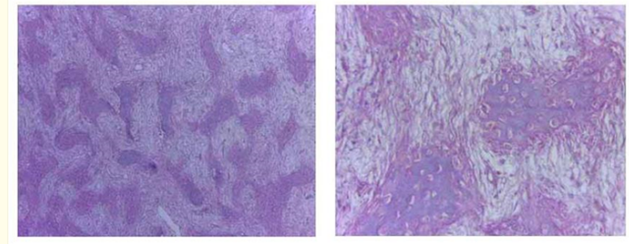

Figure 9: A and B – (H.E, E 10X and F 40X): Fibrous dysplasia: proliferation of fusiform cells related to the formation of immature bone trabecula's.

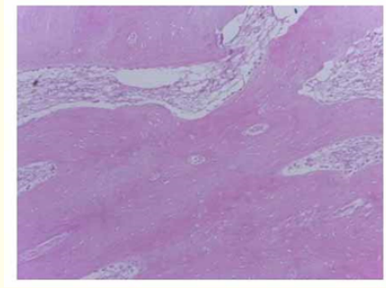

Figure 10: (H.E, 10X): Changes in Osteogenesis imperfecta: Thin Cortical and Hypercellular (Hyper osteocytes).

Correlations

As for the alterations of the Osteogenesis imperfecta we observe hypercellularity of the cortical. The diagnosis of the association of Osteogenesis imperfecta and fibrous dysplasia was made by correlation with clinical, radiological and histopathological data.

Discussion

The appearance of bone tumors in brothers and bearers of Osteogenesis imperfecta, and occurring at the same site, is a fact not yet described in Western literature. So we have no way to compare our current description to another similar case. However, there are some reports of benign and malignant bone tumors in the appendicular skeleton associated with imperfect osteogenesis.

Kutnowski M and colleagues in 1979 the first case of multiple myeloma associated with OI [11]. Already Chen Y and collaborators described in 2018 the concomitance of type 1 OI and multiple myeloma in an adult female patient treated with bisphosphonates for 10 years, with the result of an atypical incomplete femur fracture [10].

Lasson U and colleagues in 1978, Reid BS and collaborators in 1979 and Takahashi S and fellow workers in 2004 described osteosarcoma in patients with OI localized in the femur, who were amputated [13,16,17].

In 1995 Gagliardi JA and collaborators a 21-year-old female patient with OI with osteosarcoma in the right proximal femur, with bilateral intramodular stems in the femur and vertebral arthrodesis for the correction of kyphoscoliosis and spinal instability. Being initially undergoing chemotherapy treatment due to refusal for surgical intervention. Progressing with tumor growth, pelvic invasion and scapular metastasis; after 2 high-dose cycles of methotrexate and 1 cycle of cisplatin and Adriamycin combination. He then underwent hemipelvectomy associated with palliative chemotherapy [14].

Bedi HS and collaborators published in 1999 in the journal Pathology the description of osteosarcoma in a 37-year-old woman, with some degree of mental disability, who over the course of her life was affected with 50 isolated fractures, caused by low-energy trauma, causing extensive bone deformities. The author warned of the difficulty of characterization between Osteosarcoma and other benign findings, such as bone fall hypertrophy, due to the difficulties of radiological differentiation in resulting from the deformities, associated with difficult clinical evaluation [18].

Maiya S and collaborators published in 2002 the association of type 1 OI with right hip osteosarcoma in a male child, who was treated with chemotherapy, and resection of the tumor and placement of a stem in the right femur. Due to complications, after 4 and a half years, he was chosen for the placement of an endoprosthesis. Until the date of its publication, no metastases had been observed, showing good quality of life [15].

In 2021 Ferreira DG and collaborators described a 32-year-old male patient with type 3 OI. It was the first case of telangiectatic osteosarcoma described in an OI carrier. Located in his right proximal tibia, having undergone transfemoral amputation, developing in a year with pulmonary metastasis. Treated with associated chemotherapy, it remained uncomplicated until the date of case description [12].

Calonge WM and collaborators published in 2009 the finding of osteochondroma in a patient with type 1 OI. He was accompanied from 5 months of age to 18 years of age, with a family history corresponding to OI in the paternal lineage, and with a mother affected by multiple osteochondromes [19].

A 29-year-old female patient with type 3 OI suffering from chondrosarcoma in the right knee was described by Mandziak DG and Clayer M in 2013. Initially, a biopsy with 0.5 mm trefin was performed with initial laudo of Enchondroma, but due to the size of the tumor, the suspicion for Chondrosarcoma remained. In this way, he opted for an open biopsy, correcting the histopathological diagnosis for chondrosarcoma. Patient was then subjected to a knee disarticulation, with good clinical response [20].

In Bombay, India, a bone cyst in the metaphysical region of the distal femur and proximal tibia of the lower limb was in a patient with OI, and numerous associated bone deformities, without a positive family history for OI [21].

The distal fibula plays an important role in the static stabilization of the ankle, along with the distal tibia, the tibiofibular syndesmosis and other ligaments that form part of the deltoid ligament and the lateral ligaments. In immature skeletons the inaptitude in this bone segment can lead to abnormalities in valgus and growth deficit, as well as lower limbs with asymmetries of length [22-24]. Several studies recommend reconstruction when opted for distal fibula resection, to mitigate risks of instability, with descriptions of techniques with varying degrees of complexity and limitations [23,25]. Although the literature recommend reconstruction of the distal fibula, the patients described in our study showed no signs of instability, as well as complaints during their follow-up, developing with good functionality of the joint and proper walking and without deformities.

Conclusion

Due to the uncertainty of data regarding the overall incidence of bone tumors, the presence or absence of the association of bones tumors with imperfect osteogenesis, more specifically that of type 5, cannot be affirmed. In this way more studies are needed as to the epidemiology of these associated pathologies.

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Conflict of Interests

The authors declare that there is no conflict of interest.

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