

CHALLENGES IN SURGICAL ORTHOPEADIC TREATMENT IN A CASE OF PYCNODYSTOSIS: SOMETIMES YOU WIN, SOMETIMES YOU LEARN.

Summary: Pycnodysostosis is a rare skeletal dysplasia caused by a lysosomal storage disorder, which is, in turn, caused by a mutation in the cathepsin K enzyme gene. This study reports the case of a 16-year-old patient suffering from pycnodysostosis with dental/maxillofacial (ho trovato anche "dento-skeletal"), spine and appendicular skeleton dysmorphism. In order to correct the bilateral femoral deformities, we performed osteotomies and synthesis with intramedullary nails. We treated the right femur first; the patient later developed the following complications post-operatively: severe anaemia and a systemic Staphylococcus Hominis infection. The left femur was then subsequently treated with a revision of the intramedullary nail - priorly implanted for a diaphyseal fracture in the patient's country of origin - a corrective osteotomy and the positioning of a new nail. Post-operatively, the patient suffered a per-subtrochanteric compound fracture of the left femur. At the last radiographic follow-up 14 months post-operatively on the right femur and 5 months post-operatively on the left femur, there was complete consolidation of the osteotomy and satisfactory correction of the deformity with restoration of a correct loading axis of the right side and initial consolidation of the osteotomy and per-subtrochanteric fracture of the left side. The patient walks autonomously without pain and his quality of life has significantly improved.

Keywords: Pycnodysostosis, bone diseases, skeletal deformities, femur fracture, femoral intramedullary nail.

Introduction

Pycnodysostosis (OMIM 265800) is a rare skeletal dysplasia caused by a lysosomal storage disorder, transmitted in an autosomal recessive manner, the exact prevalence of which is unknown, though it is, in any case, less than 1 in 100,000 [1]. The genetic cause can be found in the mutation of the CTKS gene (locus 1q21), which causes a deficit in the activity of cathepsin K enzyme. This enzyme, expressed by the osteoclasts, partakes in the bone resorption process, thus a deficit of said enzyme leads to osteosclerosis, the formation of abnormal bone matrix with increased density and a predisposition to pathological fractures of long bones in particular [2, 3, 4, 5]. The clinical manifestations are heterogeneous: delayed growth associated with short stature, craniofacial dysmorphisms with delayed closure of the cranial sutures, acro-osteolysis and pathologic fractures that are difficult to heal. The following are sometimes associated to the aforementioned pathologies: endocrinological issues, haematological issues and upper airway obstruction associated with OSAS [6, 7, 8, 9]. The diagnostic suspicion arises in the presence of short stature, skeletal dysmorphism and a history of repeated fractures.

Case report

The authors describe the case of a patient of 17 years and 7 months, weighing 37 kg at a height of 137cm, who comes from Algeria, specifically from an ethnic group of the Sahara Desert with a high percentage of consanguineous marriages. The **patient** (boy) came to us with a diagnosis of pycnodysostosis and a history of numerous prior fractures, two of which affecting the right femur and one the left femur. The radiograph showed: dolichocephaly, elongated sellar region, flattened mandibular profile, hypertelorism, limiting sclerosis vertebral somatic with "diapason shaped" vertebrae, right-convex dorsal scoliosis, oval-shaped iliac wings with poor development of the acetabular roofs, multiple previous fractures of the femoral shaft and a procurvatum deformity, previous fractures of the medial third of both tibias, brachitelefalangia (non ho trovato la traduzione) of the toes and hands with fragmentation of the distal phalanges, bilaterally curved radius. (Fig. 1, 2, 3). (controllate bene tutta questa sezione perché non sono sicurissima di tutti i termini tecnici)

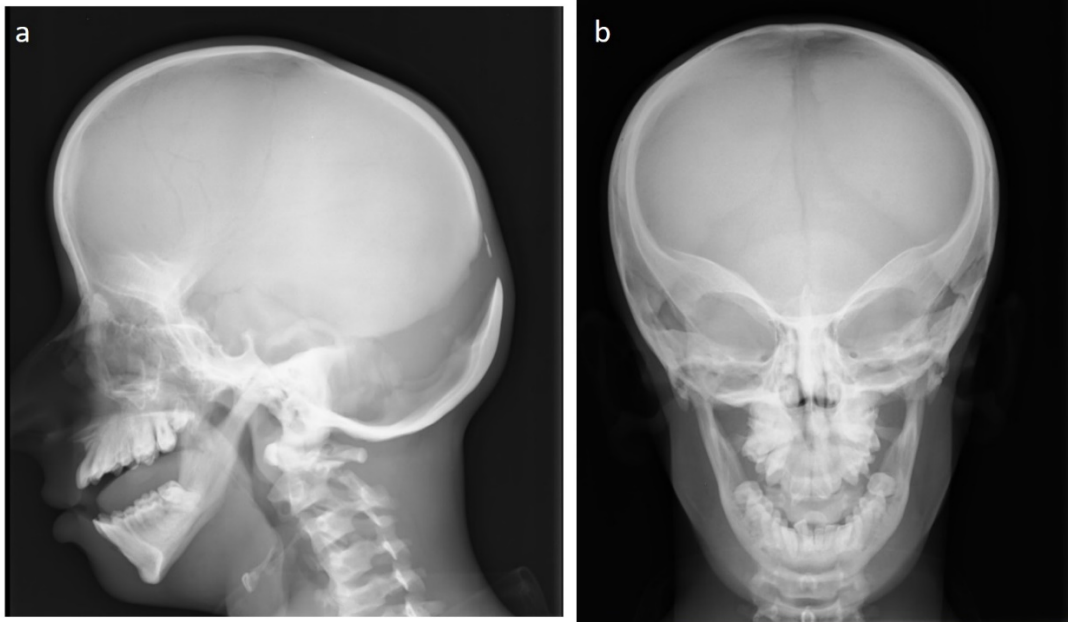


Fig. 1. Skull X-rays: a) Anteroposterior view; b) Lateral view.

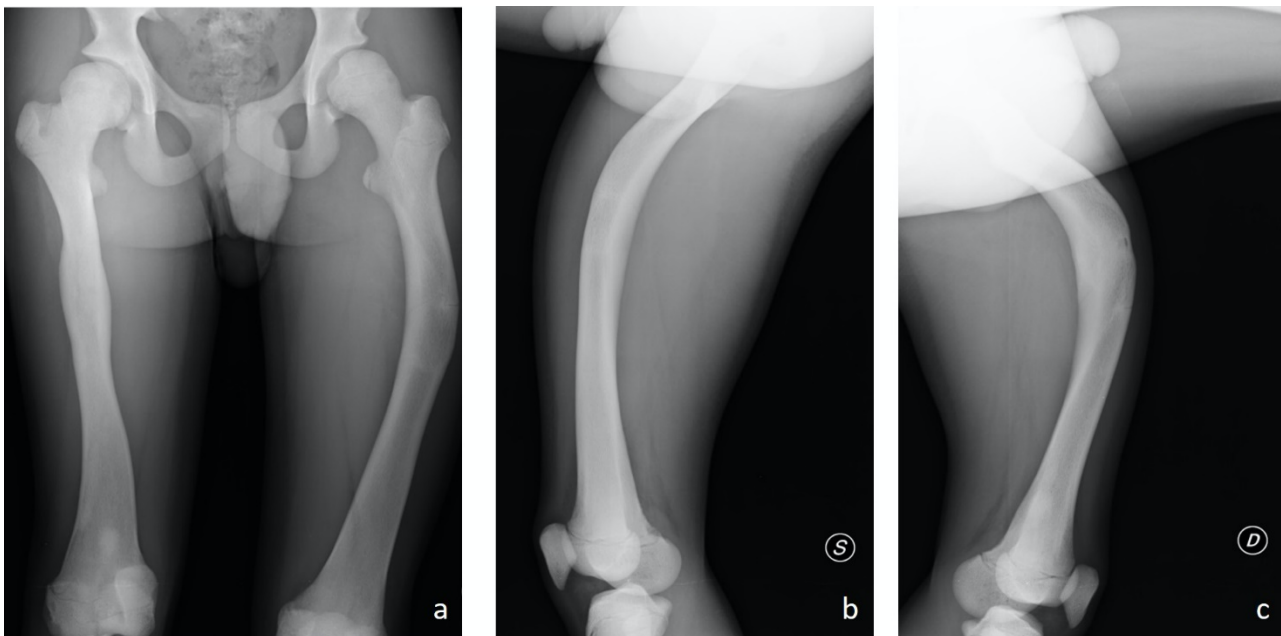


Fig. 2. a) Anteroposterior X-ray of the pelvis and the femurs showing alterations of the acetabular development, femoral deformities and signs of previous fractures; b) Lateral radiograph view of left femur; c) Lateral radiograph view of right femur.

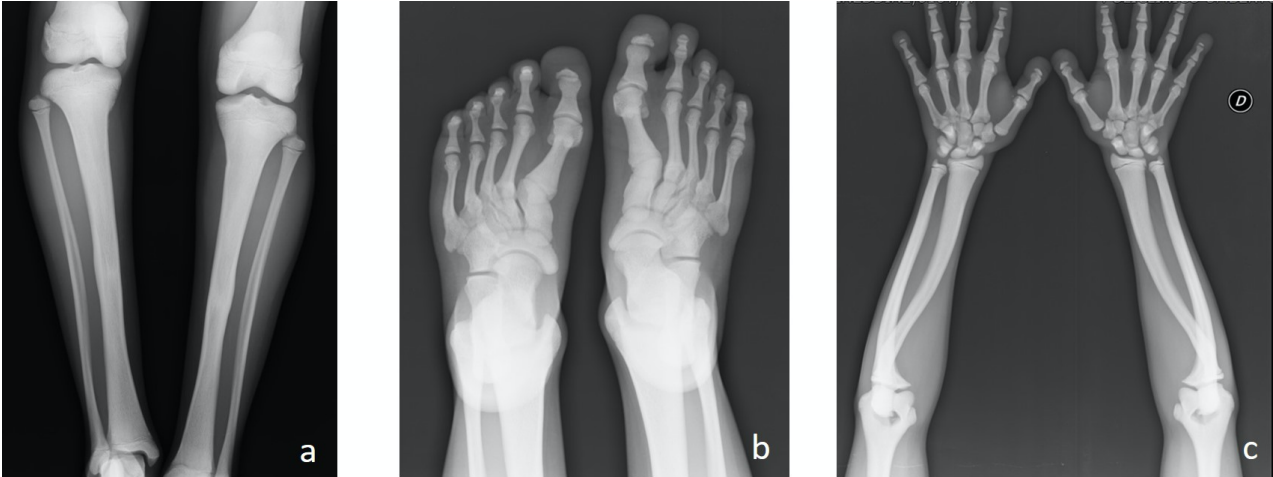


Fig. 3. a) anteroposterior view X-ray of bilateral tibia and fibula showing signs of previous fractures; b) dorsoplantar view X-ray of left and right foot with hallux valgus and partial bone resorption of distal phalanges; c) X-ray of right and left forearm and hand showing deformity of the radius and partial bone resorption of distal phalanges.

The physical examination revealed milk-coffee coloured skin staining in the sternal region, some alterations of the **dental bite(?) (non trovo traduzione per eruzione dentaria)**, a heterometry of the lower limbs of about 3 cm with a recurvatum deformity of left knee and bilaterally pronated feet with forefoot abduction, mostly on the right side. The prescribed therapy was surgical correction of both femurs by means of osteotomies and osteosynthesis with intramedullary nails, in order to prevent the onset of new fractures at the apex of the deformities and improve lower limb functionality and quality of life. The CT examination of the lower limbs showed: on the right femur, prior fractures of the medial-proximal third with medial cortical thickness of 7 mm, lateral cortical thickness of 7 mm and a reduction in the diameter of the medullary canal, which was around 7 mm; on the left femur, prior fractures with medial cortical thickness of 3.5 mm, lateral cortical thickness of 5.5 mm and a minimum diameter of the medullary canal of 9.5 mm (Fig.4).



Fig. 4. Three-dimensional Ct scans of the lower limbs showing femoral and tibial deformities: a) Anteroposterior view; b) Right lateral view; c) Left lateral view.

In February 2019, the patient underwent surgery to correct the deformity of the right femur procurvatum by means of wedge osteotomy and synthesis with an Adolescent Lateral Femoral Nail ALFN DePuy Synthes 8.2mm diameter intramedullary nail. During the surgery, we encountered marble bone consistency with complete obliteration of the medullary canal, which made reaming the canal very difficult and caused one of the drill bits to break (Fig. 5).

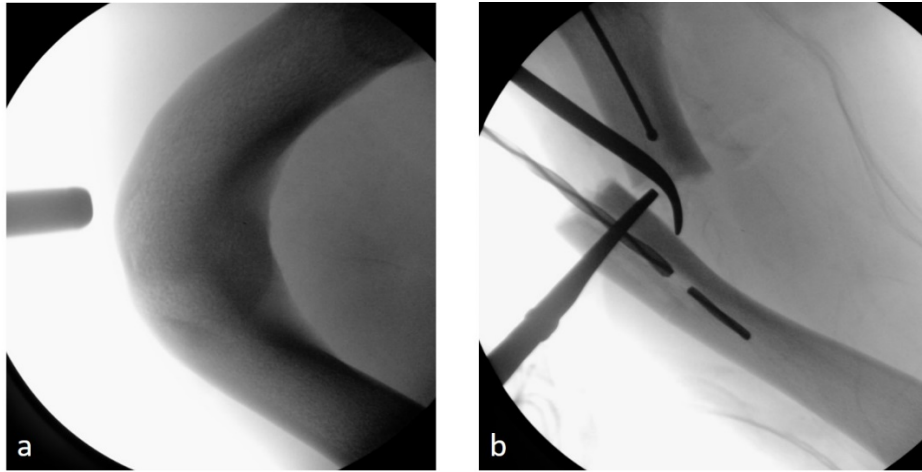


Fig. 5. Intraoperative X-rays of the right femur: a) Initial condition of deformity; b) Breakage of the drill bit.

Following a risk-benefit assessment to calculate the technical difficulties and the extension of the surgical times, along with its associated risks, we decided it was inconvenient to remove the drill bit as this did not hinder the positioning of the nail within the medullary canal. The surgery continued with moderate blood loss and satisfactory deformity correction. In the immediate post-operative period, the patient spiked a persistent fever, reaching a peak body temperature of $>38^{\circ}\text{C}$ on day 4 and a simultaneous increase in CRP ($45900\ \mu\text{g/L}$) and neutrophils ($10.25 \times 10^9/\text{L}$) levels. Three blood cultures were performed, one of which was positive for *Staphylococcus hominis* while the other two were negative; the patient was set up with specific antibiotic therapy and the infection was resolved in about two weeks. The patient also developed progressive post-operative anaemia, reaching, on the 5th day, a Hb value of $6.2\ \text{g/dL}$, 17.2% HCT, $\text{PLT } 231 \times 10^9/\text{L}$. His platelet aggregation test results showed no functional impairment; a supplementation of iron and folin was administered, resulting in a progressive increase in haemoglobin values. On the 7th post-operative day, the patient began motor function re-education in bed with passive and active mobilisation of the hip and right knee. On the 15th post-operative day a radiograph was performed, which showed satisfactory results, and he began motor function re-education in a standing position, deambulating with walking aids and partial weight bearing (Fig. 6).



Fig. 6. Anteroposterior X-ray of the right femur at the 15-day follow-up.

Upon discharge, which occurred 20 days after surgery, the boy was in good general condition, walking with 2 Canadian crutches and taking iron and folic acid supplements orally. Once he returned to his country of origin, the patient found it difficult to access hospital facilities in order to carry out his rehabilitation and follow-ups. It was also difficult for us surgeons to communicate effectively with local caretakers and the patient's clinical information was only obtainable via e-mail through with the collaboration of a humanitarian organisation. Follow up radiographs were received forty and seventy days after surgery, showing satisfactory results. Full weight bearing without walking aids was achieved two months after surgery, with complete **articulation** of the hip and right knee. About eight months after the surgery on the right femur, the boy suffered an accidental fall with subsequent fracture of the proximal third of the diaphysis of the left femur and **underwent reduction surgery and osteosynthesis** with an intramedullary nail in an Algerian hospital. We have no precise medical records of this event. By analysing the radiographs, we deduced that our colleagues encountered considerable difficulty in performing the synthesis of the fracture, as they were not able to place the nail far enough inside the medullary canal. In fact, there was a considerable proximal protrusion of

the nail and the ipsilateral iliac wing appeared altered, which led us to assume that our colleagues had carried out said alteration to allow hip movement. The patient was now 18 years and 4 months old and had painful symptoms with severe functional deficit of the left femur. We therefore recommended intramedullary nail revision surgery. In November 2019, we removed the synthesis **medium** and performed a corrective wedge osteotomy and positioned a new Lateral Femoral Nail LFN DePuy Synthes 10mm diameter intramedullary nail, with a dynamic proximal screw and a distal screw (Fig. 7). During the surgery, we encountered a non-displaced fracture of the medial cortex, around 1 cm distally from the lesser trochanter, and therefore decided not to place additional means of synthesis.

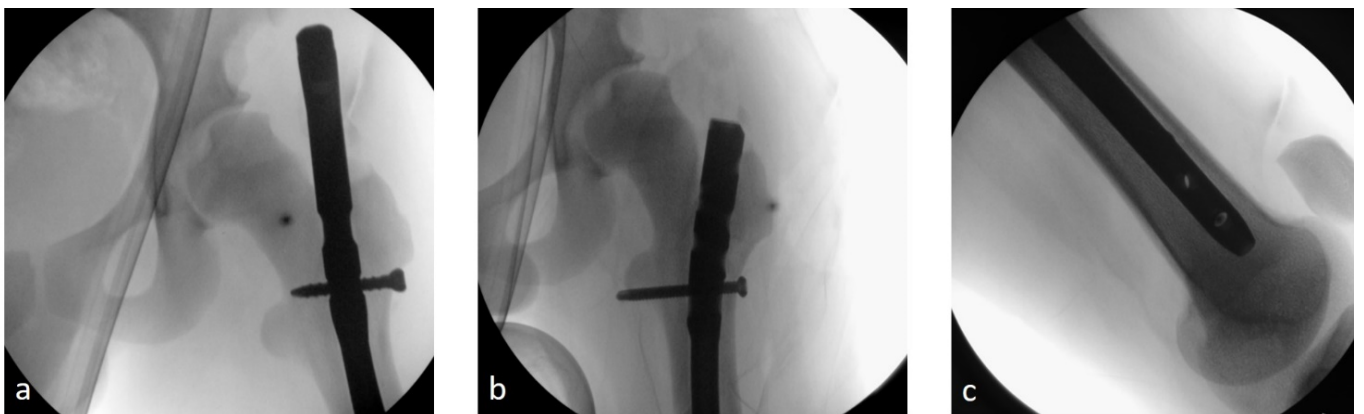


Fig. 7. Intraoperative X-ray of the left femur: a) initial condition with proximal protrusion of the femoral nail and altered shape of the iliac bone; b) X-ray of proximal femur performed after positioning the new nail; c) X-ray of the distal femur performed after positioning the new nail.

The immediate post-operative period was avoid of complications. On the 5th post-operative day, the patient started motor function re-education in bed with active and passive mobilisation of the hip and knee, and was placed in a seated position. On the 15th postoperative day, a radiograph was performed and the patient began deambulatory motor function re-education with progressive weight bearing recovery. The boy was then discharged in good general condition twenty days after surgery and returned once again to his country of origin. The radiographic follow up forty days after the

surgery, received by e-mail, showed a new per-subtrochanteric fracture of the left femur with partial proximal mobilisation of the intramedullary nail, thus instructions were given prohibiting weight bearing for forty-five days (Fig. 8).

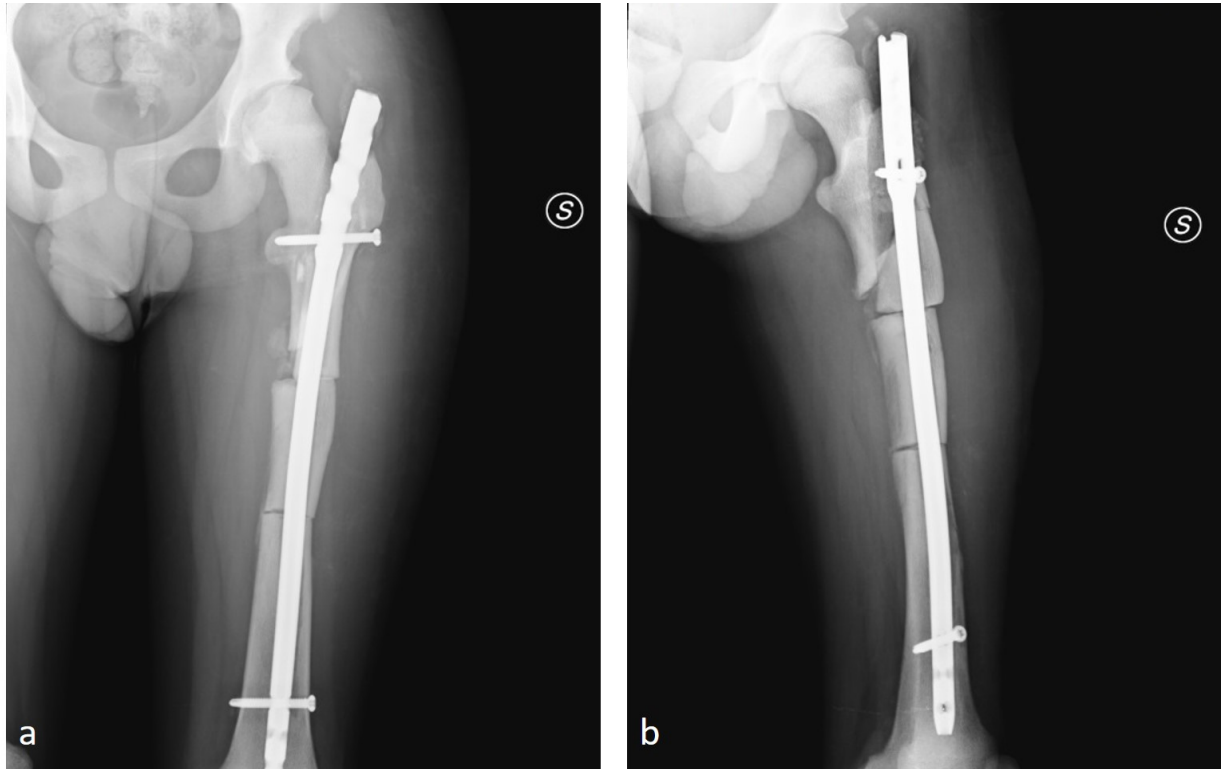


Fig. 8. X-rays of the left femur performed at forty postoperative days showing a new per-subtrochanteric fracture and partial proximal migration of the nail: a) anteroposterior view; b) Lateral view

We did not receive further information from the patient until they performed new bilateral radiographs, now five months after the last surgery on the left limb and fourteen months after the surgery on the right limb. The left limb showed initial consolidation of the per-subtrochanteric fracture and osteotomy, with a good correction of the deformity and a good axial loading, with a slight deterioration in the proximal mobilisation of the nail; the right limb showed a satisfactory consolidation of the osteotomy and correct positioning of the synthesis medium (Fig.9).

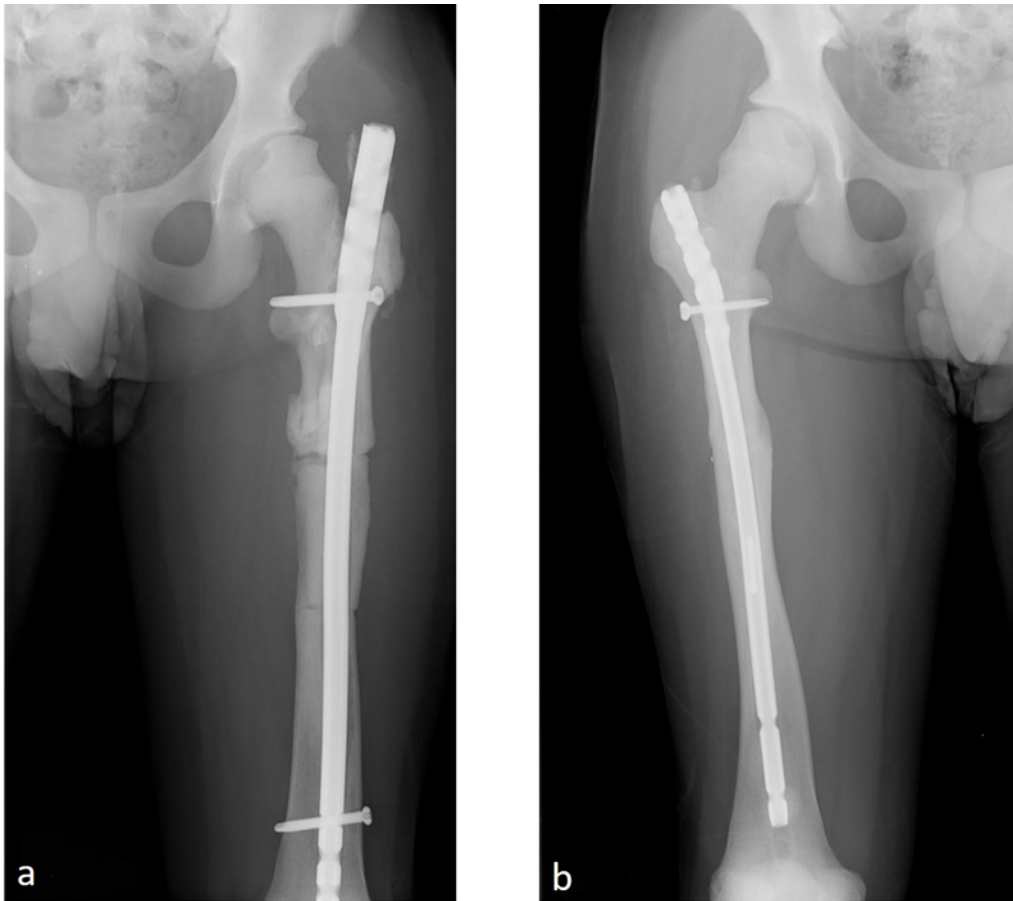


Fig. 9. a) X-ray of the right femur performed at fourteen months from surgery; b) X-ray of the left femur performed at five months from surgery.

We were told that the articulation of the hip and knee was bilaterally complete and void of pain, the patient walked independently and reported an improvement in his autonomy and quality of life. Despite the difficulties encountered during the follow-ups, we hope to obtain future updates on the patient's clinical and radiographic conditions that will confirm the good evolution of his medical framework.

Discussion

Pycnodysostosis is a rare disease that can cause heterogeneous clinical manifestations. Diagnostic suspicion is fundamental in cases of patients with short stature, associated with skeletal dysmorphisms and a history of repeated fractures [10, 11]. The differential diagnosis should include osteopetrosis, dysosteosclerosis, cleidocranial dysplasia and idiopathic acroosteolysis. In the case

of atypical fractures, especially of the femur, it should include hypophosphataemia, osteoporosis, osteoporosis-pseudoglioma syndrome, osteogenesis imperfecta, osteopetrosis [2]. The treatment of these patients is multidisciplinary. With regard to the orthopaedic treatment, it is necessary to correct the skeletal deformities of the long bones through osteotomies and subsequent synthesis with intramedullary nails. In the literature, there are few studies regarding this surgical treatment [12]. The use of plates for the synthesis of fractures in these patients is not recommended due to the increased risk of new fractures occurring above and below the plate itself, due to the resulting elastic modulus. What our experience has shown, in agreement with several authors, is that in pycnodysostosis the bone is fragile, even though it is sclerotic and has a marble-like consistency. This leads to multiple intra-operative technical difficulties both in the execution of osteotomies, the preparation of the intramedullary canal and subsequent insertion of the nail, with an increased risk of fracturing or micro-fracturing events that do not show up in the radiographs taken during the aforementioned steps. Therefore, a careful pre-operative study is required in order to set up the most suitable strategy and back-up plan in case of difficulty. The study of the bone segment, including the measurement of the diameter of the intramedullary canal, is necessary in order to have anatomical intramedullary nails of different diameters and multiple drill bits to be used in the event of possible instrument damage. The iatrogenic breakage of the drill bits is a possible complication [13, 14]. Furthermore, it is advisable to perform osteotomies with a chisel, possibly in combination with a **forage (non trovo traduzione, "reamer" forse?)** with small diameter drill bits to facilitate introduction, in order to avoid the use of the oscillating saw, which can increase the risk of bone necrosis. With regard to fracture healing, given the biological characteristics of the bone, several authors describe a delay in consolidation and a tendency towards pseudoarthrosis [15,16]. Our experience suggests that, despite a good surgical result and good clinical condition of the patient, it is still necessary to respect the appropriate times of full weight bearing abstention post-operatively. In fact, the analysis of the clinical case, given the presence of the per-subtrochanteric fracture found thirty days post-operatively in the left femur, on which the full weight bearing was granted fifteen days after surgery, suggests that intra-operative microfractures may have occurred and needed to be addressed more cautiously when granting weight bearing. These considerations may require further reflection on the

rigidity resulting from the insertion of the distal locking screw of the nail, which would therefore require a more prolonged abstention from weight bearing. Furthermore, some authors have shown that the consolidation of the fracture in these patients is not influenced by the biological stimulus on the bone given by the weight bearing [16]. Our clinical case also allows us to underline the importance of careful post-operative clinical laboratory monitoring and clear and effective communication with the patient and his parents, regarding the benefits and risks associated with surgery.

Conclusions

The approach for patients with pycnodysostosis must be a multidisciplinary one. Orthopaedic surgeons must take into account, in their pre-operative planning, the multiple technical difficulties they may encounter in relation to the particular characteristics of the bone, which has a marble-like consistency and is fragile at the same time, in order to ensure the presence of suitable instruments in the operating room. The surgical approach that we suggest, in case of fractures or deformities of the long bones in these patients, is the execution of corrective osteotomies and subsequent synthesis with an anatomical intramedullary nail of adequate diameter. Abstention from full weight bearing must be assessed in relation to the rigidity obtained from the synthesis. Radiographic follow-ups are necessary to monitor bone callus formation, as well as to detect any new fractures. Clinical and laboratory monitoring in the immediate post-operative period is essential to identify any complications.

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