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ORIGINAL STUDY

Autologous bone marrow injection in the management of simple bone cysts in children

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The majority of simple bone cysts (SBC's) is not symptomatic and remains undiagnosed or is discovered fortuitously. A number of simple bone cysts are only diagnosed after a pathological fracture which occurs as a presenting symptom. Fractures are managed either conservatively or surgically, based on criteria such as the age of the child and the type and localisation of the fracture. The risk for fracture can be evaluated radiographically. In the absence of a fracture risk, plain radiographic follow-up is sufficient. In case of a high fracture risk, percutaneous aspiration and injection of bone marrow may be performed. The result of this treatment in 21 simple bone cysts with a high risk for fracture is reported. Slow regression of the cyst and progressive healing were obtained in 15 cases (71.4%) whereas no response was noted in 3 cases (14.3%) and recurrence in another 3 (14.3%), after a mean follow-up of 37.1 months. Guidelines are proposed for the follow-up and management of SBC.

INTRODUCTION

Historically the first descriptions of simple bone cyst (SBC) were made in the second half of the XIXth century, in anatomopathological studies which described "cystic degeneration of bone". In 1926, Adams *(1)* described a lesion which he called "fibrocystic disease of the humerus" and concluded that the preferential localisation of the lesion in the proximal part of the humerus and femur is related to maximal stress areas. The radiological and histological definition of the lesion was given by Jaffe and Lichtenstein in 1942 *(27)*.

Unicameral or solitary bone cyst (SBC) is a lytic bone lesion affecting children. The incidence is around 1/10 000 children each year *(30)*. It represents 3% of all primary bone tumours *(38)* and it is the third bone lesion in frequency in children after non ossifying fibroma and osteochondroma.

Taking into account 1151 SBC's from the largest series in the literature *(10, 11, 29, 31, 39, 47, 48, 51)*, there is a male predominance (66% of boys and 34% of girls). It is essentially a paediatric pathology since 93% of the cysts occur before the age of 20 years.

The aetiology remains unknown but various hypotheses have been put forward : local disturbance of bone growth owing to mechanical stress *(1, 27)*, disturbance of lymphatic drainage *(16)* venous obstruction *(14, 40)*, osteolysis due to lysosomal enzymes *(23)* or oxygen scavengers *(33)*.
Secondary SBC's have been described associated with non ossifying fibroma *(8)*, fibrous dysplasia or enchondroma *(55)*. One case of post-traumatic SBC has been reported *(36)*.

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Fig. 1. — Left : typical radiological aspect of a simple bone cyst : a centered metaphyseal oval lytic lesion without septation. Middle : blowed aspect and septation after two fractures and callus invasion. Right : the "fallen fragment sign" of Reynolds has a specificity of 100%.

Considering 1569 SBC's from the largest series published *(3, 10, 11, 22, 31, 39, 47, 51)*, the most common cyst localisations are the proximal humerus (52%) and proximal femur (27%). Less frequent sites are mid- or distal humerus (3%), mid- or distal femur (3%), proximal tibia (5%), calcaneus (3%), distal tibia (2%), fibula (2%), radius (0.5%), ulna (0.5%) and others (2%).

Calcaneal SBC differs from other localisations. Its discovery is most often fortuitous. It appears at a later age, in adolescents or in adults. Pathological fracture is rare and no treatment is required as the outcome is generally favourable *(53)*.

SBC is generally solitary. Only one case of multiple SBC has been described *(15)* with involvement of calcaneus, metacarpal, radius and ulna.

Macroscopically the cystic cavity contains a straw-colored fluid. The fluid may be blood-tinted of frankly bloody in cases with pathological fracture or following attempts to insert a needle into the lesion. Occasionally, partial or complete septation of the cyst may be seen. Microscopically, the cyst is lined with a thin layer of fibrous connective tissue. Thicker areas of the cyst wall contain multinucleated giant cells.

The cyst fluid is comparable to plasma *(16)* and contains lysosomal enzymes *(23)*. The intracystic pressure is increased in comparison with normal bone marrow pressure *(14)*.

The cyst activity is related to its proximity to the physis. An SBC is considered active when it remains close to the physis (< 0.5cm) because growth of the cyst is faster than bone growth. It is latent when far away from the physis (> 0.5cm) *(40)*.

Clinically, the majority of SBC's are painless and remain undiagnosed. The discovery of a humeral SBC generally occurs after a pathological fracture occurring as a presenting symptom. Femoral SBC's are diagnosed after they have fractured or because the child presents with pain and limping due to microfracture of the cyst wall. Fortuitous finding is also possible.

Radiographically (fig 1), SBC appears as a centered metaphyseal oval lytic lesion with possible septation (more frequent after fracture or treatment). The cortical bone may be made thinner but the subperiosteal bone is respected. After one or more fractures, a blowed aspect is possible due to callus invasion by the SBC (fig 1). The "fallen fragment sign" described by Reynolds *(44)* is present in 10% of SBC's at the time of diagnosis and has a specificity of 100% (fig 1). Plain radiographs are often sufficient to make the diagnosis. MRI is useful for doubtful cases. The lesion has a high signal in T2-weighted images and an intermediate signal in T1-weighted images (fig 2). Fluid-fluid levels are never present, contrary to aneurysmal bone cyst (ABC) where fluid levels are present in 66% of cases *(52)*. Septa are present in only 37.5% of cases and are usually incomplete, in contrast with ABC (complete septa in 100%) *(52)*. Bone scan shows

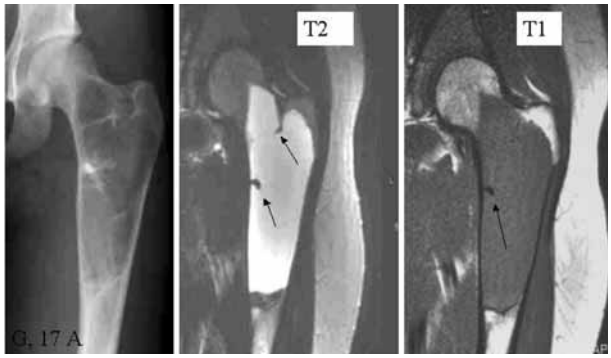

Fig. 2. — On MRI, the cyst displays a high signal in T2-weighted image and an intermediate signal in T1-weighted image. Fluid-fluid levels are never present. Septation is present in only 37.5% of cases and is usually incomplete (arrows).

reduced isotope uptake but this examination lacks specificity. Increased isotope uptake may be seen after fracture or in case of cyst healing.

The natural history of SBC is that of a lesion which originates in the center of cancellous metaphyseal bone, followed by centrifugeal expansion. In case of cortical weakening, pathological fracture is possible. Healing may occur either spontaneously (which shows the potential of the cyst wall for bone formation) or after a fracture. The final outcome is generally disappearance of the cyst after skeletal maturity or evolution to a latent ossified cyst. In rare cases, a voluminous diaphyseal cyst persists.

Growth repercussions are rare but possible for juxtaepiphyseal SBC and premature epiphyseodesis has been reported after fracture *(7, 25, 35)* and may lead to limb length discrepancy, coxa vara, or humerus valgus. Epiphyseal involvement is also possible but it always occurs after at least two fractures *(42)*.

A simple bone cyst represents a mechanical threat for subsequent pathologic fracture. The fracture risk can be evaluated by two means : the cyst index of Kaelin and Mc Ewen *(31)* and the cyst diameter index according to Ahn and Park *(3)*. When the cyst index is more than 4 for a humeral SBC and more than 3.5 for a femoral SBC, the risk for fracture is high *(31)*. Mechanically, a cyst can be considered healed when the index is less than 3, with a cortical thickness more than 2 mm *(31)*. A cyst occupying more than 85% of the bone diameter is at high risk for fracture *(3)*.

The present study aimed at assessing the therapeutic value of one single autologous bone marrow injection, with bony healing of the cyst as the end point.

MATERIALS AND METHODS

Percutaneous injection of autogenous bone marrow was performed in 21 consecutive patients (table I) with a mean age at operation of 10.0 years (range 2 to 20 years). The classical male predominance was noted (14 boys and 7 girls). The cyst location was the proximal femur in 9 cases (43%), the proximal humerus in 7 (33%), the distal femur in 2 (9.5%), the distal tibia in 2 (9.5%) and the humeral shaft in one case (5%). Fifteen cysts (71%) were multiloculated and 6 (29%) uniloculated.

Twelve patients (57%) had sustained at least one previous pathologic fracture. The diagnostic circumstance was a pathologic fracture in all the 8 humeral cases (100%) with a mean number of 1.9 fractures per patient (range 1 to 4). The femoral cysts were found incidentally in 5 cases (46%), in 3 cases by radiological examination for limp (27%) and in 3 other cases after a pathologic fracture (27%) (mean number of fractures per patient 0.3 ; range 0 to 1). The presence of a fracture at the time of injection necessitated postoperative immobilisation in two cases. One patient had already undergone surgical curettage on two occasions and presented with a further recurrence. One other cyst had been previously treated by steroid injection, without success.

At the time of injection, 14 cysts (67%) were active whereas 5 cysts (24%) were latent according to Neer *(39)* ; another two occurred after physeal closure.

The fracture risk was evaluated in every case by two methods : the cyst index *(31)* and the cyst diameter related to metaphysis *(3)*. The mean cyst index at the time of injection was 4.6. The mean cyst diameter was 86% of the metaphysis diameter.

The minimal cortical thickness was less than 1 mm in 14 cases (67%) and less than 2 mm in 5 other cases (24%). According to one or more of these criteria, all the SBC's were at high risk for fracture before treatment.

The surgical procedure *(18)* was performed under general anaesthesia. The cyst was localised under fluoroscopy. A large trocar (12 gauge diameter, Unimed, Switzerland) was first introduced into the upper part of the cavity, then a second one into the lower part. The cyst fluid was allowed to flow out spontaneously and was then slowly aspirated. The final volume of fluid collected was measured, and a sample was sent for cytological study. No attempt was made to disrupt the lining membrane. A third trocar was used to obtain bone marrow from the anterior part of the iliac crest. One single suction was sufficient in all cases to obtain the desired volume, equal to the volume of fluid collected. The bone marrow was injected through one of the trocars until it was overflowing by the second trocar. The patients stayed in hospital overnight and were then discharged. No immobilisation was required for non fractured cysts. Those with fractures were immobilised until fracture healing.

Only autologous bone marrow was injected in the last 19 patients, but in the first 2 cases bone marrow and methylprednisolone acetate (MPA) at a dose of 40mg had been injected together. One single bone marrow

Table I. – The patient series

Case	Patient	Sex	Age (years) at injection	Location of the bone cyst	Initial lesion diameter (1)	Metaphyseal position (2)	Multi loculated	Finding circumstance	Presence of fracture at injection	Number of previous fractures	Previous treatment	Treatment	Follow-up	Result (3)	Mechanical healing (4)
N°1	BS	M	9	proximal humerus	>90%	< 0.5 cm	+	fracture	-	1	-	Bone Marrow + 40 mg MPA	39	complete healing	+
N°2	JV	F	8	proximal humerus	> 90%	< 0.5 cm	+	fracture	-	1	-	Bone Marrow + 40 mg MPA	38	complete healing	+
N°3	FS	M	10	proximal humerus	> 90%	> 0.5 cm	+	fracture	+	4	Bone	Bone Marrow	95	recurrence and fracture	-
N°4	JN	F	12	proximal humerus	> 90%	> 0.5 cm	+	fracture	-	1	-	Bone Marrow	41	partial healing	-
N°5	BL	M	2	proximal humerus	> 90%	< 0.5 cm	+	fracture	-	2	-	Bone Marrow	39	partial healing	-
N°6	BF	M	2	proximal humerus	> 90%	< 0.5 cm	+	fracture	-	2	-	Bone Marrow	8	partial healing	-
N°7	CC	M	18	proximal humerus	> 90%	> 0.5 cm	+	fracture	-	3	-	Bone Marrow	14	complete healing	+
N°8	DM	F	3	proximal femur	> 90%	< 0.5 cm	-	fracture	-	1	80 mg MPA	Bone Marrow	54	complete healing	+
N°9	SG	M	12	proximal femur	> 90%	< 0.5cm	+	incidental finding	-	0	-	Bone Marrow	26	complete healing	+
N°10	GM	F	5	proximal femur	> 85%	< 0.5 cm	-	fracture	+	1	-	Bone Marrow	76	complete healing	+
N°11	GBG	M	3	distal tibia	> 85%	< 0.5 cm	+	incidental finding	-	0	-	Bone Marrow	107	complete healing	+
N°12	LM	M	6	proximal femur	> 85%	< 0.5 cm	-	limp	-	0	-	Bone Marrow	24	complete healing	+
N°13	DPO	M	5	proximal femur	> 85%	< 0.5 cm	+	fracture	-	1	-	Bone Marrow (2x) 2nd after 7M	23	recurrence and fracture	-
N°14	LB	M	19	humeral shaft	> 80%	> 0.5 cm	+	fracture	-	1	-	Bone Marrow	24	no response	-
N°15	LQ	M	19	proximal femur	> 85%	< 0.5 cm	+	incidental finding	-	0	-	Bone Marrow (2x) 2nd after 7M	23	no response	-
N°16	GB	F	17	proximal femur	> 85%	closed physis	+	incidental finding	-	0	-	Bone Marrow	40	complete healing	+
N°17	MC	F	13	proximal femur	> 85%	< 0.5 cm	+	limp	-	0	-	Bone Marrow	40	no response	-
N°18	DJ	M	16	distal femur	77%	> 0,5 cm	-	incidental finding	-	0	-	Bone Marrow	8	partial healing	-
N°19	DL	F	20	distal femur	60%	closed physis	-	incidental finding	-	0	-	Bone Marrow	7	partial healing	+
N°20	RJ	M	10	proximal femur	> 90%	< 0.5cm	+	limp	-	0	-	Bone Marrow	13	fracture after 6 weeks	-
N°21	LY	M	2	distal tibia	> 90%	< 0,5cm	-	fracture	-	2	-	Bone Marrow	20	complete healing	+

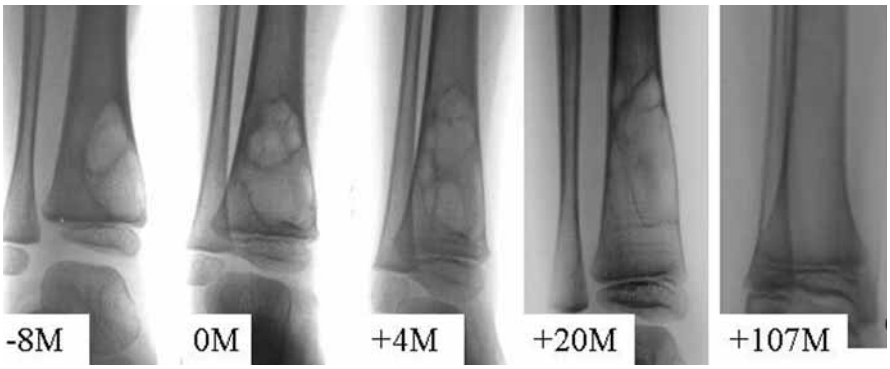

Fig. 3. — A 3-year-old boy with a distal tibial SBC. The cyst was initially monitored. The cyst was in an expanding phase. When the fracture risk became important (cyst diameter > 85% metaphysis), a percutaneous bone marrow injection was performed. Progressive healing occurred and was completed after 107 months.

injection was performed in 19 cases (90%) ; an additional injection was necessary in only 2 cases (10%).

The mean follow-up was 37.1 months (range : 7 to 107 months).

Postoperative assessment was performed with monthly radiographs for the first three months and every 6 months thereafter. The films were digitised with a high-resolution scanner. The digital pictures were analysed using the Scion image analysis software *(49)*. Bone density was measured and helped to distinguish healed and cystic zones. The cyst index *(31)* was calculated by delineating the area of the cyst, measuring its surface, and relating the latter to the diameter of the humeral diaphysis. The relative cyst diameter index *(3)* was determined by the ratio of the cyst diameter to the diameter of the metaphysis. The minimum cortical thickness over the cyst was also measured.

The final results were classified in 4 groups according to Capanna *(11)*. "Healing" is obtained when the cyst is filled with bone and the overlying cortex is thickened. "Healing with residual" describes a healed cyst with small residual areas of osteolysis. "Recurrence" is defined by the presence of large areas of osteolysis and cortical thinning which developed following initial signs of healing. "No response" is when there is no evidence of response.

RESULTS

Analysis of the cyst fluid confirmed in every case that the lesion was a simple bone cyst. Based on the relative cyst diameter index *(3)*, all the cysts except three were at risk for fracture before being treated. The response to treatment was monitored by the decrease in the cyst index and the relative diameter of the cyst, and by the increase in bone density.

Table II. – Global results with bone marrow injection in a series of 21 SBC's

RESULTS (N = 21)		
complete healing	10	47.6%
complete disappearance	4	19.0%
minor residual cystic areas	6	28.6%
partial healing	5	23.8%
recurrence	2	9.5%
no response	3	14.3%
postoperative fracture	1	4.8%

Complete healing (table II) was obtained in 10 cases (47.6%) with complete disappearance of the cyst in 4 children (19%) (fig 3) or persistence of minor residual cystic areas in the other 6 cases (28.6%). We obtained partial healing with improvement of the cyst index, reduction of the cyst diameter and cortical thickening in 5 children (23.8%) (fig 4). The fracture risk was decreased but was still present in these patients.

Recurrence occurred in 2 cases (9.5%) with re-fracture. The first case was treated by intramedullary nailing and went on to healing. The second was immobilised in a plaster cast, and a further bone marrow injection was performed, achieving partial healing.

One proximal femoral cyst fractured 6 weeks after the bone marrow injection procedure when

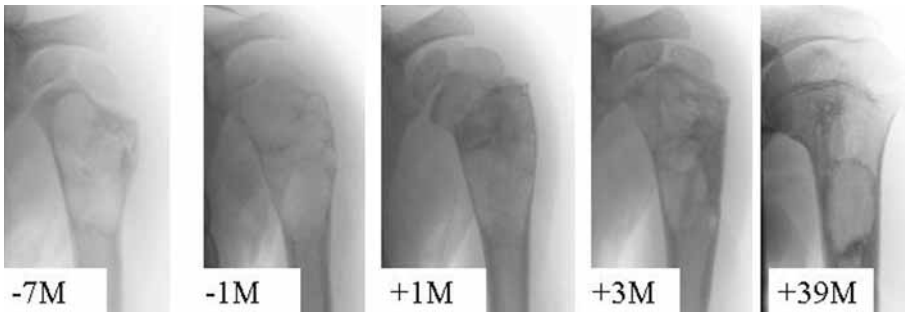

Fig. 4. — A 2-year-old boy with a proximal humeral SBC. He had already sustained two fractures. Progressive healing occurred after injection ; partial healing is achieved after 39 months, with a latent cyst.

the child fell at school (fig 5). Fracture healing as well as healing of the cyst were achieved after intramedullary nailing.

No response was obtained in 3 other cases (14.3%).

All the patients resumed their activities without restriction immediately after the injection or 3 months after radiological healing of fracture when present.

Fig. 5. — A 10-year-old boy who sustained a fracture 6 weeks after the bone marrow injection procedure. He underwent intramedullary nailing, and the osteosynthesis was protected by a plaster cast for 6 weeks. The nails were removed 9 months after fracture. The cyst partially reossified. The child recovered complete mobility. The fractured leg is 1 centimeter shorter than the contralateral side.

DISCUSSION

Historically, curettage and bone grafting in the treatment of SBC has been disappointing because of the very high recurrence rate : 33% of 259 SBC's for Campanacci *et al (10)* and 45% of 177 cases for Spence *et al (51)*. Furthermore this aggressive operation has a high rate of complications such as premature epiphyseal closure (4%) or wound infection (1%) *(39)*. Percutaneous steroid injection was introduced by Scaglietti in 1974 *(46)*. In a large series of 141 SBC's, Campanacci *et al (10)* reported complete healing in only 50%, partial healing in 25%, recurrence in 15% and no response in 10%. One case of avascular necrosis of the femoral head has been reported after steroid injection in a proximal femoral SBC *(10)*. This method has become very popular owing to its simplicity and low morbidity ; however, 50% of patients require more than one injection *(41)* and an average of 3 to 4 injections of methylprednisolone acetate are generally necessary to obtain healing *(11, 28)*.

More recently, bone marrow has been proposed as an alternative to steroid *(13, 18, 19, 34, 56)*. Bone marrow injection will promote the osteogenic phase of the bone cyst. Using this technique, Yandow *et al* obtained complete healing in 67% of the cases, partial healing in 17% and no response in 17% *(56)*.

Numerous other treatments have also been reported : cystography *(28)*, plaster-of-Paris pellets *(43)*, Ethibloc injection *(2)*, hydroxyapatite *(26)* or triphosphate calcium implantation *(4, 12)*, multiple

Table III. – Recommendation for SBC management in children

HUMERAL SIMPLE BONE CYST
uncomplicated lesion
cyst index < 4 and cyst diameter < 85% radiographic follow-up
cyst index > 4 or cyst diameter > 85% percutaneous bone marrow injection
fracture complication
stable and undisplaced orthopaedic treatment
displaced intramedullary nailing
FEMORAL SIMPLE BONE CYST
uncomplicated lesion
cyst index < 3.5 and cyst diameter < 85% radiographic follow-up
cyst index > 3.5 or cyst diameter > 85% percutaneous bone marrow injection, activities restriction until cyst index is < 3 and cortical are larger than 2 mm
fracture complication
child < 6 years orthopaedic treatment
child > 6 years intramedullary nailing or proximal femoral nail

percutaneous drilling with a Kirschner wire *(32, 50)*, perforation of the cyst wall with a cannulated screw *(20)*, intramedullary nailing *(29, 45)*.

Our treatment seems to be acting by two mechanisms : firstly by relieving the pressure within the cyst, which is thought to be an important pathogenic factor *(14, 16, 20, 32, 54)* and secondly by the effect of the bone marrow. The use of two large gauge trocars is critical in order to achieve long lasting decompression, which is a requisite for success. In addition, red marrow has been shown to improve osteogenesis in both experimental models and in man *(6, 9, 17, 21)* and osteogenic stem cells have been demonstrated in the marrow *(5, 37)*.

Recurrence was noted in only two cases (9.5%). A negative outcome is not immediately predictable, as there may be an initial period of improvement, followed by recurrence. The first case was a voluminous humeral cyst in a 10-year-old boy who had undergone curettage and bone grafting on two occasions without success. The cyst had resulted in four previous fractures. The cyst recurred and a fifth fracture occurred 89 months postoperatively, but it was related to a high-energy trauma. Healing was then obtained after intramedullary nailing. The second case with recurrence was a large femoral cyst in a 5-year-old boy who had sustained a fracture at the time of injection. A second bone marrow injection was made 7 months later, without success, and a further fracture occurred after 23 months. A plaster cast was applied until radiological fracture healing and a third bone marrow injection was then performed, resulting in partial healing. These two cases presented one or more risk factors for recurrence : age < 10 years, activity, volume, humeral cyst *(10, 24, 41)*.

The case which presented a postoperative fracture (fig 5) was a large femoral cyst in a 10-year-old boy. A pathological fracture occurred 6 weeks after the injection procedure when the child fell at school. This fracture may be considered as a complication of the cyst wall perforation with the two large trocars. Intramedullary nailing was followed by healing of the lesion.

No response was observed in 3 cases (14.3%) but no further fracture occurred in these 3 patients after a follow-up of 23, 24 and 40 months respectively.

Overall, the treatment proved efficient in 71.4% of the patients. In 47.6% the fracture risk was cleared, and healing of the cyst was obtained. Femoral cysts seem to progress less rapidly than humeral cysts. In another 23.8% of the children, the fracture risk was significantly decreased.

Percutaneous injection of bone marrow is a safe and reliable method of treatment for simple bone cyst at risk for fracture. The operative method is very simple. One-day surgery is possible. Only one complication (4.8%) was observed associated with the procedure (a pathological fracture six weeks after injection). No immobilisation is needed postoperatively, except in case of fracture.

Our proposed recommendations are summarised in table III. Uncomplicated lesions are monitored, with determination of cyst index and cyst diameter. When the risk of fracture is high, a percutaneous bone marrow injection is performed and in case of a femoral SBC, restriction of activities is mandatory. When a humeral fracture occurs, it is generally a stable non-displaced metaphyseal fracture and conservative treatment is sufficient. Cyst healing is frequent after fracture. In case of a displaced frac-

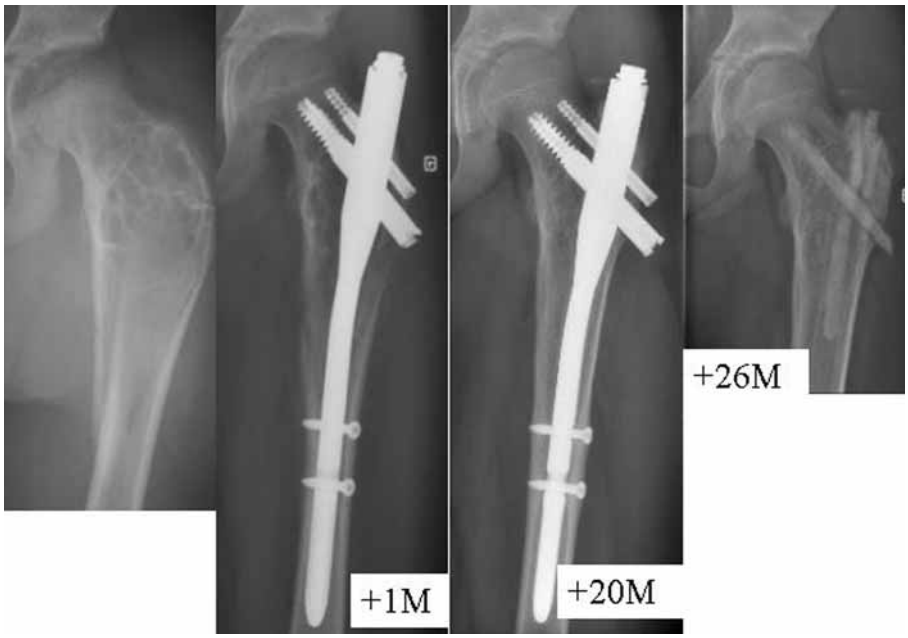

Fig. 6. — A 10-year-old boy who presented with a pathological fracture of the femur secondary to a large SBC. Osteosynthesis was performed with a proximal femoral nail. Complete healing was obtained and the nail was removed after 20 months. Lyophilised cortical struts were implanted into the nail track. Full mobility was recovered 3 months after hardware removal. The fractured leg is 12 mm longer than the contralateral side, due to growth stimulation.

ture, intramedullary nailing is performed to stabilise the fracture and to treat the cyst. In case of a femoral fracture, surgical treatment is preferable, except in the small child (< 6 years) where conservative treatment is possible. Intramedullary nailing sometimes requires an additional plaster cast immobilisation in case of a very large cyst. A possible alternative technique in this particular case is the proximal femoral nail (fig 6).

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