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ORIGINAL STUDY

Treatment outcome in 60 children with pathological fractures of the humerus caused by juvenile or aneurysmal bone cysts

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The treatment of pathological fractures of the humerus caused by juvenile or aneurysmal bone cysts (JBC/ABC) should be a single approach with a high success rate and low complication rate. This study evaluates how day by day treatment concepts fulfil these aims.

Children below 15 years of age with a pathological fracture of the humerus caused by a JBC or ABC between 01.01.2001 and 31.12.2010, were investigated by chart review in four major paediatric trauma centres. Age, gender, fracture localisation, X-ray findings, treatment and outcome - assessed by the Capanna classification (I to IV), were analysed.

60 children [41male, 19 female; mean age: 9 years (4-14 years)] with 43 JBC and 12 ABC were included as well as five cysts, who could not be classified definitively. First treatment was non-operatively in 33 children. Of these 27 cysts did not improve; likewise the supportive installation of cortisone in six patients did not change the outcome. The first treatment consisted of elastic stable intramedullary in 13 children; up to three nail exchanges included. But only six of these reached (nearly) complete resolution (I/II). Overall the combined mechanical and biological treatment with curettage, elastic stable intramedullary nailing, (artificial) bone substitute and in some cases growth factors was performed as the 1st-line treatment in nine patients and further in 2nd or 3rd-line treatments in 13 humeral cysts. More than half of these reached a complete or nearly complete resolution of the cyst (12x I, 5x II, 1x III, 4x IV).

Major complications in all operated patients were six nails not removable and two children with upper extremities length differences.

Healing rates are low for non-operative treatment, elastic stable intramedullary nailing alone and by using cortisone for cysts resolution in pathological fractures of the humerus. Data support a combined mechanical and biological treatment with curettage, elastic stable intramedullary nailing, (artificial) bone substitute and the use of growth factors.

Keywords : bone cyst; pathological fracture; children; humerus.

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INTRODUCTION

Pathological fractures are the most common presentation of juvenile or aneurysmal bone cysts in children (*29*). Both types of cysts weaken the cortex, predisposing the bone to pathological fractures which occur most often in the proximal metaphysis of the humerus (*7*). No causal therapy currently exists for juvenile and aneurysmal bone cysts because their definite aetiology has remained unknown since their first description (*31*). In contrast to a random finding of a juvenile or aneurysmal bone cyst, a pathological fracture often needs immediate treatment due to pain and (more rarely) due to instability of the fracture. A wide range of different treatment options exists (*6,11,23,25*), from the principle of 'watch and wait' for spontaneous consolidation, which occurs in around 15% of all cysts after fracture (*7,20*), decompression of the cyst by cannulated "decompression" hollow screws (*1,12*) to combinations of osteosynthesis and biologicals (*17,26*). In addition, the filling of the cysts is reported: with cortisone (*28,32*), bone marrow (*5,33*) or bone grafts (*6,14*). Another approach is the stabilisation of the bone in combination with cyst decompression by elastic stable intramedullary nailing (*18*). This procedure can also be combined with curettage, different kinds of bone substitute (*3,7,17*) and individual or combined application of growth factors (*26*). However, none of these various treatments has been evaluated in a level 1 randomized controlled trial; mainly retrospective case series are published referring to one institution with different the cyst locations or combinations of pathological fractures and random findings of bone cysts (*16*). Another problem is of promising short-term results, for example early studies with percutaneous injection of methylprednisolone acetate, which cannot later be substantiated when using clear in- and exclusion criteria (*13*). Failure rates of about 80% for cortisone, 64% for isolated curettage and 50% for combined procedures with bone marrow are reported in literature (*28*). A similar problem seems to exist for elastic stable intramedullary nailing and the application of biologicals. Around a decade ago surgeons began to use elastic stable intramedullary nailing more frequently for stabilizing pathological fractures of juvenile and aneurysmal bone cysts. Following stabilization, very high success rates in the complete healing of the cysts were, and still are, reported in the literature (*18,24*). However, other studies could not confirm this and reported a prolonged healing period and the requirement for the exchange of the elastic stable nails once, twice or up to four times during therapy (*26,27*). Because of this Kanellopoulos and his colleagues described, some years ago, a novel combination therapy of osteosynthesis and biologicals (*17*). Their treatment concept employed successfully demineralised bone matrix and autologous bone marrow injection in addition to intramedullary nailing; but no long term results or further case series were published.

The German society of paediatric surgery has defined treatment goals in their guidelines for the evaluation of nowadays and future treatment concepts (*16*):

— A single approach should lead to complete healing.

— The duration of the treatment concept should be as short as possible.

— Treatment should offer a very high success with a low complication rate.

— A treatment concept should offer the child a fast recovery and participation in all age-related activities without any restrictions in sporting activities or contact with his peers.

The aim of this study is to evaluate the actual day-by-day treatment in different clinics focused on pathological fractures of the humerus and to describe how current treatment concepts fulfil the aims of the guidelines in daily practice.

PATIENT AND METHODS

The study population comprised all children and adolescents below 15 years of age with a pathological fracture of the humerus caused by a juvenile or aneurysmal bone cyst treated in one of the four participating paediatric surgery trauma centres between 1 January 2001 and 31 December 2010. Children with an asymptomatic juvenile or aneurysmal bone cyst as well as those without a pathological fracture were excluded from further investigations.

The selected paediatric surgery trauma centres were located in different parts of Germany; two in urban cities and two in smaller cities with a more rural community. Each was a referral for paediatric fracture treatment with experts on call.

The retrospective data collection from medical charts and images in each clinic included for each patient: gender, age, localization of pathological fracture (proximal or distal metaphysis, diaphysis), cyst type (defined by radiological imaging or histopathological examinations), method of non-operative or operative treatment, type of osteosynthesis, type of bone substitutes and use of biologicals. Short-term follow up comprised peri- and postoperative morbidity, time and number of refractures and major complications such as growth plate arrest.

The outcome of each treatment cycle was classified by X-ray according to the scheme used by Capanna, either at the last recorded visit or at the time a further treatment was arranged due to failure of the earlier concept or became necessary due to a refracture (*2*):

— Grade 1 = healed – the cyst was completely filled in and the cortical margin thickened

— Grade 2 = healed with residual cyst – the cyst was consolidated with bone and the cortical margin thickened but there were still residual cyst parts

— Grade 3 = recurrence – the cyst initially consolidated with bone, but large areas of osteolysis and cortical thinning subsequently recurred

— Grade 4 = no response – the cyst showed no evidence of response to the treatment.

Grades 1 and 2 were defined as success; grades 3 and 4 represented a failure in treatment. Afterwards all data were anonymised and sent to the main study centre for analysis.

Statistical analysis remained descriptive due to the heterogeneity of treatment concepts.

RESULTS

60 children [mean age: 9 years (4-14 years)] fulfilled the study criteria; twice as many boys (n = 41) as girls (n = 19). The pathological fractures occurred in the proximal metaphysis in 38 children and in the diaphysis in 19 children. Bone cysts were juvenile in 43 cases and aneurysmal in 12; five cysts could not definitely be classified as juvenile or aneurysmal by X-ray (Table I).

During the treatment period, histopathological examination confirmed the diagnosis of 24 juvenile and 7 aneurysmal bone cysts; one further case of each was later classified by magnetic resonance imaging.

More than half of all humeral bone cysts were treated non-operatively by bandage during first-line treatment [Gilchrist ®] but, whereas only 6 of 33 children reached complete or almost complete resolution of the cyst (Capanna I/II), 22 needed further treatment methods (Table II).

Treatment with elastic stable intramedullary nailing alone in the 1st or 2nd treatment cycle was successful in 8 of 19 children. In treatments of 7 children using cortisone with or without osteosynthesis in the 1st, 2nd and 3rd treatment cycle, two reached Capanna II, the others were classified as 1´ Capanna III and 4´ Capanna IV.

In all treatment cycles, combined therapy concepts of osteosynthesis and biologicals, such as stabilisation with elastic stable intramedullary nailing, complete curettage of the cyst, filling the defect with bone substitutes and (sometimes) added growth factors, were successful in most cases (n = 22 ; 12´ Capanna I, 5´ II, 1´ III, 4´ IV) and always reached Capanna I or II if growth factors had been added (n = 11; 9´ Capanna I, 2´ Capanna II).

As well as a total of 20 refractures in 7 children, two further major complications arose: in six

Table I. — Bone cyst type and localisation of the pathologic humeral fractures: n = 60 (% in brackets)

	Localisation of the pathological fracture / bone cyst	
Cyst type	*proximal metaphysic: n = 42 (70)*	*diaphysis: n = 18 (30)*
Juvenile bone cyst: n = 43 (72)	31 (52)	12 (20)
Aneurysmal bone cyst: n = 12 (20)	7 (12)	5 (8)
Not classified: n = 5 (8)	4 (6)	1 (2)

Table II. — Treatment cycles and outcome during the study period between 01.01.2001 and 31.12.2010

First line treatment **Ö second line treatment** **c third line treatment**	**1st cycle n = 60**	**2nd cycle n = 31**	**3rd cycle n = 14**	**Outcome measured by Capanna [*]**			
				I	**II**	**III**	**IV**
Conservative (non-operative) approach	**33**			**3**	**3**	**2 [2]**	**25 [20]**
Ö cortisone (~3x)		4		-	1	-	3 [2]
c bone substitute (S)			1	-	-	-	1 [1]
c ESIN			1	-	-	-	1 (~)
Ö cortisone (~3x) + ESIN		2		-	-	1 [1]	1 (#,~)
c cortisone			1	-	1	-	-
Ö curettage + bone substitute (A)		2		-	1	1 [1]	-
c ESIN + curettage + bone substitute (A)			1	-	-	1 [1,~]	-
Ö ESIN		6		-	2	-	4 [4]
c ESIN			1	-	1	-	-
c ESIN + curettage + bone substitute (A/H)			1	-	1	-	-
c curettage + bone substitute (A, A/S)			2	1 (A/S)	-	-	1 (A)
Ö ESIN + bone substitute (S)		5		-	1	-	4 [3](#)(~)
c ESIN + bone substitute (A,S)			3	-	-	1 (S)	2 (A, A/S)
Ö ESIN + curettage + bone substitute (A, S)		2			1 (A)		1 (S) [1]
c ESIN			1				1 [1]
Ö ESIN + curettage + bone substitute (S) + growth factor		1		1 (~)	-	-	-
Bone substitute (S) without curettage	**1**			**1**	**-**	**-**	**-**
ESIN	**13**			**2**	**4**	**3 [3]**	**4 [3]**
Ö ESIN + curettage + bone substitute (A, S)		2		1 (S,~)	1 (A)	-	-
Ö ESIN + curettage + bone substitute (H) + growth factor		4		3	1 [1]	-	-
c bone substitute (H) + growth factor			1	1	**-**	**-**	**-**
ESIN + curettage	**1**			**-**	**-**	**1 [1]**	**-**
Ö curettage + bone substitute (A)		1		1	-	-	-
ESIN + hollow screws	**1**			**-**	**-**	**-**	**1 [1]**
Ö hollow screws + cortisone		1		-	1	-	-
ESIN + curettage + hollow screws + cortisone	**1**			**-**	**-**	**-**	**1 [1]**
Ö conservative (non-operative)		1		-	-	-	1 [1]
c curettage + ESIN			1	-	1	-	-
ESIN + hollow screws + bone substitute (S) + antibiotics	**1**			**-**	**1**	-	-
ESIN + curettage + bone substitute (A, H, S)	**3**			**1 (A)**	**1 (S)**	**-**	**1 (H)**
ESIN + curettage + bone substitute (H) + growth factors	**6**			**5**	**1**	-	-

ESIN Elastic stable intramedullary nailing

A autologous, allogenic; H heterologic; S synthetic;

* Number of those with further treatment cycle(s) in brackets.

Growth arrest of the proximal physis with visible length differences of the humerus (n = 2; length difference 4 and 7 cm)

~ Implant removal not possible (n = 6)

patients removal of the nails was impossible and in two children a growth arrest of the proximal physis occurred. In these last two cases the results was a visible limb length difference of 4 cm and 7 cm with functional limitations.

DISCUSSION

This study evaluated 105 different day-by-day treatment cycles in 60 children with a juvenile or aneurysmal bone cyst. It is one of the few studies that focus on the single cyst location 'humerus' combined with a cyst presentation as an 'acute pathological fracture' (*16*).

The total number of the study population appears low, but earlier reports about this rare condition often focus on only 20 patients or fewer, or include further locations such as femur, calcaneus, mandible or spine (*7,25*).

In line with the epidemiological literature on this kind of bone cyst, twice as many boys are affected as girls in our study, and juvenile bone cysts comprise more than 70% of humeral bone cysts (*34*).

To evaluate the success or failure of a treatment method one should focus on objective outcome criteria such as the Capanna classification using the evaluation of patient's X-rays, which was the approach in our study (*2,15*). It shows that, in most cases, a conservative (non-operative) approach fails in the aim of resolving the bone cyst; only 6 of 33 healed completely or in most part. This very low success rates are in accordance with the literature (*8,29*).

But, in evaluating a treatment, it is also of importance that success be reached in a short time period such as in the 1st, and not the 3rd, treatment cycle. The patient should experience minimal stress by the absence of refractures and redo surgery and a very low rate of co-morbidities such as sport restrictions or motion limitations (*16*). A current paper emphasizes the importance of a successful primary treatment: Donaldson and his colleagues report that, following a failed primary treatment of juvenile bone cysts, no spontaneous healing occurred in any of the 24 patients over a period of seven years, although nearly all growth plates were closed at last follow-up with a mean patient age of 17 years (*8*).

To focus again on the conservative (non-operative) approach, our study demonstrates that this method led to most redo treatments and even combining with multiple cortisone injections (with or without intramedullary nailing) did not improve the success rates or minimize the complications. The total failure of multiple cortisone injections, giving no complete healing in any treatment cycle or combination in our study, might be related to the small number of only seven patients, but the review by Donaldson and his colleagues confirmed these results (*6*). This supports the conclusion that injections of cortisone should not be recommended for the treatment regime of juvenile or aneurysmal bone cysts.

Another common treatment method for pathological fracture caused by juvenile or aneurysmal bone cysts is the elastic stable intramedullary nailing of the affected long bone *(18,24)*. Following the primary nonoperative approach, elastic stable intramedullary nailing was the second common primary treatment of choice. But complete or partial healing of the cyst was achieved in only 6 of 13 patients; even combined with the use of this technique in the 2nd cycle after conservative treatment, the success remains moderate with redo surgery and a further treatment cycle needed in 10 out of 19 patients. Some studies in the literature report a success rate of about 50% in using this technique without open curettage or combined methods (*27*). The long-term use of elastic stable intramedullary nails while waiting for the healing of the cysts can lead to changing of the nails being necessary or to the removal of the implants being very difficult, if not impossible, as seen in six of our patients.

Further, we have to mention that two of our patients suffered a growth arrest of the proximal metaphysic plate with a relevant limb length discrepancy (shortening) and motion problems. Both these occurred after initial non-operative treatment and a later switch to elastic stable intramedullary nailing; in one case combined with multiple cortisone injections and in the other with bone substitutes leading to further changing of the nails and further bone substitute implantation. Whether this major complication is a direct effect of the nails affecting

the growth plate during the operation or a result of insufficient primary treatment resulting in further growth of the cysts thus destroying the plate, cannot be determined retrospectively (*10,19*). According to the post operatively x-rays the nails did not affect the growth plate.

In recent literature, biologicals (*3,30*) or combinations of osteosynthesis and biologicals attract more attention (*7,15,25*), but long term results are still rarely reported and these referring to the experiences of single centres with one combination (*3,17,33*). One finding of our multi-centre study is that the outcome varies greatly between different combinations of osteosynthesis and biologicals. Overall, the combined treatment with open curettage, elastic stable intramedullary nailing, (artificial) bone substitute (*9,22*) and (sometimes) growth factors (*21*) was performed successfully in 17 of 22 children as a 1st or 2nd line treatment. But those without added growth factors comprised all the failed treatments, success depended also on whether an autologous or synthetic bone substitute was used. Because of the very small numbers, the bone substitutes were not divided into different products, only categorised into their different origin material (A autologous/allogenis, H heterologic, S synthetic) (*9*). Our study emphasizes that the 'best' bone substitute for the treatment of juvenile and aneurismal bone cysts with a pathological fracture has not yet been found, and that multi-centre-trials are necessary both to eliminate the uncertainties of single centre studies and to study the side effects and complications of the different bone substitutes. We believe that results from trials of their use in non- or malunion in adults cannot be transferred into the every day treatment of bone cysts in children (*4*). Bone substitutes and additional growth factors vary widely in their biological characteristics, their origin and their risk profile and only a common study safety protocol could diminish the individual treatment risk for the child with a pathological fracture due to a juvenile or aneurismal bone cyst (*22,25*).

CONCLUSION

The success rate, in the treatment of pathological fractures of the humerus caused by JBC or ABC, is low in non-operative treatment, in elastic stable intramedullary nailing alone and in combinations with cortisone. Our results support a combined mechanical and biological treatment concept of osteosynthesis and biologicals, with open curettage, elastic stable intramedullary nailing, (artificial) bone substitute and suggested use of growth factors. But the best bone substitution and growth factors have to be evaluated, yet.

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