

Treatment of aneurysmal bone cysts with allograft

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Abstract

Background: Patients with aneurysmal bone cyst pose diagnostic and therapeutic difficulties. Multiple therapeutic options have been described.

Objective: To evaluate the results obtained in patients treated with curettage and filling with bone allograft.

Methods: Sixteen cysts, corresponding to 15 patients were evaluated, with a minimum follow-up of 28 months and a median follow-up of 83 months.

Results: Average age was 10 years (range 3-16). The main complication was recurrence in 37.5% of patients, being more frequent with physeal involvement (62.5% vs. 12.5% without involvement; $p = 0.05$). The recurrence rate was unchanged for both sexes, for different ages and regarding the use or not of high-speed burr.

Conclusion: We think that the treatment performed is safe, but recurrence rate is high, similar to that reported in other series.

Key words: Aneurysmal bone cyst; allograft.

Level of Evidence: IV

TRATAMIENTO DE QUISTES ÓSEOS ANEURISMÁTICOS CON ALOINJERTO

Resumen

Antecedentes: Los pacientes con quiste óseo aneurismático plantean dificultades diagnósticas y terapéuticas. Se han descrito múltiples opciones terapéuticas.

Objetivos: Evaluar los resultados obtenidos en pacientes tratados con curetaje y relleno con aloinjerto óseo.

Materiales y Métodos: Se analizaron 16 quistes, correspondientes a 15 pacientes, con un seguimiento mínimo de 28 meses y una mediana de seguimiento de 83 meses.

Resultados: La media de la edad era de 10 años (rango 3-16). La principal complicación fue la recidiva (37,5%), que fue más frecuente cuando existía compromiso fisario (62,5% frente al 12,5% sin compromiso; $p = 0,05$). La frecuencia de recidiva no varió en ambos sexos, para las distintas edades analizadas y respecto al uso o no de fresa de alta velocidad.

Conclusión: Consideramos que el tratamiento realizado es seguro, pero tiene una alta tasa de recidivas, similar a las publicadas en otras series.

Palabras clave: Quiste óseo aneurismático; aloinjerto.

Nivel de Evidencia: IV

Conflict of interests: The authors have reported none.

Introduction

The aneurysmal bone cyst (ABC) is a lesion of the pseudotumoral type, and it can be defined as a cavity filled by blood and divided into sub-cavities by connective tissue partitions that contain fusiform cells, multinucleated giant cells, hemosiderin storage areas and some trabecular bone. The process is locally destructive, with great tendency to recur.^{1,2}

This condition is scarcely frequent, with approximate rates of 0.14 per 100,000 inhabitants. It represents 1 to 1.4% of primitive bone tumors.³ Although it can show at any age, it prevails among children and the youngest up to 20 years old.

In general, it poses diagnostic and therapeutic challenges because of its topography, its locally aggressive profile with great bone destruction, the associate fractures in pathologic bone and the high percentage of local recurrence. Multiple therapeutic options have been described, such as radiotherapy, local or systemic chemotherapy, sclerotherapy, cryotherapy, selective arterial embolization, etc. They can be given as the unique therapeutic approach or as surgical treatment adjuvant therapies. As an example of surgical approach we can mention curettage and bone graft filling of cavities, which is considered as the treatment of choice.

In the Orthopedics Department of the Sanatorio Americano Montevideo, curettage and bone graft filling of cavities is the therapeutic option most frequently used. The aims of this study are: to recognize the main characteristics that ABCs show in the population that we have treated; types and percentages of complications found after treatment; and the relationship between recurrence and age and sex of patients along with type and localization of ABCs.

Materials and Methods

We evaluated all the patients younger than 18 years old with diagnosis of ABC, treated using only one therapeutic approach, between March 2003 and February 2010 at our center. Patients were monitored until December 2012, in which we ended our study.

Diagnosis of ABC was based on the tripod of medical history, images (X-rays and magnetic resonance imaging [MRI] and pathology by incisional biopsy, in all the patients. Pathologic assessment was always performed by the same technical team.

Treatment was based on the thorough curettage of the cavity of the ABC using a simple curette to do away with all the internal membranes that were stuck to the walls of the ABC. In seven patients, apart from the conventional curette, we used high-speed drilling as an adjuvant method to remove the membranes. Then we filled the resulting cavity with bone allograft, provided by the National Institute of Organs and Tissues Transplantation (INDT, by

its Spanish acronym) in the form of chips of lyophilized cortico-cancellous bone, which was re-hydrated using saline solution during 20 minutes before insertion.

Demographic and medical variables analyzed were: age and sex, sign/s or symptom/s that motivated medical consultation, the affected bone, the location of the ABC within the bone, growth plate involvement (assessed in X-ray and MRI), the type of ABC,³ the progression phase (Enneking stage)³, the Cappana imaging classification,³ the diagnosis interval (defined as the time passed between the onset of symptoms and the diagnosis), the diagnosis-to-treatment interval (defined as the time passed between the confirmation of the pathologic diagnosis and the surgery), adjuvant treatments given and history of recurrence. Moreover, we evaluated immediate and remote postoperative complications.

Diagnosis of recurrence was made using the classification of the treatment X-ray outcomes, as stated by the Cappana's⁴ scheme, later adopted by other authors,^{5,6} which specifies four possible types of response to treatment:

- Grade 1 = Healing. Complete bone healing of the ABC cavity, with marginal cortex thickening.
- Grade 2 = Incomplete healing. Bone healing and marginal cortex thickening, but there still are residual parts of the ABC with persistence of small areas of osteolysis.
- Grade 3 = Recurrence. At first the ABC heals, but later great areas of osteolysis and cortex thinning show again.
- Grade 4 = Lack of response. The ABC did not show evidence of response to treatment, with growth persistence.

Grades 1 and 2 are defined as a success, whereas grades 3 and 4 are therapeutic failures.

With respect to the statistical analysis of the data, the main characteristics of the patients were summarized by percentages in the case of the qualitative variables, and by means (averages) and medians in the case of the quantitative variables. We used the chi-square test (or the Fisher's exact test, as required) to compare percentages, and the Mann-Whitney test or the Kruskal-Wallis test to compare averages/medians between two or more groups.

To estimate the time free from recurrence, we used the Kaplan-Meier method, and we summarized it by the median and its 95% confidence interval (95CI). We used the log-rank test to compare the distribution of these times among groups or strata of the analyzed variables.

We considered as a significance level a value of 0.05. The statistical processing of the data was carried out with the program SPSS v. 15 (SPSS Inc., Chicago, Illinois, USA).

All the information gathered for this study is confidential, and it was managed as stated by the ethical norms for epidemiological research studies. The patients' identity was managed only by the medical doctors that participated in the assistance process. We created a computing database with the sole purpose of processing the collected

data, keeping information about the patients unidentified by means of a code given to every patient, which was only known to the study researchers.

Results

In the aforementioned amount of time, we treated 15 patients and 16 ABCs, because one patient showed two ABCs in different locations. There was only one case of comorbidity—von Willebrand disease. The time median of the global follow-up of the analyzed patients was 83 months (ranging from 28 to 109). The age average of medical presentation or onset of symptoms was of 8 years old (ranging from 2 to 15) and of 10 years old (ranging from 3 to 16) at the time of treatment. In 75% of the cases there was no delay in consultation, with patients consulting the doctor the very first day on which symptoms showed. In the remaining 25%, the delay was from 14 to 53 days.

The medical/X-ray initial diagnosis was mistaken in 25% of the cases, in which diagnosis was that of a simple bone cyst.

The median of the diagnosis interval was of 6.5 months (ranging from 13 days to 75 months). On the other hand, the median of the diagnosis-to-treatment interval was of 3 months (ranging from 1 to 24).

In all the patients with pathologic bone fracture as the initial symptom, we first treated the fracture, non-surgically or surgically as indicated and, once the fracture was healed, we treated the ABC.

We used high-speed drilling in 7 patients (43.75%) as an adjuvant to conventional curettage. In one case, apart from allograft we used autograft of non-vascularized fibula to fill the great bone defect.

The main demographic and medical characteristics of the assessed patients are shown in Table 1.

X-ray evaluation of the treatment results as outlined by the Capanna's classification⁴ showed 62.5% of satisfactory results. Therefore, 37.5% of the treated patients showed recurrence of the condition, with a time median until recurrence of 22 months (95CI: 12-33), a minimal time of 10 months and a maximal time of 40 months. On the other hand, patients with no recurrence showed a follow-up median of 76 months (95CI: 60-92), minimum of 37 months and maximum of 104 months.

Although we verified a greater proportion of recurrence among the females, this difference was not statistically significant (45% vs. 28% among the males; $p=0.245$). Along this lines, and without showing statistical significance either, among the females we verified less time free from recurrence (median time of 61 months vs. 84 months; $p=0.392$).

The age average at the time of the first medical consultation was similar among the patients with and without recurrence (respectively 7.5 years vs. 8.4 years old on average; $p=0.509$). In turn, taking as cut-off point an age of 10

years old, we verified more frequent recurrences among the patients younger than 10 (57% vs. 22% in children of 10 years of age and older), with differences non-statistically significant.

The analysis suggests a possible relationship between ABCs with physeal involvement and recurrence. Out of the eight ABCs with physeal involvement, five recurred (62.5%), whereas out of the eight ABCs with no physeal involvement, only one (12%) recurred ($p=0.049$).

We verified a shorter diagnosis interval in the patients that showed recurrence (median time of 8.3 months vs. 14.7 months in those with no recurrence; $p=0.042$). With respect to the interval between the diagnosis and the surgery, although it was greater among the patients who showed recurrence (median of 2.6 months vs. 6.6 months), this difference was not statistically significant.

At the time of analyzing recurrence related to the use of a high-speed drilling as adjuvant treatment, we detected no differences: three recurrences in six patients we use high-speed drilling in (50%) vs. four recurrences in 10 patients who received conventional curettage (40%).

Recurrence was associated neither with the type of reason for first medical consultation nor with the affected bone.

It is worth mentioning that, out of the six patients with recurrence, five were operated on again using the same procedure; four showed good results, whereas one showed a second recurrence which required a third surgery with the same procedure too and, eventually, the outcomes were good. Therefore, in 80% of the patients operated on again once, we got satisfactory results (one of type 1, and three of type 2). The last one of the six patients with recurrence does not want to be subject to another surgery (Figures 1 and 2).

With respect to the complications associated with treatment, not to mention recurrence, in the early postoperative period one patient suffered a superficial infection of the surgical wound that healed with outpatient antibiotic treatment; and two patients suffered late complications: one suffered an upper limb shortening of approximately 5 cm for involvement of the humerus proximal physis, with no functional impairment; and the other one suffered a lower limb shortening of approximately 2.5 cm as sequel to the fracture of a femur shaft lesion, with no functional impairment either. No patient died, no patient suffered amputation. No patient suffered residual pain, mal-alignment or function impairment that alter daily life, as verified during the latest follow-up consultation. Results are detailed in Table 2.

Discussion

In 25% of the patients there was no initial medical/X-ray diagnosis of the ABC, what evidences one of the characteristics of this condition regarding the difficulties for diagnosis, even though there are routine imaging studies

Table 1. Main demographic, medical and treatment characteristics of the 15 patients assessed (16 cysts treated)

Case	Sex	Age at diagnosis	Age at treatment	Reason for consultation	Bone	Physical involvement	Type of ABC	Enneking	Capanna	Treatment
1	M	4	6	Fracture	Humerus	Yes	Classic	2	2	Curettage + Allograft + High-speed drilling + Fibula autograft
2	F	13	13	Fracture	Humerus	Yes	Classic	2	2	Curettage + Allograft
3	M	13	13	Finding	Ilium	No	Classic	2	2	Curettage + Allograft
4	F	9	9	Pain	Tibia	Yes	Classic	2	2	Curettage + Allograft
5	F	8	8	Fracture	Humerus	Yes	Classic	2	2	Curettage + Allograft + High-speed drilling
6	F	4	5	Fracture	Humerus	Yes	Classic	2	2	Curettage + Allograft + High-speed drilling
7	M	13	14	Fracture	Femur	No	Classic	2	1	Curettage + Allograft + High-speed drilling
8	M	7	7	Fracture	Humerus	Yes	Classic	2	2	Curettage + Allograft
9	F	10	11	Tumor	Tibia	Yes	Classic	2	1	Curettage + Allograft
10	M	15	16	Fracture	Humerus	No	Classic	2	2	Curettage + Allograft + High-speed drilling
11	F	10	10	Finding	Tibia	Yes	Classic	2	1	Curettage + Allograft
12	F	10	10	Fracture	Tibia	No	Classic	2	1	Curettage + Allograft
13	M	10	10	Fracture	Femur	No	Classic	2	2	Curettage + Allograft
14	M	6	6	Fracture	Femur	No	Classic	2	3	Curettage + Allograft
15	F	12	12	Fracture	Humerus	No	Classic	2	1	Curettage + Allograft + High-speed drilling
16	F	3	3	Fracture	Tibia	Yes	Classic	2	2	Curettage + Allograft + High-speed drilling

F= female; M= male



▲
Figure 1. Case 6: Five years old, fractured aneurysmal bone cyst at proximal humerus level; recurrence after treatment with curettage with high-speed drill and bone allograft filling. Recurrence was treated in the same way with good results at the end of the study.

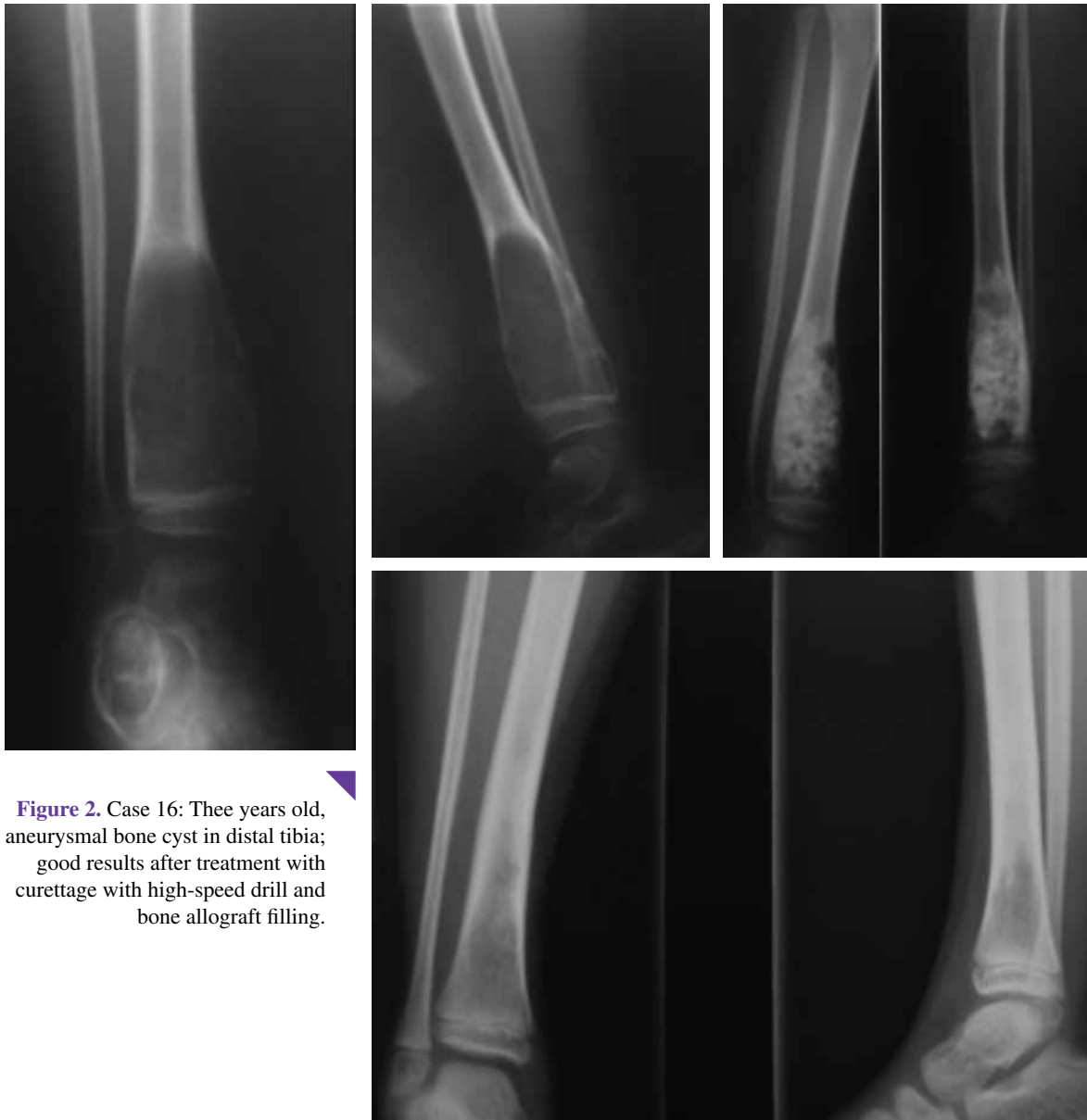


Figure 2. Case 16: Three years old, aneurysmal bone cyst in distal tibia; good results after treatment with curettage with high-speed drill and bone allograft filling.

available. This highlights the importance of the pathologic analysis of the lesion. It is also very important that the pathologist is trained in bone tumor pathology.

The sex relationship recorded in our study coincides with that of other series—this condition is slightly more frequent among females;³ nine of the 15 patients were females and six, males.

Literature affirms that the presentation of an ABC as the fracture of a pathologic bone might not be frequent;³ however, this was the most frequent reason for medical consultation in our series (75%). As background, in a study published by Bollini et al.,⁷ in 1998, the fracture of a pathologic bone was also the main reason for con-

sultation, in 27 children and adolescents with ABCs (8 patients).

With respect to the recurrence rates records of 37.5%, they are similar to those reported by other authors administering this kind of treatment (Table 3), and recurrence is the main complication. In the study carried out by Bollini et al.,⁷ in 27 ABCs in children and adolescents, 41.6% of the cases suffered recurrence of the lesions in long bones after treatment with curettage; age average at diagnosis time was 10 years old, with a follow-up average of 5 years. Freiberg et al.⁸ recorded 29% of recurrences in seven patients with curettage and bone grafting, whereas Ramírez et al.⁹ got a global rate of recurrence of 27.5%

Table 2. Main medical results and verified complications in the 15 patients assessed (16 cysts treated).

Case	Complications	Recurrence	Results (Ca-panna)	Treat-Rec interval (months)	Follow-up (months)	Time free from recurrence (months)
1		Yes (1)	3	40	109	40
2		Yes (1)	3	25	94	25
3		Yes (1)	3	23	55	23
4		Yes (2)	3	19	102	19
5	A five cm-shortening, mild limitation of motion	Yes (1)	3	18	50	18
6		Yes (1)	3	10	28	10
7			1		97	97
8			1		104	104
9			1		81	81
10			1		64	64
11			1		63	63
12			1		49	49
13	Shortening of 2,5 cm		1		85	85
14			1		91	91
15			1		96	96
16	Superficial infection		2		37	37

Table 3. Recurrence rates reported in treatment with curettage

	Number of cases	Treatment	Recurrence
Bollini et al. ⁷	27	Curettage	41.6%
Ramirez et al. ⁹	29	Curettage plus grafting or resection	27.5%
Mankin et al. ¹⁰	150	Curettage plus bone grafting or poly-methyl-methacrylate	20%
Moller et al. ¹¹	19	Curettage plus bone grafting	31%
Freigberg et al. ⁸	7	Curettage plus bone grafting	29%
Olivera et al.	16	Curettage plus bone grafting	37.5%

in 29 patients treated with curettage plus bone grafting or bone resection. Mankin et al. revised a series of 150 primary ABCs treated mainly with curettage and implan-

tation of chips of allograft or autograft or poly-methyl-methacrylate; the main problem they were faced with was local recurrence (20% of the patients).¹⁰ In 1992, Moller

et al. published a study in which they treated 19 patients with curettage of the ABCs plus bone grafting. They got 31% of recurrences; five of them were operated on again with no new recurrence. They recommended this procedure as treatment of choice, in spite of recurrence rates, that's why the patients have to be monitored regularly with both medical history and images.¹¹ Most of the studies that have been published agree on the fact that recurrence shows generally two years before the surgery. In our series, median time until recurrence was 22 months.

Some factors, such as a younger age, the female sex, the affected bone, physeal contact, the morphologic type, and the aggressiveness profile of the lesion have been associated with an increase in recurrence rates.¹²⁻²¹ In our series, we found statistic significance only in the relationship between recurrence and ABCs with physeal involvement. In turn, we found greater recurrence rates in the female sex (45% vs. 28% in the male sex), and also in patients < 10 years old; in these cases, though, we did not find statistical significance, perhaps because of the small size of the sample.

The need to supplement the treatment with adjuvant therapies is a controversial issue. Although some authors have reported a decrease in recurrence rates using adjuvant therapies, many have not appreciated substantial benefit. The theoretical advantage of widening the necrosis area in the tissues to reach residual tumor cells after curettage is intriguing, especially in the case of aggressive or recurrent lesions. Unfortunately, many of the popularized adjuvant therapies that are actually in use, such as liquid nitrogen and phenol, have brought about complications such as local and systemic toxicity, tissue necrosis, fracture and osteonecrosis. This highlights the need of an adjuvant therapy that is safe and easy to administer.²² In this context, high-speed drilling for curettage is described as an adjuvant treatment that decreases recurrence rates. Gibbs et al. got recurrence rates of 12% after using high-speed drilling in 34 patients as a treatment adjuvant to conventional cyst curettage, compared to rates of approximately 30% published by other authors who used only conventional curettage. Out of this study it can be concluded that it is possible to get local control rates of almost 90% with thorough curettage using mechanic drilling and no other adjuvant therapies in patients with an ABC in his/her limb.¹² Ramirez et al. suggest that this method "revive" the cavity walls for them to bleed and incorporate better the bone used to fill the cavity, and at the same time, it completes the resection of the intracavitary partitions and crests.⁹ In our series, there was no statistically significant difference in recurrence rates between those patients that received high-speed drilling as adjuvant treatment and those that did not.

Large bone defects resulting from either curettage or resection are difficult to treat. There are several reconstructive options to fill these defects and give bone integrity, such as grafting with bone autograft or allograft, and nu-

merous bone substitutes. Shih et al. assessed 104 patients with lesions that left considerable bone defects after extensive intracavitary curettage and that were filled with frozen allograft; 12 were ABCs. They showed complete incorporation of the allograft and formation of new bone within the cavity in 83% of the patients. They concluded that, for large bone defects, the reconstructive technique that uses allograft provides greater resistance, easy fixation and cyst defect remodeling, although results show slowly.²³ In one patient of our series, with a great lesion in the proximal metaphysis-diaphyseal area of the humerus, apart from allograft we used autograft of non-vascularized fibula to fill the bone defect. Non-vascularized fibula grafts are technically easier to use than vascularized grafts and offer excellent bone structural support to the receptor. However, they can take several months to get incorporated. In 1995, Khan et al.²⁴ published a study that suggests that ABC recurrence is very frequent after curettage and cancellous bone grafting and recommends that, when resection of the ABC is not possible, treatment consist of curettage and fibula autograft combined with cancellous allograft. Elimination of the medial third of the fibula does not cause handicap and the fibula regenerates completely in three months. Abuhassan et al.,²⁵ in a series of eight patients (7 with open growth plates) show the role of the periostium in the regeneration of the bone defect; the average size of the resected piece was 5.12 cm; all the patients showed complete regeneration of the bone defect within 3 to 9 months, with neither joint instability nor range of motion deterioration; average follow-up was 11.5 years. The patient in our series that received curettage, allograft and non-vascularized fibula autograft suffered a recurrence; later treatment consisted of new curettage and allograft and, eventually, results were good. There were no complications in the area the graft was taken from; there was no functional sequel in such lower limb either.

Literature about growth disorders related to surgical procedures is not conclusive. Rizzo et al.²⁶ did not record growth stoppage in 15 patients with juxta-epiphyseal ABCs treated with intracavitary curettage and bone grafting; however, Capanna et al.²⁷ report early fusion in five of 39 patients with juxta-epiphyseal ABCs. Moreover, Green et al.²⁸ (1 of 8 cases, 12.5%) and Lampasi et al.²⁹ (1 of 7 juxta-epiphyseal ABCs, 14.3%) report growth stoppage. Ramírez et al., in their series of 29 patients treated with curettage plus bone grafting or resection, recorded three cases of growth stoppage.⁹ The patient in our series with a physeal lesion at proximal humerus level shows a shortening of approximately 5 cm in the upper limb, with no functional impairment in daily life. This patient had been treated twice, at 8 and 9 years old, because of recurrence, what increases the likelihood of physeal injury. Many authors highlight the importance of preserving the physis in the treatment of ABCs, especially in small children. When an ABC contacts the growth plate, it is nec-

essary to perform blunt curettage to preserve the child's growth potential. Later recurrence is usually easier to treat than a bridge of epiphysiodesis and its consequences.⁷ On the other hand, when a juxta-epiphyseal ABC is located in a bone that the patient can do without, for some authors it is worth performing a more aggressive approach. An ABC that contacts the physis can lead to its deterioration because of both the growth of the ABC itself and a iatrogenic injury. Cryosurgery, embolization and radiotherapy are inadequate options for these places in children, because of complications that include growth plate stoppage, skin necrosis, postoperative fracture, progression to sarcoma, joint rigidity and osteonecrosis. Several authors have considered resection as the treatment of choice, due to lower recurrence rates as compared to curettage and bone grafting. In children older than 10 to 12 years old, inclusion of the growth plate into the resection can provide safer margins. However, it is recommended performing the resection preserving the growth plate, even in patients >10. In smaller children, the lesion has to be removed sub-periostically up to the edge of the physis, and the distal cut has to be given a few millimeters above the growth plate. Resection adjacent to the growth plate has to be rounded off with blunt curettage. To stimulate regeneration, it is essential to leave the periostium as intact as possible.²⁹

In our series, there was one patient with multicentric presentation of ABC at femoral shaft and acetabulum ipsilateral level. ABCs in different locations in one patient are exceptional. Up to date, the few multicentric ABCs reported have more frequently been found in males, as in our case, and the patients assessed have not shown chromosomal disorders.³⁰

Finally, and not failing in acknowledging that the main limitations of this study are the small size of the sample and the fact that it is a retrospective study, it is worth mentioning that the patients were treated by different surgeons in many cases, because of which surgical treatment uniformity and exact comparisons result impossible. The technique specifically used in each case depends on the surgeon's preferences. On the other hand, thoroughness of the initial curettage, one of the key aspects of treatment, probably varied among surgeons. This may represent a bias, as the fact of including in the sample the patient that was treated with fibular autograft together with the proposed technique may.

Conclusions

The ABC is a pseudotumoral lesion, locally aggressive and difficult to treat. Symptoms at onset and images many times do not give clear diagnostic criteria and it is necessary to rule out the diagnosis of other tumors. Therefore, the biopsy and the pathologic assessment by a professional trained in bone tumor pathology are essential.

The choice of the method of treatment many times depends on the surgeon's experience and the tradition at a given center; however, the ABC localization, its type, its activity, its size, its relationship with the growth plate and the patient's age have to be taken into account. Most patients are treated with curettage and bone grafting. Although, according to international literature, this treatment is associated with recurrence rates of about 30% (37.5% en our series), it is a safe method, with lower rates of serious complications as compared with other treatments. Recurrence seems to be greater in ABCs with physal contact, as deduced from the assessed bibliography, what coincides with our results. Both the patient and his or her family have to be informed about the perspectives of undergoing surgical treatment by stages; and what's more, the patient has to be closely monitored. The use of allograft is an attractive alternative for patients with an immature skeleton whose defects to fill are too large for their limited autograft stock, not to mention the allograft osteoconductive properties. Nowadays, there are strict health protocols for the management of the bone tissue to graft, in the assessment and choice of the donor, and also in the processing, conservation and move of the piece, what provides greater safety in terms of the transmission of infectious agents. However, the interest for synthetic bone substitutes is growing.

Other therapeutic approaches such as intra-lesional injection of sclerosing agents, cryotherapy, radiotherapy and embolization have been proved for lesions less affordable by surgery or for recurrent ABCs, due to the far from negligible serious complication rates they are associated with. Extra-lesional resection eliminates the whole lesion, but it can imply an extensive surgery with prolonged immobilization, the need of great amounts of bone graft, and morbidity at the growth plate level; therefore, they are spared for aggressive or recurrent lesions in areas that the patient can do without.

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