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Retrospective Study

Sclerotherapy as a primary or salvage procedure for aneurysmal bone cysts: A single-center experience

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Abstract

BACKGROUND

Aneurysmal bone cysts (ABC) are benign cystic bone tumors of an osteolytic and locally aggressive nature. As an alternative to the primary treatment of choice, which consists of curettage with bone grafting, alternative treatment methods with promising results have been described. At our department, we have, in recent years, used percutaneous sclerotherapy with polidocanol. The objective of this study was to identify the healing rate and safety of sclerotherapy with polidocanol.

AIM

To identify the efficacy and safety of sclerotherapy with polidocanol in primary and recurrent ABC.

METHODS

Twenty-two consecutive patients (median age 12.5 years; range 1-27) with 23 ABCs treated with sclerotherapy with polidocanol from 2016-2021 were included retrospectively. Eleven patients (48%) had undergone different forms of previous treatment with recurrence. Under general anesthesia and fluoroscopic guidance, repeated percutaneous injections of 4mg polidocanol/kg body weight were performed. Through review of the electronic medical records, the following were identified: healing and recurrence rate, number of treatments, gender, age, comorbidity, location of the tumor and side effects / complications, as well as any previous surgery for ABC. The median length of radiographic follow-up was 19.5 mo.

RESULTS

All ABCs except one (96%) showed healing or stable disease after a median of 4 (range 1-8) injections. Complete clinical and radiographic healing was observed in 16 cysts (70%), while partial radiographic healing with resolution of pain was seen in 6 cases (26%) and considered as stable disease. The cyst that failed to heal had

previously undergone curettage twice with recurrence. One patient with a large pelvic ABC experienced, right after two injections, a sudden drop in blood pressure, which could quickly be reversed. One patient with a juxtaphyseal ABC in the femoral neck showed a minor limb length discrepancy because of deformity. Beyond that, no complications were observed.

CONCLUSION

Percutaneous sclerotherapy with polidocanol appears to be a safe alternative for treatment of aneurysmal bone cysts. In our series of both primary and recurrent cysts, it showed the ability to achieve healing or stable disease in 22 of 23 cases (96%). Further studies are needed to decide if this provides a long-lasting effect.

Key Words: Aneurysmal bone cyst; Bone tumor; Sclerotherapy; Polidocanol; Healing rate; Complications

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Core Tip: This retrospective study presents the first outcomes after implementation of sclerotherapy for aneurysmal bone cysts (ABC) at our department. Compared to other series, 48% of our cohort consisted of patients with recurrent ABC after previous treatment or failed surgery. Sclerotherapy showed a high potency to achieve healing or stable disease and a low rate of adverse events in both treatment groups. We can recommend it as standard treatment both for primary and recurrent ABC, keeping in mind that randomized multicenter studies would be needed to provide evidence for the superiority of one treatment method.

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INTRODUCTION

Aneurysmal bone cysts (ABC) are rare benign bone tumors, usually affecting children and adolescents¹. Patients mostly present with pain, with or without swelling, and sometimes with a pathological fracture.

Radiologically, these lesions are expansile and osteolytic and can be locally aggressive (Figure 1). On magnetic resonance imaging (MRI), fluid-fluid levels are diagnostic, and soft tissue expansion can be seen. It is the gold standard to verify the diagnosis with biopsy.

The traditional treatment, curettage and bone grafting, has shown high rates of morbidity and recurrence[1-4]. As a result of that, several other treatment options have been explored: embolization, radiotherapy, wide excision and sclerotherapy with different agents and more[5-9]. In recent years, percutaneous sclerotherapy, especially with polidocanol, alcohol or doxycycline, has shown promising results with similar recurrence rates and low morbidity compared to open surgery[10-17]. There are several series published with polidocanol as primary treatment, but to our knowledge, there are no larger reported series on polidocanol as a salvage procedure. In our series, 48% of the cysts were treated with polidocanol for failed surgery or recurrence after previous treatment.

In this study, we present our experience with percutaneous polidocanol treatment for primary and recurrent ABC with focus on healing rate, recurrence and complications.

MATERIALS AND METHODS

In this single-center retrospective study design, all patients treated for ABC with percutaneous sclerotherapy from 2016-2021 were included. In 2016, sclerotherapy was introduced as standard therapy for primary and recurrent ABCs at our institution. Through review of the electronic medical records, the following data was identified: healing and recurrence rate, number of treatments, gender, age, comorbidity, location of the tumor, side effects and complications, as well as any previous surgery for ABC. Twenty-two patients with a combined number of 23 ABCs were identified. The various characteristics are shown in Table 1. Imaging at first presentation included conventional radiographs and MRI in all patients. Furthermore, a histological sample was available in all patients, either from previous surgery or collected with open biopsy. In five patients, open biopsy was performed simultaneously with the first sclerosant injection (Figure 2).

Sclerotherapy was performed under general anesthesia. The cyst was punctured percutaneously with a 1.0 or 1.2 mm trocar needle under fluoroscopic guidance. In classic ABC, bloody fluid from the cyst can be aspirated at the beginning of treatment. The cyst was injected with 4 mg Polidocanol (Aethoxysklerol®) per kilogram bodyweight, as described by Brosjö *et al*[10], mixed with contrast agent Iohexol (Omnipaque®). Before injection, the needle with trocar was directed in all cystic areas to break down possible septae. During injection, contrast agent was used to ensure that all parts of the cyst

Table 1 Demographic data and treatment details

Patient-ID	Age at presentation	Gender	Location	No. of injections	Ossification	Previous treatment	Follow-up (mo)	Histologic result
1	13	M	Pubic bone	5	Complete	Curettage + bone graft	13	Classic ABC
1	13	M	Sacrum	3	Partial	None	13	Consistent with ABC
2	13	F	Distal fibula	5	Absent	Two curettages + bone graft	37	Classic ABC
3	10	M	Ischium	6	Partial	None	29	Classic ABC
4	6	M	Scapula	7	Partial	None	24	Classic ABC
5	25	F	Proximal femur	3	Partial	Two curettages + bone graft	8	Classic ABC
6	14	M	Ileum	6	Partial	None	16	Consistent with ABC
7	4	M	Distal fibula	3	Complete	None	4	Consistent with ABC
8	12	F	Distal tibia	1	Complete	Curettage + bone substitute	31	Classic ABC
9	16	M	Proximal tibia	4	Complete	Curettage + bone graft	33	Classic ABC
10	6	M	Distal tibia	8	Complete	Triamcinolone injection	47	Consistent with ABC
11	5	F	Proximal fibula	3	Complete	Curettage + bone substitute	38	Classic ABC
12	15	M	Ischium	2	Partial	None	4	Consistent with ABC
13	14	M	Distal fibula	4	Complete	Curettage + bone graft	23	Classic ABC
14	25	M	Acetabulum	1	Complete	Two curettages + bone graft	35	Classic ABC
15	10	F	3. metatarsal	4	Complete	Curettage + bone substitute	19	Classic ABC
16	10	M	Proximal femur	3	Complete	None	26	Classic ABC
17	27	M	Proximal radius	1	Complete	None	11	Classic ABC
18	16	M	Proximal fibula	5	Complete	None	6	Classic ABC
19	18	M	Proximal femur	2	Complete	Three curettages + bone graft	20	Consistent with ABC
20	9	M	Ischium	4	Complete	None	16	Classic ABC
21	7	F	Distal tibia	6	Complete	None	5	Classic ABC
22	1	F	Proximal femur	6	Complete	None	9	Classic ABC

ABC: Aneurysmal bone cysts.

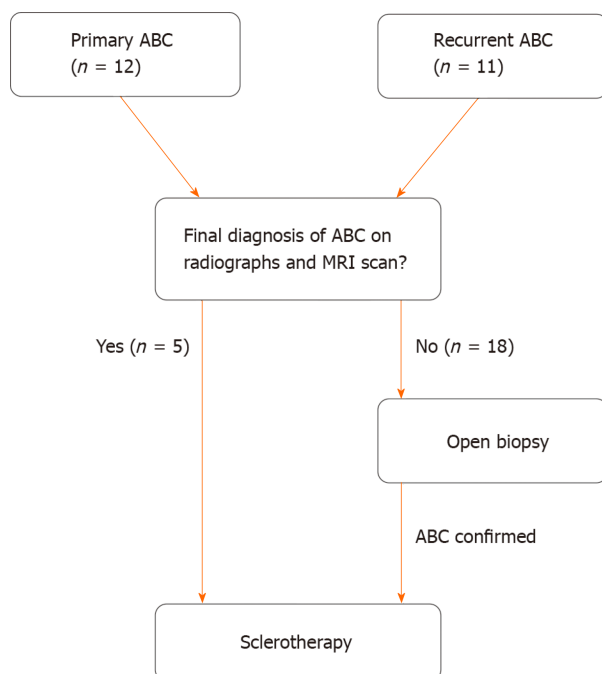
were treated (Figure 3). After injection, the needle was flushed with saline or previously aspirated blood, and after needle removal, pressure was applied at the site for at least two minutes to prevent extravasation.

The procedure was repeated every 4-6 wk, following the example of Brosjö *et al*[10], until satisfactory radiographical and clinical healing of the cyst was seen. Healing was defined as resolution of pain on clinical examination in addition to complete ossification on radiographs (Figures 1 and 4). Partial ossification or stable disease was determined as resolution of pain on clinical examination in addition to thickening of cortex and partial ossification without increase in cyst size on radiographs (Figure 5). The median radiographic follow-up was 19.5 mo (range: 4-47 mo).



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Figure 1 Radiographs of an aneurysmal bone cyst in the proximal fibula of a 5-year-old girl. A: At presentation; B: After three injections of polidocanol; C: At 38 mo follow-up



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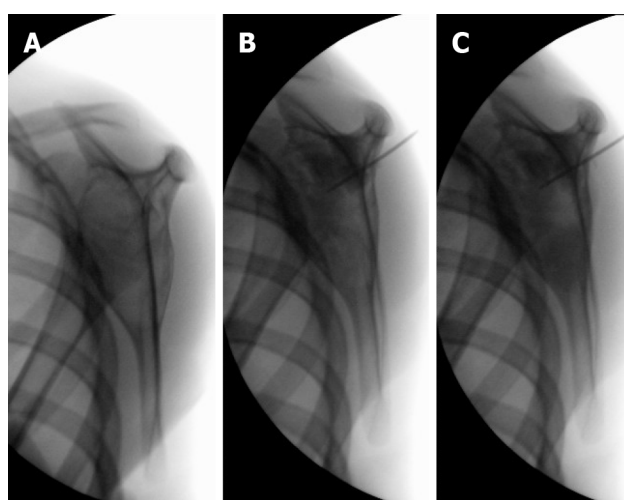
Figure 2 Flowchart of the algorithm from initial diagnosis to final management. ABC: Aneurysmal bone cysts; MRI: Magnetic resonance imaging.

RESULTS

The summary of the patient characteristics and treatment results is shown in Table 1. The median age at beginning of treatment was 12.5 years (range: 1-27), and males accounted for 68% of patients. Of the 23 cysts, eleven had undergone previous surgical intervention (48%) with subsequent recurrence, wherein ten cysts had been treated with curettage and bone grafting/bone substitute and one with glucocorticoid injection (for details see Table 1). Histopathologically, the diagnosis was confirmed in 17 cases, and in the remaining six cases, the sample was consistent with aneurysmal bone cyst. There were no tumors with an ABC-like area (previously called secondary ABC) or malignancies.

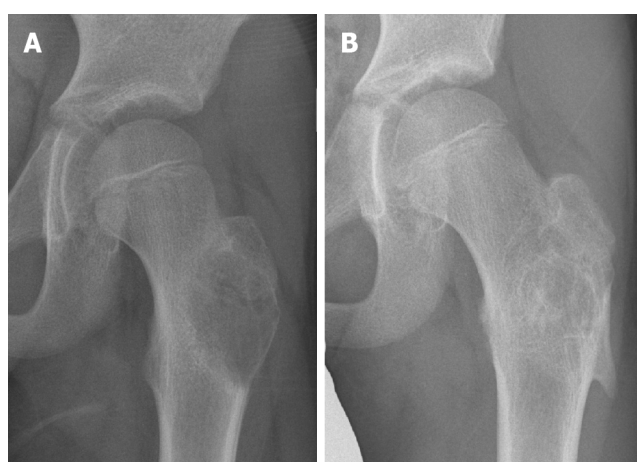
All cysts except one (96%) showed healing or stable disease after a median of four (range: 1-8) injections. Complete ossification was observed in 16 cysts (70%), while partial ossification with complete resolution of pain were seen in six cases (26%), which were considered as stable disease. There were no recurrences in the follow-up period.

The cyst in the distal fibula that failed to heal had previously undergone curettage twice with recurrence. During the course of five polidocanol injections, it showed recurring radiolucency in different parts of the cyst, and the patient displayed persistent pain. Finally, extended curettage with high-speed burring and bone grafting with polidocanol as adjuvant was performed, and the cyst healed without recurrence.



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Figure 3 Intraoperative fluoroscopy images showing sclerotherapy of an aneurysmal bone cyst in the scapula. A: Before injection; B: During injection with polidocanol and contrast agent; C: After injection



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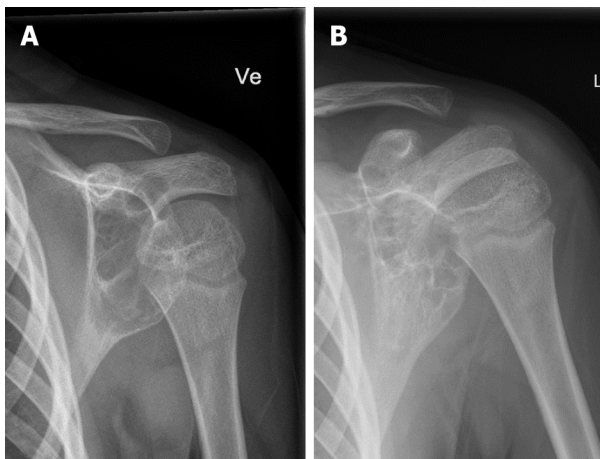
Figure 4 Radiographs of an aneurysmal bone cyst in the proximal femur showing complete ossification. A: At presentation; B: At 26 mo follow-up after sclerotherapy.

Due to a possible allergic reaction, one patient with a large cyst in the ischium showed a sudden drop in blood pressure to 60 mmHg systolic right after injection of polidocanol/iohexol in two settings, which could quickly be reversed after a bolus of ephedrine and fluid.

One patient with a juxtaphyseal ABC in the femoral neck, who was only 18 mo old at the beginning of treatment, developed a minor limb shortening because of deformity in the trochanteric area at 9 mo follow-up, possibly requiring further orthopedic treatment in the future. Beyond that, no complications, such as skin necrosis or infections, were observed.

DISCUSSION

In this study, we present our experience with percutaneous sclerotherapy of ABC with polidocanol. In our series, 96% of all cysts showed satisfactory treatment response with complete resolution of pain, with 70% showing complete ossification and 26% showing partial ossification without increase in cyst size. There were no recurrences in the follow-up period, but one cyst failed to heal, and treatment was converted to extended curettage and bone grafting with polidocanol as adjuvant. The healing rate of 96% in this study is comparable to the results published in recent literature, with healing rates ranging from 83%-100% [10-13,17-20], except for one study discussed further below. The studies comparing sclerotherapy with polidocanol with curettage found healing rates slightly in favor of sclerotherapy (93.3% *vs* 84.8% and 100% *vs* 82%, respectively) and showed lower morbidity in the sclerotherapy group [11,17].



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Figure 5 Radiographs of an aneurysmal bone cyst in the scapula showing partial ossification. A: At presentation; B: At 24 mo follow-up after sclerotherapy.

There is no agreement about the clear definition of successful treatment, or healing, in the literature. As applied in this study, most authors accept the following clinical and radiological signs as successful treatment: Resolution of pain, restoring of function, increasing sclerosis and cortical thickness without increase in cyst size[12,13,17,18].

One study showed less favorable results in both groups: Failure of sclerotherapy with polidocanol and need for further treatment in 34.5% of cases as well as a 38.5% recurrence rate with need for further treatment after intralesional curettage [21]. The authors find a possible explanation for these less satisfactory results in the more accurate cyst size measurement based on MRI scans and higher initial cyst volume in their study compared to similar studies[21]. Furthermore, MRI scans might be more sensitive to detect residual cyst activity (*i.e.*, fluid-fluid levels) than conventional biplanar radiographs, though the clinical importance of this finding remains unclear.

Apart from polidocanol, other sclerosing agents have been used for ABC with promising results. Publications on sclerotherapy with ethanol (in one study combined with Surgiflo®) and doxycycline showed success rates ranging from 68%-100% and 86%-100%, respectively, making them comparable to treatment with polidocanol[14,15,22-25]. At this stage, no sclerotherapy modality has been proven superior, and the treatment choice is usually dependent on regional preference and experience.

The general disadvantage of sclerotherapy is the need for repeated treatments in most cases, which, in this patient age group, usually requires general anesthesia.

Our cohort consisted of 12 primary ABCs and 11 cysts that had undergone previous surgical intervention with subsequent recurrence. To our knowledge, there are no larger reported series on polidocanol as a salvage procedure. In this series, 10 of the 11 recurrent ABCs (92%) showed satisfactory treatment response after sclerotherapy (Table 1).

One recurrent cyst, which had previously undergone curettage twice, failed to heal. Five injections of polidocanol were performed, but the patient showed persistent pain, and radiologically recurrent osteolytic areas were observed in different parts of the cyst. Finally, extended curettage with high-speed burring and bone grafting with polidocanol as adjuvant was performed, and the cyst healed without recurrence. We argue that it can be difficult to address all areas of a recurrent cyst, which in some cases consists of many subcavities. Especially if there are bony septae, it can be challenging to reach a certain subpart of the cyst percutaneously.

There are other described methods for ABC as salvage treatment or in patients where sclerotherapy or open surgery are contraindicated or not feasible. Selective arterial embolization has shown good results and is primarily used in the spine and other anatomically difficult locations, as well as a preoperative adjuvant to surgery. However, it is a technically demanding, operator-dependent procedure with potentially serious side effects due to ischemia, and it requires that a feeding vessel to the cyst can be identified[26,27].

Furthermore, there are pharmacological treatments available as rescue therapy for ABC. In several studies, denosumab, a monoclonal antibody inhibiting osteoclast formation and activity, has been shown to achieve re-ossification of ABC[6, 28-30]. However, serious side effects have been described. Some patients demonstrated severe hypo- or hypercalcemia under or after denosumab treatment[30,31]. Moreover, knowledge regarding the long-term consequences of denosumab on the growing skeleton is lacking so far. A related medical therapy is the use of bisphosphonates, such as zoledronic acid, which also inhibits osteoclast activity. They are widely used to successfully treat and manage various unresectable or metastatic bone tumors. Two smaller studies, with five and eight patients, respectively, have shown positive clinical and radiological effects of bisphosphonates in ABC without adverse events[32,33]. The authors even suggest bisphosphonates as treatment of choice in spinal ABC without neurological deficit or instability[32].

Based on the results of the present study, sclerotherapy with polidocanol might be another alternative salvage procedure to stabilize refractory or recurrent ABC. It can be considered before advancing to salvage treatments with a spectrum of more serious adverse events, as described above. However, further studies with more patients and longer follow-ups are needed to decide whether this is of lasting effect.

There was one adverse event observed in our cohort: A ten-year-old boy with a large cyst in the ischium showed a sudden drop in blood pressure to 60 mmHg systolic right after injection of polidocanol/iohexol in two settings. The reaction could quickly be reversed after a bolus of ephedrine and fluid. This phenomenon has also been described by other authors[18,34]. Like in the present study, it is usually harmless and quickly reversible, but in two cases, severe reactions have been described: One patient developed hypovolemic shock and cardiac arrest needing resuscitation, and the other one presented ventricular tachycardia with a sharp drop in blood pressure[18,34]. Both patients are reported to have recovered completely, but these observations necessitate this procedure only to be performed in a controlled setting with monitoring of vital signs.

Other authors reported minor complications to sclerotherapy, *e.g.*, skin induration, hypopigmentation, minor inflammatory reactions, ulceration or temporary pain[10,12,13,17,19,20]. On the other hand, the studies comparing sclerotherapy to curettage and/or resection found a higher rate of clinically pertinent complications and poorer functional outcomes in the surgery group[11,17,21].

One important limitation of this study is the short radiological follow-up in some patients. The retrospective study design meant that the follow-up was planned individually by the treating surgeon, not following a standard plan. Some patients showing signs of healing and resolution of pain in the first year after treatment were discharged and informed to contact our department again should pain or other symptoms recur. For these patients, our department is the responsible center for treating ABCs. The electronic medical journal showed no contacts to our or other hospitals in the region concerning their previous ABC in the following months and years. Furthermore, it was ensured that the place of residence was still in our region. The authors therefore argue that recurrence with clinical signs most likely would have been detected in these patients.

The other limitations of this study consist primarily of the number of patients, the retrospective study design and the lack of a control group. Randomized multicenter studies would be needed to provide evidence for the superiority of one treatment method for aneurysmal bone cysts.

CONCLUSION

This study supports evidence in the current literature that percutaneous sclerotherapy with polidocanol is an efficient and safe alternative to conventional surgery for the treatment of aneurysmal bone cysts. It can especially be recommended for cysts in difficult anatomic locations where open surgery would cause significant morbidity. Based on the present study, it may also be considered as a salvage procedure for failed surgery or multiple recurrences. Further studies are needed to decide if this provides a long-lasting effect and which of the discussed treatment methods is superior for primary or recurring aneurysmal bone cysts.

ARTICLE HIGHLIGHTS

Research background

As an alternative to the traditional treatment of aneurysmal bone cysts (ABC), which consists of curettage with bone grafting, alternative treatment methods with promising results have been described. At our department, we have been using percutaneous sclerotherapy with polidocanol for primary and recurrent ABC. To our knowledge, this is the first larger series reporting on polidocanol as a salvage procedure.

Research motivation

The main challenge with aneurysmal bone cysts is their locally aggressive nature and a high risk of recurrence. Therefore, there is a need to find evidence for the best available treatment, which optimally shows high efficacy and at the same time low morbidity and low rates of recurrence.

Research objectives

The main objective was to identify the efficacy and safety of sclerotherapy with polidocanol in primary and recurrent ABC. The outcomes of this study, especially regarding recurrent ABC, propose sclerotherapy as a relevant treatment method to be considered.

Research methods

This is a single-center retrospective study, where all patients treated for ABC with percutaneous sclerotherapy from 2016-2021 were included. The data was collected through review of the electronic medical records.

Research results

In our series, sclerotherapy with polidocanol showed the ability to achieve healing or stable disease in 96% of cases (100% in primary ABC and 92% in recurrent ABC). These results support the positive experience with sclerotherapy for primary ABC in the recent literature and open the debate about sclerotherapy as a possible salvage treatment. The median length of radiographic follow-up was 19.5 mo. Further studies with longer follow-up are needed to decide if this provides a long-lasting effect.

Research conclusions

Based on the present study, sclerotherapy with polidocanol may also be considered as a salvage procedure for failed surgery or multiple recurrences. This can be a valuable alternative to other salvage treatment methods, which may have higher morbidity.

Research perspectives

Given the variety of possible treatment methods, future research should focus on randomized clinical trials to identify the gold standard treatment for primary and recurrent ABC.

FOOTNOTES

Author contributions: Weber KS designed and performed the research and wrote the paper. Jensen CL and Petersen MM designed the research, contributed to the analysis and supervised the report.

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