

Is sclerotherapy with polidocanol a better treatment option for aneurysmal bone cyst compared to conventional curettage and bone grafting?

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ABSTRACT

Background: The standard treatment of Aneurysmal bone cyst is curettage and grafting and is associated with high morbidity. Hence minimal invasive alternative treatment methods such as sclerotherapy are gaining much popularity. Though sclerotherapy has been attributed to reasonable cure rates, undetermined tissue diagnosis often impedes with initiation of treatment. This study examines if sclerotherapy with polidocanol based on clinic-radiological picture is comparable with the standard intralesional curettage and bone grafting. Attempting biopsy and treatment simultaneously based on the clinico-radiological presentation makes this study unique.

Methods: We divided 48 patients into two treatment groups. Group 1 treated with percutaneous sclerotherapy using polidocanol and group 2 those treated with extended curettage and bone grafting. We assessed time to healing and recurrence, pain relief, and radiological outcome using modified Neer's criteria for the radiological healing of the bone cysts. 31 patients from Group 1 and 17 from Group 2 were available for study. The minimum follow-up was 2 years.

Results: At last follow-up, 100% in Group 1 and 82% in Group 2 had achieved complete healing and there was no statistical difference in outcome at 24 months ($p = 0.255$). Complications in Group 1 were injection site necrosis, pain and hypopigmentation, all of which resolved spontaneously. In Group 2, three patients had recurrence. Despite similar healing rates, we found higher incidence of clinically pertinent complications, poor functional outcomes and increased cost of treatment associated with intralesional excision.

Three cases were excluded from sclerotherapy group as the final diagnosis turned up to be secondary ABC.

Conclusions: Percutaneous sclerotherapy using polidocanol is a highly effective, cost efficient and safe treatment option with good cosmesis and reduced morbidity. In this study, we found comparable outcomes for both treatment methods however this will require confirmation in larger studies.

1. Introduction

An aneurysmal bone cyst (ABC) is a benign expansile lytic lesion of the bone classified under tumour like lesion of the bone. It consists of blood filled spaces separated by septae encompassing osteoid tissue and giant osteoclast cells.¹ Although benign, ABC can be a rapidly growing and destructive with no malignant transformation. This bone lesion is found mostly in the second decade of life (85% presented before 20 years of age) often affecting the metaphysis of long bones.² It can also develop secondary to other primary bone tumours, such as giant cell tumours, hemangiomas, osteoblastomas, chondroblastomas, telangiectatic osteosarcomas, fibrous dysplasia and non-ossifying fibroma but the clinical

features resembled the associated lesion.³ Secondary ABC is considered to be a secondary blow out in a preexisting lesion. Patients often presents with pain and swelling and rarely with a pathological fracture.⁴

Radiologically it is an expansile, lytic bone lesion of the metaphysis with thinning of cortex and subperiosteal new bone formation. Multiple fluid-fluid level and soft tissue expansion on MRI are diagnostic, while solid soft tissue component within the lesion is suggestive of secondary ABC.⁵ Though pathognomonic X-ray and MRI findings are diagnostic; biopsy is the gold standard.

The standard treatment of Aneurysmal bone cyst is curettage with bone grafting and is associated with high morbidity and recurrence.⁶ Various adjuvant techniques such as high speed burrs and cryotherapy

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have been tried to reduce the rate of recurrence but with increased morbidity. Hence minimal invasive alternative treatment methods such as sclerotherapy, radiotherapy, embolization are gaining more popularity.⁷

This study focuses on the comparing radiological and clinical outcome of the ABCs treated by curettage with bone grafting (CBG) and polidocanol sclerotherapy based on the clinic radiological diagnosis. Modified Neer's criteria for radiological healing of bone cysts is used to assess the radiological outcome at regular intervals.⁸

2. Materials and methods

From 2008 to 2018, 48 ABCs were diagnosed and treated at our institution. Among these, 31 cases were selected for sclerotherapy with polidocanol (ST) (Group I), all cases diagnosed as primary ABC based on the clinico-radiological picture and treated since 2012 irrespective of the size and site of the lesion. Intralesional curettage with bone grafting (CBG) was done in 17 cases (Group II). CBG was the treatment option for ABC in our institution until 2012 and the records were retrospectively reviewed. All the patients were followed up for a minimum period of 2 years. Preoperative evaluation of the lesion consisted of plain radiographs and MRI, occasionally CT scan was also done. A comparative study of radiological outcome of 31 patients treated with polidocanol sclerotherapy and 17 cases treated with curettage and bone grafting were retrospectively reviewed based on Modified Neer's criteria for healing of cystic lesions. All cases of secondary ABCs were excluded from the study. Patients diagnosed as primary ABCs treated with polidocanol sclerotherapy (n = 31) were categorised as group 1 and those by curettage and bone grafting (n = 17) as group 2.

This study was done after getting the approval from Institutional Review board, ethical committee and informed consent from the participants.

2.1. Statistical Analysis

Data collected was analysed by IBM SPSS (Statistical Package for Social sciences) Version 23. Data collected at the end of the test was analysed by Fisher's exact test.

2.1.1. Operative technique of sclerotherapy

Provisional diagnosis of ABC is made based on the clinical presentation and the radiological features of the lesion (Plain X-ray and MRI scans showing definite fluid-fluid levels). Procedure is done under CT guidance under local anaesthesia (2% Xylocaine) taking care of aseptic precautions (Fig. 1). First an attempt is made to get the sample of the lining cells using core biopsy needle in all cases.⁹ In classic ABC, we rarely get solid tissue, only blood is obtained (Fig. 2a). About 10ml of



Fig. 1. CT guided biopsy from Ischium.

blood aspirate along with lining tissue specimen if obtained in the core biopsy needle is sent for pathological examination (Fig. 2b). 18G needle is then introduced through the same site and is used to break the septa within the lesion by moving it in all directions. The sclerosant is then injected with a syringe and held sealed for 10 minutes (Fig. 2c). This step is crucial in preventing extravasation of the sclerosant and prevent soft tissue necrosis. The amount of sclerosant to be injected is determined based on the size of lesion calculated from the CT images at the time of procedure (1ml 3% polidocanol per 1cm³ of the lesion) and no more than 12ml(360mg) sclerosant was injected into any lesion. The sclerosant used was 3% polidocanol (hydroxypolyethoxydodecan) available in 2ml ampoules; 1ml = 30mg polidocanol.

Patients were reviewed at 10 days following the first injection, subsequently assessed at 3months, 6months, 12 months and 24 months. Radiological assessment of the lesion (cortical sclerosis, volume reduction, and cavity opacification) along with the clinical assessment of the symptoms of the patient were performed on the outpatient basis during the follow-up (Fig. 3, Fig. 4). Resolution of pain on clinical examination and thickening of cortex on radiological examination without any increase in the cyst size are features suggestive of healing. If any of these features were absent on follow up a second dose of the sclerosant was administered. Patients were strictly instructed to avoid sporting and arduous physical activities until the radiological healing of the lesion. Radiological assessment was done using modified Neer's criteria for the radiological healing of the bone cysts (Table 1).

2.1.2. Operative technique of intralesional curettage and bone grafting

The surgical technique consists of three stages: Stage 1 (intralesional excision of the tumour); Stage 2 (extended curettage); Stage3 (Reconstruction and graft application).

After the exposure of the involved bone, a cortical window of the size of the longest longitudinal dimension of the tumour is made, to make sure to expose the whole tumour. All the gross tumours were removed with hand curettes. Bone defects after curettage were filled with Autogenous iliac crest bone grafts. Autogenous fibular strut graft was applied to add structural support. All the patients had clinical and radiological evaluation at regular intervals.

3. Results

Summary of the treatment of both the groups listed in Table 2. The mean age in the first group was 17.8 years and in the second group was 14.8 years. The lesion occurred mainly during the second decade of life in both the groups though it can affect any age. Only one cases occurred in patient above 40 years.

Males accounted for 52.1% of the study group (Table 2). Pain and swelling were the chief complaints in majority of the patients at diagnosis in the both the study groups with pain seen in all patients. No case presented with pathological fracture in our series.

Femur was the most commonly involved bone, accounting for 14 cases, followed by tibia (12 cases). Distal femur and proximal tibia accounted for commonest site single. Site wise distribution of primary ABC summarised in Table 3. Pre-operative Enneking scores of the lesions listed in Table 4.

Aspirated bloody fluid and cell bloc were sent for histopathology in all cases. Only in three cases we were able to obtain wall linings by curetting. In 28 cases, the report came to be consistent with ABC or smear with no atypia. Three cases from the initial group were excluded from polidocanol group as the histopathology reports turned out to be ABC secondary to GCT.

Mean duration for cortical healing was 4 months in the sclerotherapy group. Mean number of injection per patient was 1.09. Twenty eight patients were healed by a single dose of polidocanol and three patients required second injection. Curettage group showed graft union in 5.6 months on an average. Autologous iliac crest graft was used in most cases and fibular strut graft was incorporated in two cases. Main

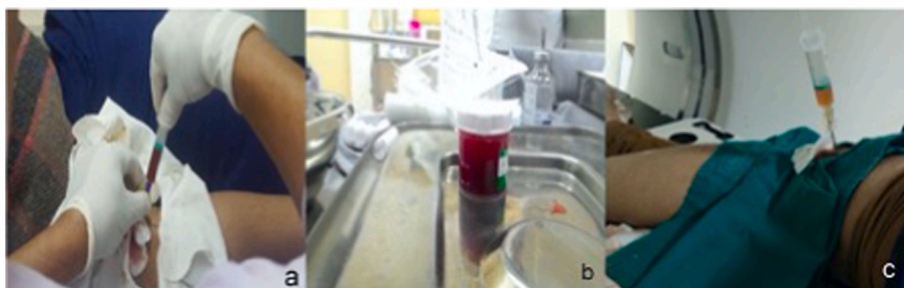


Fig. 2. Bloody fluid aspirate(a),(b) and Injecting the sclerosant(c).



Fig. 3. X ray showing healing of proximal phalanx of 3rd toe at presentation(a), 3 months(b), 6 months(c) and 1 year(d).

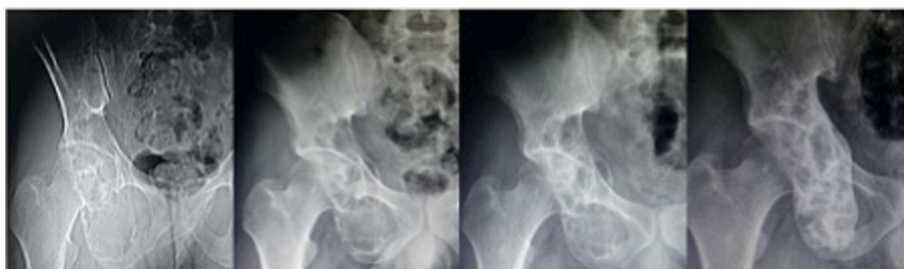


Fig. 4. X ray showing healing of ischium at presentation(a), 3 months(b), 6 months(c) and 1 year(d).

Table 1

Modified Neer’s criteria for radiological healing of bone cysts.

Grade 1	Healed cyst	Cyst filled with formation of new bone with or without small, static, radiolucent area(s) <1cm
Grade 2	Healing with defect	Static, radiolucent area(s), <50% of the diameter of the bone with enough cortical thickness
Grade 3	Persistent cyst	Radiolucent areas >50% of the diameter of the bone and with a thin cortical rim; no increase in cyst size;
Grade 4	Recurrent cyst	Cyst reappeared in a previously obliterated area or a residual radiolucent area has increased in size.

Table 2

Summary of both groups.

	Sclerotherapy(Group I)	Curettage + Bone grafting (Group II)
Number of patients	34	17
Mean age in years	17.67 (4–45)	14.88 (10–34)
Gender (M:F)	18:13	7:10
Avg. no. of Treatments	1.06	1.23
Mean Treatment duration	4 months	5.6 months
Recurrence	0	3

Table 3

Site wise distribution of ABC in each group.

Location	Frequency	Percent
Clavicle	2	4.2
Femur distal	9	18.8
Femur proximal	3	6.3
Femur shaft	1	2.1
Fibula	1	2.1
Humerus proximal	3	6.3
Humerus shaft	2	4.2
Ilium	2	4.2
Ischium	2	4.2
Metacarpal	2	4.2
Metatarsal	1	2.1
Phalanx foot	2	4.2
Phalanx hand	1	2.1
Radius distal	2	4.2
Sacrum	1	2.1
Scapula	1	2.1
Talus	2	4.2
Tibia distal	4	8.3
Tibia proximal	7	14.6
Total	48	100.0

problem faced was early graft resorption. There were no case of post-surgical infection in our series. In the curettage group, three patients had recurrence. Two patients had sclerotherapy as the subsequent

Table 4
Preoperative Enneking stage in both the groups.

Enneking	Sclerotherapy	C + BG
Latent	5	3
Active	17	9
Aggressive	9	5
Total	31	17

procedure, which eventually healed during further follow-up and one case was treated by repeated curettage.

The modified Neers' criteria (Table 1) were used to assess the radiological outcome at regular intervals of 3, 6, 9 and 12 months (Table 5). In the sclerotherapy group; at the end of 24 months follow up there were 19 grade1 and 12 grade2. While in the curettage group, there were 11 patients in grade1, 3 in grade2 and 3 cases had recurrence within years. The clinical and radiological outcome at the end of two years showed no statistical difference between the two groups in our series, p value > 0.05 (Table 5). In fact two cases which recurred following curettage were eventually treated with sclerotherapy. In spite of similar healing rates, we found higher incidence of clinically pertinent complications, poor functional score and increased cost of treatment associated with intralesional excision. Two patients from sclerotherapy group had injection site complications such as ulcerations and hypopigmentation which healed spontaneously with serial dressings.

4. Discussion

An aneurysmal bone cyst is regarded as tumour like lesion and not a true neoplasm.¹⁰ Some considers it as an intraosseous arteriovenous fistula, while others regard it as post traumatic or de novo lesion.¹¹ This attracts controversy regarding its characterisation and treatment.

Various treatment options from extensive extended curettage to minimally invasive sclerotherapy have been described and practiced widely. Each treatment options have got its own fair share of advantages and disadvantage. The current accepted way of treatment remains intralesional curettage with or without bone grafting. High recurrence rate and growth disturbance has been reported with this procedure in lesions close to epiphyseal plate. High speed burring and cryotherapy were tried as adjuvants to reduce recurrence.¹² However, complications like excessive bleeding, physéal damage and incomplete tumour removal were common with these procedures.¹³ At times surgical access becomes challenging due to anatomical constraints. Endoscopic curettage was experimented in such cases but long term results are awaited.⁸ Other accepted treatment modalities includes intralesional procedures like radiation therapy, cryotherapy, sclerotherapy, selective embolization and extralesional en-bloc excision with/without reconstruction.¹⁴

En-bloc extralesional excision helps to removes the entire tumour, but it usually involves extensive surgery, bone grafts, growth arrest and prolonged immobilisation.¹⁵ Radiotherapy, once popular has now been abandoned due to radiation induced malignant changes.⁴

Embolization which has been employed to reduce intra operative blood loss has proven to be an effective method. Surgically inaccessible lesions can be dealt with super selective embolization of the feeding vessels.¹⁶ Downside of this procedure is that, not all the cysts have a

Table 5
Post OP Neer's score in each group.

Post OP NEER	3 M		6 M		12 M		24 M	
	1	2	1	2	1	2	1	2
1	1	0	3	2	8	5	19	11
2	18	10	23	12	22	10	12	3
3	12	7	5	3	1	2	-	-
4	-	-	-	-	-	-	-	3
Fisher's exact test p value	0.640		0.961		0.471		0.255	

definitive feeding vessel that can be embolised with a potential complication of ischemia of the adjacent neurovascular structures.

Coming to sclerotherapy, it has shown promising results in treating primary ABC. It acts by damaging the endothelium of blood vessels, initiating the intrinsic pathway of blood coagulation by activating factor XII and causing thrombosis and local fibrosis. Several sclerosants have been used till date for treatment of various medical conditions, like hypertonic saline [HS], hypertonic dextrose, glycerine based sclerosants, sodium salicylate lidocaine, alcohol.¹⁷

Dubois et al. and Juhan et al. have concluded use of absolute alcohol as safe and effective method for treating ABCs in technically challenging and high risk candidates.^{18,19} Use of alcohol gel in deep and inaccessible lesions by Batisse et al. proved to be clinically and radiologically efficient.²⁰

At present Polidocanol (hydroxypolyaethoxydedocan) has been considered as the sclerosant of choice in the treatment of varicose veins, telangiectasias, venous malformations.²¹ Polidocanol has extraordinary record of safety and efficacy which has been proved clinically over half a century. Lefebvre et al. demonstrated immediate thrombosis with complete ossification of the lesion within 2 years with the use of polidocanol.²² Based on previous study by Varshney et al. sclerotherapy is found to be very effective and acceptable treatment option for ABC.²³

The downside of previous studies was the delay in treatment due to difficulty in getting adequate tissue for confirming the diagnosis. Needle biopsies rarely confirm the diagnosis by itself, it often becomes a diagnosis of exclusion and correlation with the clinical and radiological presentation.²⁴ Many a times multiple attempts of biopsies have been reported before initiation of treatment which often dulls the charm of this treatment.

Considering ABC as a tumor like lesion rather than a true tumor, in this study we proceed with sclerotherapy simultaneously with needle biopsy. We expect three outcomes in such a scenario, (a) biopsy conclusive of ABC, (b) biopsy suggestive of secondary ABC and (c) biopsy inconclusive. In the first two categories the treatment protocol is straight forward. In former proceed with follow-up and in second category proceed with the definite treatment options prescribed for that specific lesion. In our series we had three cases which turned out to ABC secondary to GCT, which were later excluded from the study. In the last category we strongly rely on the clinical presentation and the radiological picture to proceed with the treatment. Mahnken et al. demonstrated combined sensitivity and specificity of 83% and 70% respectively with conventional radiography and MR imaging in diagnosing ABC.²⁵ MRI helps to demonstrate multiple fluid filled cystic lesions separated by a thin septum indicating collection of blood.⁵ Demonstration of fluid-fluid level (FFL) of more than 2/3rd of the total volume on MRI correlates with the benign nature of the lesion.²⁶ On the contrary, features of secondary ABC exhibits features of the concomitant lesion both radiologically and clinically.³ Areas of solid regions within the lesion should raise the suspicion of secondary ABC and in such cases every effort should be made to get tissue from those areas for biopsy. Once the diagnosis of secondary ABC is made then the treatment is based on the underlying primary lesions. In this series 3 cases turned out to be ABC secondary to GCT which were later treated by curettage and bone grafting. It is important to consider aggressive lesions like giant cell tumours and osteosarcomas when MRI shows solid soft tissue mass. TelangiectaticOS(TOS), a rare subtype of osteosarcoma is one lesion that mimics ABC and should not be missed. Gadolinium enhanced MRI demonstrates thick and nodular enhancement of soft tissue around cystic spaces, suggestive of sarcomatous lesion in the case of TOS and secondly ABCs do not demonstrate necrosis.²⁷

Munk et al. have reported a constellation of¹ a young age,² expansile lesion with a thin low-signal rim,³ increasing signal with augmented T2 weighting, and⁴ possibly a lobulated contour and/or fluid levels within it strongly suggests the diagnosis of aneurysmal bone cyst.²⁸ Along with the imaging studies, blood parameters such as hemogram and serum ALP helps us to differentiate from the aggressive neoplasms. ALP levels

were not elevated in any of the cases with primary ABC. Presence of typical clinical features and radiological findings along with a blood-rich aspirate devoid of overtly malignant cells strongly supports the diagnosis of ABC.²⁴ Based on aforementioned evidences we keep patients with strong clinico-radiological picture of ABC under close follow-up despite an inconclusive biopsy. We look for radiological regression of the lesion and clinical improvement of symptoms.

In our series the results were good in 31 patients treated with polidocanol, with 100% healing at 2year follow up including lesions considered aggressive. On the contrary, 82% in curettage group showed complete healing with recurrence in 3 cases. However, there was no statistically significant difference between the two groups in the final outcome. Most of our patients in sclerotherapy group had symptomatic relief by the end of 6 weeks with definitive cortical thickening seen on X ray by 4 months. This result was comparable with the study by Batisse et al.²⁰ The mean residual lesion was less than 25% of the initial lesion. These finding were similar to the findings by Ulici et al.²⁹ A mean of 1.09 injections were required in our study group, this was contrary to other studies which reported an average of 3 injections by Rastogi et al. and Brosjo et al.^{7,23} Healing pattern in the axial skeleton in our series were promising and comparable with the study by Brosjo et al.⁷ There was no recurrence in sclerotherapy group compared to the curettage and bone grafting group. A few cases that recurred after curettage were treated subsequently with polidocanol sclerotherapy (Fig. 5).

In our series we did not have any cases which later turned to be a malignant or aggressive lesions on follow-up. We have found our technique to be more time efficient and cost effective by reducing the time to start of treatment and reducing additional biopsy attempts. It also reduces unnecessary exposure to higher dose harmful radiations which the patients are exposed to when subjected to multiple fluoroscopy or CT guided procedures. The approval of patients were very strong as the technique had better cosmesis and were performed as a day care procedure. Potential complications included injection site pain, hypopigmentation and injection site necrosis due to extravasation. All of these subsided spontaneously. Prevention of the extravasation is supposed to be the key to control local complications. In this study we would like to point out to the fact, ABCs are tumour like lesions and not true tumours and hence be treated like tumour like lesions. This way we would be able to take away huge burden physically, psychologically and financially from the patients and at the same time cure the lesion. However, sclerotherapy is not considered suitable in lesions causing neurovascular compromise that warrants surgical intervention.

5. Conclusion

In this study we would like to emphasis mainly on our two observations. Firstly, We have found comparable outcomes at the end of two years for both treatment methods which supports similar studies published earlier. Hence, percutaneous sclerotherapy for treating aneurysmal bone cyst using polidocanol may be considered as an effective, cost efficient and safe treatment option with good cosmesis and reduced morbidity compared to intralesional curettage and bone grafting. This is especially true in case of cysts involving inaccessible areas. Secondly, diagnosis and treatment of ABC may be proceeded simultaneously based on the clinic-radiological presentation rather than awaiting tissue confirmation, which helps patients to a large extend both physically and financially. The limitation of our study is what we believe the strength of this study. Though diagnostic biopsy were routinely done, many a times results were inconclusive but we adhered to the diagnosis of ABC based on the clinic-radiological picture. Though we did not have any misdiagnosis in our series this will require confirmation in larger studies, until then the possibility of a missed diagnosis has to be entertained.

Ethics committee and consent

This study was done after getting the approval from Institutional



Fig. 5. Recurrence after curettage and grafting(a), subsequently treated with sclerotherapy(b).

Review board (AIMSIEC/27/2017) and informed consent from the participants.

Declaration of competing interest

None.

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