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Percutaneous Ethibloc injection in aneurysmal bone cysts

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Abstract *Objective.* To investigate whether the injection of Ethibloc into aneurysmal bone cysts can be an effective treatment modality.

Design and patients. Ethibloc is an alcoholic solution of zein (corn protein) which has thrombogenic and fibrogenic properties. Ten patients with aneurysmal bone cysts were treated with CT-guided percutaneous injection of Ethibloc into the cyst cavity. Ethibloc injection was the primary treatment in five patients. Four patients had recurrence following previous curettage and bone grafting and one patient had not responded to injection into the lesion of autologous iliac crest bone marrow aspirate. Three patients needed a second injection. The median follow-up was 27 (6–60) months.

Results and conclusion. Symptoms were relieved in all patients. At imaging, seven patients had resolution of the lesion and three had partial response at the most recent follow-up. Complications consisted of a local transitory inflammatory reaction in two patients and an aseptic abscess in one patient. This relatively simple, minimally invasive procedure makes an operation unnecessary by stopping the expansion of the cyst and inducing endosteal new bone formation. This technique may be used as the primary management of aneurysmal bone cysts excluding spinal lesions.

Key words Aneurysmal bone cyst · Percutaneous · Ethibloc · Zein

Introduction

Aneurysmal bone cyst (ABC) was recognised and described as a distinct clinicopathological entity by Jaffe and Lichtenstein in 1942 [1]. It is a benign, usually expanding lesion of bone, containing blood-filled spaces and is seen, most frequently, in teenagers. While this is a benign condition, the lesion may behave in an active and aggressive fashion. The most common sites are the metaphysis of the long bones and the spine.

Traditionally the treatment of choice for an ABC has been surgical [2, 3], but recurrence is a problem. The rate of recurrence after curettage with or without bone grafting varies from 18% to 59% [4–9]. Phenol [10], liquid nitrogen [11, 12] and bone cement [13] have all been used to minimise recurrence following the curettage of

benign cystic tumours of bone. Surgery can be difficult, particularly if the spine, pelvis or an epiphysis is involved. Embolisation with gelfoam either alone or followed by surgery is helpful in the spine [14] and large pelvic cysts [15]. Total resection has been the treatment of choice in certain sites such as the proximal fibula, distal ulna, ribs, pubic ramus, metacarpals and metatarsals [8]. Although radiation [16–18] has been found to be effective, it has also been associated with a high rate of complications [7, 8] and is no longer recommended.

An alternative approach to treatment, the percutaneous injection of Ethibloc (Ethnor Laboratories, Ethicon, Norderstedt, Germany), a fibrosing agent, has been reported [19]. In this study, we determined the efficacy of CT-guided percutaneous Ethibloc injection into the ABC cavity. This management was used as the primary treat-

Table 1 Aneurysmal bone cysts treated by percutaneous Ethibloc injection

Patient no.	Age/Sex	Site	No. of previous surgeries	No. of injections	Follow-up (months)	Complications	Lesion resolution
1	15/F	Ilium	2	2	60	–	Yes
2	10/F	Tibia	1	2	54	Transitory local inflammation	Yes
3	13/M	Humerus	2	1	48	–	Yes
4	4/M	Humerus	0	1	36	Transitory local inflammation	Yes
5	11/M	Humerus	0	1	30	–	Partial
6	14/M	Humerus	0	2	24	–	Partial
7	12/M	Humerus	1 ^a	1	8	–	Yes
8	13/F	Tibia	0	1	12	Sterile abscess	Yes
9	16/M	Femur	0	1	20	–	Yes
10	10/M	Femur	1	1	6	–	Partial

^a Bone marrow injection

ment in five patients and after failure of surgical treatment in a further five.

Patients and methods

Ten patients with ABC were treated with percutaneous Ethibloc injection. There were seven boys and three girls (Table 1). The age varied from 4 to 16 years (mean 11.8 years). The humerus was involved in five patients, the tibia in two, the femur in two and the pelvis in one (previously included in the paper by Adamsbaum et al. [19]). Four patients had recurrence following previous curettage and bone grafting and one patient had not responded to injection of autologous bone marrow aspirate. The recurrent cases were documented radiographically and all presented with recurrent pain. Five patients had no previous surgical intervention and Ethibloc injection was the primary treatment.

Ethibloc contains an alcoholic solution of 210 mg zein (corn protein), 162 mg diatrizoate (as a radiopaque marker), 145 mg oleum papaveris (to provide a soft consistency) and 6 mg propylene glycol (to provide sterility) per millimetre of alcohol. It is available in sterilised 7.5-ml syringes, ready to be injected.

Ethibloc is licensed for injection into the pancreatic duct and into the renal artery for embolisation but is not specifically licensed for injection into bone, although the preparation has been safely injected into bone cysts at other institutions (unpublished communication). We have used the preparation for injection into bone cysts only on a named patient basis. In view of the safe use of the preparation elsewhere, and the clinical indication to treat the problem, we did not seek ethics committee approval but all patients gave full informed consent to the procedure, and all potential complications were explained.

Diagnosis

In most cases the diagnosis was based on typical radiographic features and aspiration of blood from the cyst cavity before injection of Ethibloc. The radiographic findings vary with the maturity and location of the lesion. Typically ABC is metaphyseal or metadiaphyseal, well defined, eccentric, and shows the characteristic expansile “soap-bubble” area of radiolucency. CT or MRI was helpful in confirming the benign nature of the lesion and in showing the fluid-on-fluid levels within the cystic cavity. Aspiration of blood at the time of Ethibloc injection supported the diagnosis of ABC.

Procedure

The lesions were all imaged by CT on a separate occasion prior to the procedure. The Ethibloc injection was performed under general anaesthesia using an aseptic technique. The lesion was localised using a fine needle (21–22 gauge) under CT control. A larger needle (16 gauge) was then inserted into the cyst and aspiration of blood supported the diagnosis. In some cases biopsy with a Jemshidi needle was attempted, but in all cases inadequate tissue for histological evaluation was obtained. Before injection of Ethibloc, contrast medium was injected to ensure the intracavitary location of the needle with no leakage into the soft tissues, and following this 4–8 ml of Ethibloc was injected, depending on the size of the cyst. A course of prophylactic antibiotics was prescribed. Initially the patients were kept overnight in the hospital but the last six patients had the procedure performed as a day case. The patients were forewarned against a possible pathological fracture following needling of the cyst and a ‘flu-like illness which may occur due to the body’s reaction to the foreign protein.

Patients were followed with appropriate radiographs and CT postoperatively. Initially the radiographs were repeated at 3-monthly intervals but with experience the time interval was increased to 6 months. The first postprocedure CT scan should be performed at 6 months with further reassessment by CT after 12 months unless there is a clinical indication to perform a scan earlier. The median follow-up was 27 (6–60) months.

Results

Seven of ten patients treated with Ethibloc had resolution of the lesion, and three had partial response at the latest follow-up. Of the seven successfully healed patients, three needed two injections because there was partial response to the first injection. Repair was evident on radiographs as a progressive decrease in the radiolucency, remineralisation, ossification and consolidation of the cyst and reconstitution of the bone (Figs. 2, 3). The CT scan confirmed the presence of endosteal new bone formation at the site of the lesion and, although this process was slow, there was progressive thickening of the cortex, endosteal ossification and shrinkage of the lesion (Fig. 1). In some cases a response to the Ethibloc injection was evi-



Fig. 1A Preoperative CT scan showing an aneurysmal bone cyst of the ilium with fluid-on-fluid levels. **B** Eighteen months after the second Ethibloc injection showing endosteal new bone formation with nonprogressive residual lytic areas

dent but a residual cystic component remained. Such cases were considered to represent a partial response.

Transitory local inflammatory reactions occurred in two patients and were controlled by oral analgesics. One significant complication occurred. A girl of 13 years presented with an abscess 7 days after an uneventful injection of a distal tibial cyst. Subsequent management included incision and drainage on two occasions and antibiotics. Each time, sterile pus was drained and no organisms were grown. It is likely that local leakage of Ethibloc from the cyst into the soft tissues occurred establishing a foreign body reaction with inflammation and sterile abscess formation.

Discussion

The rate of recurrence of ABC after curettage with or without bone grafting varies from 18% to 59% [4–9]. The high rate of recurrence following the surgical management of ABCs has stimulated researchers to use various treatment modalities in conjunction with curettage to minimise local recurrence. Marcove et al. [12] have successfully used adjuvant liquid nitrogen cryotherapy after curettage and reported an 82% cure rate after the first treatment; all cases were eventually controlled after repeat cryosurgery. Capanna et al. [10] used phenol to sterilise the cavity left in the bone after curettage of benign bone tumors in order to reduce the local recurrence. The recurrence rate was 41% in patients treated with simple curettage and 7% in patients treated by curettage followed by the application of phenol. Ozaki et al.

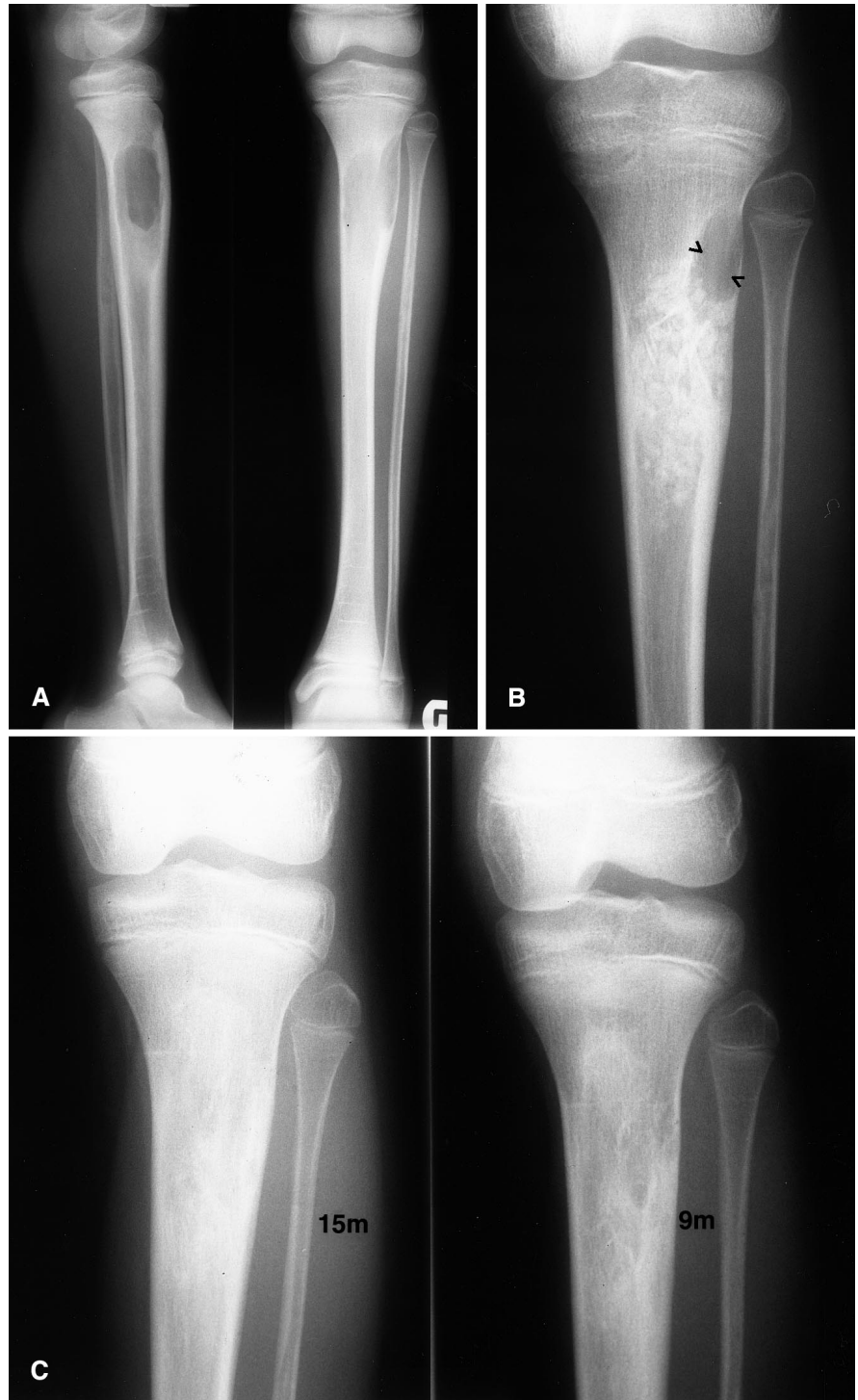
[13] packed the cavity with bone cement after extensive curettage and compared this approach with curettage and bone grafting. They found that the local recurrence rate after curettage and cement was 17% as compared with 37% after curettage and bone grafting. Surgery can be difficult, particularly if the spine, pelvis or an epiphysis is involved. Embolisation with gelfoam either alone or followed by surgery is helpful in the spine [14] and large pelvic cysts [15].

Total resection has been recommended for ABCs located in expendable bones such as the proximal fibula, distal ulna, ribs, pubic ramus, metacarpals and metatarsals [8, 20]. Partial resection is indicated for subperiosteal ABCs. Total or partial resection ensures healing in all cysts. Radiotherapy has been used for inoperable cases but significant complications have been reported including growth plate and gonadal damage in childhood [8, 21], as well as the development of secondary sarcoma [7]. Radiotherapy is no longer recommended.

It has been shown that excision remains the best form of surgical treatment [8], but usually this leads to some morbidity and impairment in the function of the extremities. There are many potential problems associated with surgical treatment, including infection and growth plate injury, in addition to a difficult surgical approach at certain sites. Immobilisation is necessary following all surgical procedures and may need to be prolonged in larger lesions, resulting in difficulties for the child and the family. An alternative minimally invasive treatment would offer significant benefits.

Ethibloc is a maize-derived product (zein), initially used in pancreatic surgery. It is an emulsion containing a mixture of zein, absolute ethanol, oleum papaveris (which maintains it in suspension), propylene glycol (a bacteriostatic substance) and a contrast medium. Ethanol enhances the necrotic effect of the zein, which is insoluble in water and precipitates progressively after dissolution of the ethanol in the aqueous medium.

Fig. 2A Aneurysmal bone cyst of the upper tibia. **B** Radiograph showing the recurrence following the curette and bone grafting (*arrowheads*). **C** The cyst healed completely following two Ethibloc injections. Radiographs were taken at 9 and 15 months following the second injection



In our study no long-term complications have been recorded to date. The presence of intracystic septa can make an equal distribution of Ethibloc inside the cyst difficult, increasing the risk of incomplete healing. Adamsbaum et al. [19] reported good results with percutaneous injection of Ethibloc in four children presenting

with benign bone cysts: two were ABCs and two were unicameral bone cysts.

One criticism of the present study is the absence of a tissue diagnosis in 8 of the 10 cases. Diagnosis in these eight was based on clinical presentation and typical imaging characteristics, which included plain radiographs, CT

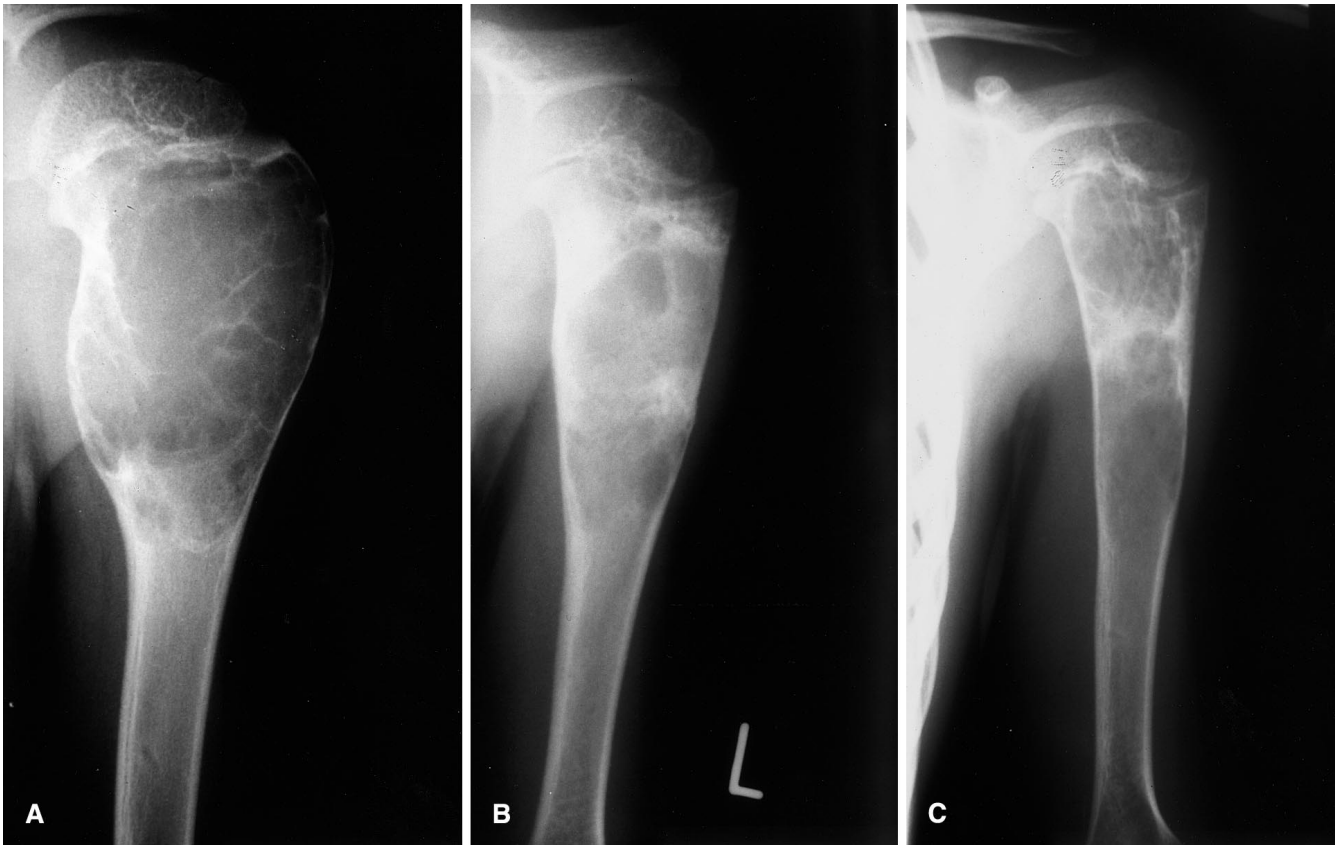


Fig. 3 **A** Preoperative radiograph showing an aneurysmal bone cyst of the proximal humerus. **B** Radiograph 4 months post-operatively showing remineralisation and the beginning of reconstitution of the bone. **C** Radiograph 18 months post-operatively showing further resolution of the lesion with some residual lucency

and MRI scans. Aspiration of blood from the cyst at the time of Ethibloc injection supported our diagnosis, and although biopsy with a Jemshidi needle was attempted in some cases, no useful material could be retrieved by this means. Open or a more invasive biopsy would have defeated the whole objective of a minimally invasive approach.

Ethibloc has been used successfully for the treatment of soft tissue venous malformations [22, 23] and lymphangiomas [24]. The precise mechanism of action of Ethibloc

is not known. It is probable that it is the thrombogenic effect of the ethanol which achieves vessel thrombosis and thus eliminates the presumed cause of an ABC. The zein component then excites endosteal repair, eventually leading to the successful resolution of the cyst.

Percutaneous Ethibloc injection may be primarily used for the local control of all primary ABCs excluding spinal lesions. We do not presently recommend injecting into spinal ABCs because of the possibility of inadvertent leak into the surrounding tissues or spinal vessels.

This relatively simple, minimally invasive procedure makes an operation unnecessary by stopping the expansion of the cyst and inducing endosteal repair. Ethibloc injection can be recommended as the primary management for aneurysmal bone cysts.

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