

TREATMENT OF ANEURYSMAL BONE CYSTS BY INTRODUCTION OF DEMINERALIZED BONE AND AUTOGENOUS BONE MARROW

BY PIERRE-LOUIS DOCQUIER, MD, AND CHRISTIAN DELLOYE, MD, PhD

Investigation performed at Cliniques Universitaires St-Luc, Brussels, Belgium

Background: On the assumption that an aneurysmal bone cyst has an intrinsic potential to heal by ossification, a new, minimally invasive protocol was developed. Demineralized bone powder mixed with bone-marrow aspirate was introduced into the cyst to halt the expansion phase and to allow the cyst to ossify. We hypothesized that, in order to induce bone-healing, cells from the cyst are needed to respond to the inductive material but that curettage or extensive surgery is not necessary. The goals of the present study were to assess cyst-healing and to determine the prevalence of recurrence associated with this new procedure.

Methods: Thirteen biopsy-proven primary aneurysmal bone cysts were entered through a small incision, and a paste of demineralized bone and autologous bone marrow was introduced with an applicator. The study group included three male and ten female patients with a mean age of 16.6 years. The cyst was located in a long bone in six patients, the pelvis in five patients, and the scapular glenoid and the calcaneus in one patient each. Five patients had not received treatment previously, whereas one had had a preoperative embolization and seven had recurrent lesions that had been treated previously.

Results: After a mean duration of follow-up of 3.9 years, healing was achieved in eleven patients.

Conclusions: This minimally invasive method is able to promote the self-healing of a primary aneurysmal bone cyst. As no curettage is required, the proposed treatment avoids extensive surgery and blood loss and is convenient for the treatment of poorly accessible lesions such as those occurring in the pelvis.

Level of Evidence: Therapeutic Level IV. See Instructions to Authors for a complete description of levels of evidence.

A neurysmal bone cyst is a benign expansile lesion that remains a diagnostic and therapeutic challenge¹. It can be either primary or secondary to another bone lesion¹⁻⁵. Biopsy is necessary to confirm the diagnosis of a primary aneurysmal bone cyst and to exclude an adjacent tumor. The most common preexisting benign lesions are giant-cell tumor, osteoblastoma, and chondroblastoma, although association with a malignant lesion such as osteosarcoma is also possible¹⁻⁵. Primary aneurysmal bone cyst is a rare lesion, with an incidence of about 1.4/1,000,000 per year⁴, and the overall prevalence is estimated to be 1% of biopsied primary bone tumors⁵.

The etiology of aneurysmal bone cyst is not clearly established. It is regarded as a reactive, highly vascular lesion resulting from local hemodynamic impairment^{5,6}, although chromosomal abnormalities also have been reported⁷. Histologically, these lesions consist of unclotted blood in cystic cavities lined with connective tissue septa containing giant cells and histiocytes as well as osteoid, which suggests a reparative process.

The natural history of an aneurysmal bone cyst is divided into four phases: lysis, expansion, stabilization, and healing⁸⁻¹⁰. Diagnosis generally occurs during the expansion or stabilization phase. Healing may occur either spontaneously⁸⁻¹⁰ or after biopsy¹¹⁻¹³, but this is uncommon. Most of these lesions require surgical treatment.

Previous surgical treatment has emphasized the necessity for complete removal or destruction of the cyst wall to decrease the risk of recurrence^{6,11}. The trigger mechanism that shifts an aneurysmal bone cyst from the lytic phase to stabilization with gradual ossification is not known. We thought that the introduction of an osteoinductive material into the cyst might trigger the ossification and hence the healing of the cyst¹⁴. We used demineralized bone and autogenous bone marrow as an inducer of the healing phase with the expectation that the cells of the aneurysmal bone cyst septa would be the responding cells. One of the potential advantages of such a method is that curettage is unnecessary, thereby allowing for a minimally invasive

approach. Such an approach would be particularly advantageous for the treatment of poorly accessible lesions such as those in the pelvis. In the present report, we describe thirteen consecutive cases of primary aneurysmal bone cyst that were treated with this technique and followed for at least two years.

Materials and Methods

Patients

Thirteen consecutive patients with a biopsy-proven primary aneurysmal bone cyst had operative insertion of a paste made of demineralized bone powder supplemented with autologous bone marrow (see Appendix). The study group included three male and ten female patients with a mean age of 16.6 years (range, eight to twenty-eight years) at the time of the operation. Six lesions were located in the long bones, including the distal part of the femur (two), the distal part of the tibia (two), the distal part of the fibula (one), and the diaphysis of the radius (one); five were located in the pelvis, including the iliopectoral ramus (three) and the iliac crest (two); and one each was located in the scapular glenoid and the calcaneus. Nine lesions were classified according to the system of Campanacci et al.¹¹ as aggressive, with periosteal Codman triangles and soft-tissue extension, whereas four lesions were classified as active, with an osseous shell margin. Eleven lesions were centrally located, and two were eccentric. All lesions were painful, and seven were associated with a palpable mass.

Five patients had had no previous treatment and were primarily managed with our protocol. One patient first had an arterial embolization, six weeks before treatment with our protocol, with use of polyvinyl alcohol particles (range, 100 to 500 μ m) associated with microcoil material. Seven patients had been referred for the treatment of a recurrent lesion following previous treatment. In this group, three cysts had recurred fol-

lowing a single curettage and bone-grafting procedure and one had recurred after two surgical procedures. Two other patients in this group had had recurrence of an aneurysmal bone cyst after preoperative arterial embolization, curettage, and bone-grafting. For one of them, this was a repeat treatment. The last patient in this group had received fourteen consecutive steroid injections without success. In this last patient, selective arterial embolization also was attempted with use of polyvinyl alcohol particles two months prior to the index procedure.

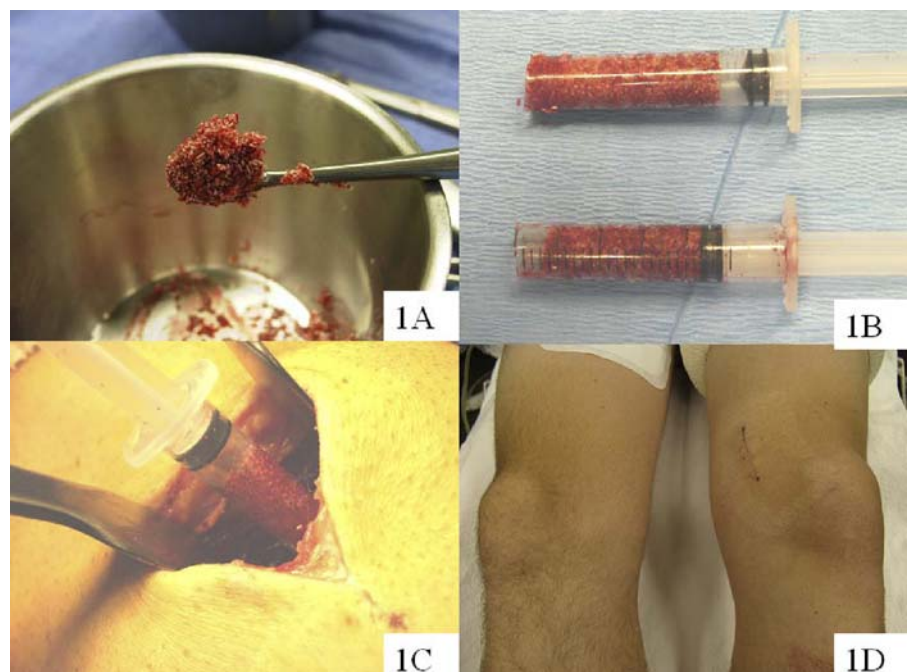
Bone Powder Preparation

The demineralized bone powder was procured from the registered tissue bank of the hospital. This powder consists of small particles of cortical bone (200 to 800 μ m) that were defatted and dehydrated in various solvents as reported previously¹⁴. Demineralization was obtained with use of a 0.6-M hydrochloric acid solution (15 mL/g bone) for fifteen hours at 4°C. The particles were rinsed with distilled water until a pH of 5.8 was reached. The residual calcium content was not evaluated. The powder was then freeze-dried and finally was sterilized with gamma irradiation at a dose of 25 KGy. The final moisture content was <5% of the wet weight. The final product, containing either 2 or 5 g of bone particles, was preserved dried in a glass bottle.

Surgical Procedure

The six patients who had undergone previous curettage and autogenous bone-grafting had no separate additional biopsy. The other seven patients had a biopsy as a separate procedure to ascertain the diagnosis of a primary aneurysmal bone cyst. Every lesion was documented with radiographs, computerized tomography, and/or magnetic resonance imaging. Before the biopsy, all imaging files were reviewed with an orthopaedic ra-

Fig. 1
Photographs illustrating the operative technique. A, Demineralized bone powder mixed with autogenous bone marrow. B, Two syringes filled with the paste. C, Minimally invasive approach to the cyst and injection of the mixture. D, The healed wound.



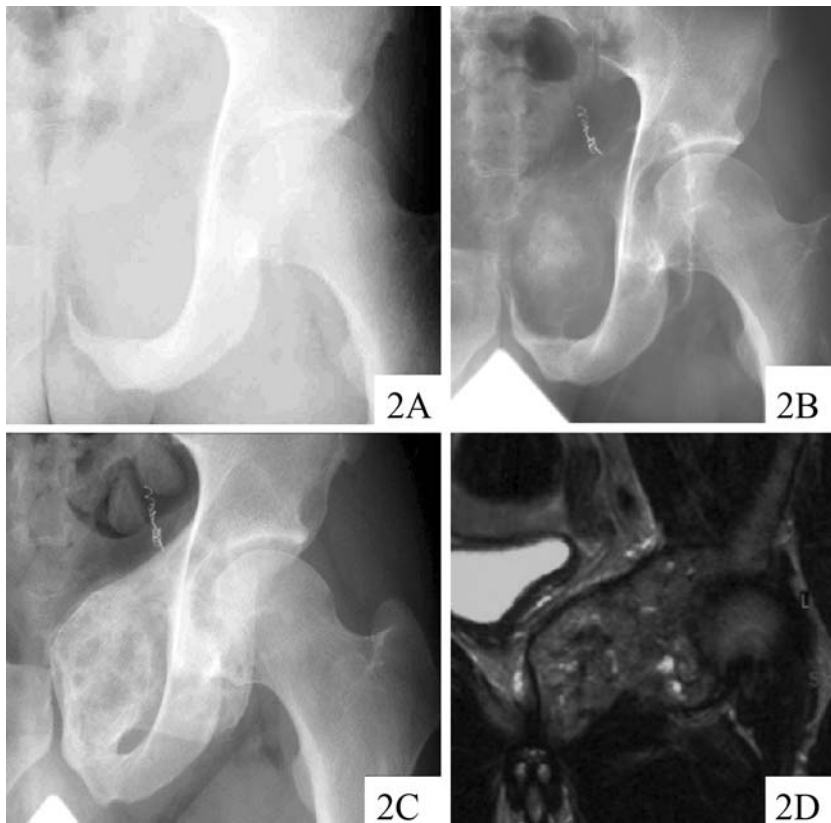


Fig. 2

A twenty-two-year-old man (Case 7; see Appendix) with an aggressive aneurysmal bone cyst involving the iliopubic ramus. Embolization was first performed six weeks prior to surgery. *A*, Preoperative radiograph showing complete lysis of the iliopubic ramus. *B*, At one month postoperatively, the micro-coil material and the inserted paste are visible. An osseous shell is beginning to surround the aneurysmal bone cyst. *C*, At twenty-two months, the aneurysmal bone cyst is healed with homogeneous ossification. *D*, T2-weighted coronal magnetic resonance imaging scan, made after thirty-five months of follow-up, showing a predominance of low-signal tissue (fibrous tissue, osseous tissue, and marrow tissue), confirming healing. Very small high-signal cavities are still present.

diologist to determine the biopsy site. In the cases of five patients, there was a three-month delay between the biopsy and the performance of the index procedure; the purpose of this delay was to exclude spontaneous healing initiated by the biopsy. The remaining two patients had aggressive lesions that were treated three and six weeks after the biopsy.

The surgical procedure was performed with the patient under general anesthesia. The cyst was localized with use of fluoroscopy. No cystogram was made to assess its vascularity. At the time of surgery, the demineralized bone powder was mixed in equal parts (g/mL) with autologous bone marrow aspirated from the anterior superior iliac crest. The paste was placed in a 2 or 5-mL syringe without a nozzle (Fig. 1), and the piston was reintroduced for injection. A minimally invasive approach through a small incision (<4 cm) permitted a small opening of the aneurysmal bone cyst cortex. A cortical window (1 cm²) was made to allow easy introduction of the syringe. Any hemorrhage that occurred during opening of the cortex ceased with the introduction of the bone paste into the cavity. No attempt was made to evacuate the cyst. Approximately one-third of the cyst volume was filled with the grafting material. A gel foam was applied to cover the entry point of the lesion. No drains were utilized. Immediate mobilization was allowed without protective splints. No physical therapy was prescribed postoperatively. Patients with pelvic and lower extremity lesions were immediately allowed full weight-bearing unless there was a risk of fracture; three such patients who were at risk for fracture used crutches until there was evidence of healing.

Evaluation

Postoperatively, radiographs were made monthly for the first three months and then every six months thereafter. The final result was classified as healing or recurrence according to clinical and radiographic criteria. In the case of healing, the cyst enlargement ceased, a peripheral osseous shell appeared around the aneurysmal bone cyst within the first three months postoperatively, the bone graft material was gradually replaced by progressive ossification of the cyst, and the lesion became non-painful. Healing was classified as complete or incomplete. Complete healing was achieved when the aneurysmal bone cyst was fully obliterated by homogeneous ossification. Incomplete healing was observed when the lesion assumed a "soap bubble" appearance characterized by the persistence of residual blood-filled cavities along with the occurrence of some new-bone formation along the septa. In the case of either complete or incomplete healing, the lesion remained stable throughout the study, with no additional expansion after the procedure. In the case of recurrence, the cyst continued to demonstrate expansion, no peripheral shell appeared within three months, the bone graft material was progressively reabsorbed, and the lesion was still painful.

Results

Five different batches of bone powder, prepared from separate donors, were used during this series. The mean quantity of demineralized bone used for the preparation was 8.9 g (range, 2 to 18 g), and the mean volume of autogenous bone

marrow aspirate was 8 mL. Blood loss did not exceed 100 mL in any patient. No patient experienced respiratory symptoms postoperatively, and pulmonary embolism was not clinically suspected in any case. The skin incisions healed uneventfully. No postoperative fevers or episodes of acute pain were observed, suggesting that no patient had a major inflammatory reaction. In all cases, a single procedure was performed.

The first sign of healing was the appearance of a peripheral shell of new bone. This shell usually became apparent approximately three months postoperatively. Any cyst that was associated with the development of this peripheral shell within three months ultimately healed and did not recur. Conversely, any cyst that did not show a peripheral shell within three months ultimately recurred.

After a mean duration of follow-up of 3.9 years (range, two to 8.3 years), healing was obtained in eleven patients. The mean age of these eleven patients was 16.2 years (range, eight

to twenty-eight years). Seven of the eleven cysts were aggressive, and four were active. The mean duration of follow-up in this group was 3.9 years (range, two to 8.3 years). Of the eleven lesions that healed, four had been primarily treated with our method and one had been treated with embolization six weeks before being treated with our protocol. The six other lesions had recurred once or twice before being treated with our protocol: three had had previous curettage and bone-grafting, one had had curettage and bone-grafting on two occasions, one had had arterial embolization associated with curettage and bone-grafting, and one had had repeated intralesional steroid injections. Seven cysts demonstrated complete healing with homogeneous ossification (Fig. 2), whereas four cysts developed a soap-bubble appearance with residual cystic areas (Fig. 3). Magnetic resonance imaging revealed that fluid levels still could be detected in these cystic remnants one or two years after the index procedure. Late recurrence was not observed in association with any of the cysts that responded to treatment.

Two cysts, both of which had been classified as aggressive preoperatively, recurred after the index procedure. The first sign of recurrence was the progressive disappearance of the bone paste within two months after its introduction. A peripheral new-bone shell did not appear within three months, and the cysts continued to increase in size. Both of these cysts were treated with more conventional methods. The first cyst, a recurrent and aggressive aneurysmal bone cyst of the posterior iliac crest in a twenty-eight-year-old woman, was treated with radiation therapy, which resulted in a stable latent lesion with nonexpansile cystic cavities. The second cyst was a very aggressive aneurysmal bone cyst of the distal part of the fibula in a ten-year-old girl. At six months after the index procedure, the patient underwent complete curettage and bone-grafting, with subsequent successful healing of the lesion.

Discussion

Curettage with or without bone-grafting is the most widely used treatment for aneurysmal bone cysts^{6,11,15-26}. Campanacci et al.¹¹ reported on ninety-one cysts that were treated with curettage and autogenous bone-grafting. Nineteen cysts (21%) recurred. Szendrői et al.²⁶ reported on twenty-six cysts that were treated with curettage and autogenous bone-grafting. Seven cysts (27%) recurred, and two were associated with infection. Arlet et al.²⁰ reported on eleven cysts that were treated with curettage without grafting. Four cysts (36%) recurred.

Although multiple options have been proposed for the treatment of aneurysmal bone cyst, only few nonablative treatments have been recommended^{6,11,15-21,27-36}. Selective arterial embolization alone was proposed as a definitive treatment as early as 1982²⁷. De Cristofaro et al.²⁸ reported two recurrences in a series of nineteen lesions that were treated with embolization alone, but complete healing was slow to occur and usually required a year or more. Boriani et al.²⁹ and DeRosa et al.³⁰ reported a low rate of recurrence in association with the use of selective arterial embolization for the treatment of spinal lesions, and Murphy et al.²⁷ and Wallace et al.³¹ reported on the



Fig. 3
An eleven-year-old girl (Case 4; see Appendix) with an active diaphyseal radial aneurysmal bone cyst. A, Pre-operative radiograph showing a voluminous active cyst (56 × 32 mm) surrounded with a peripheral reactive bone shell. B, Postoperative radiograph made after twenty-five months of follow-up, demonstrating healing with latent, nonexpansile cystic areas.

use of this method as a primary treatment for pelvic lesions.

Selective arterial embolization is most often utilized as a preoperative modality to limit blood loss at the time of surgery. Green et al.³⁷ reported no recurrences in a study of eight patients in whom embolization was performed before curettage and bone-grafting (seven patients) or as the definitive procedure (one patient). Papagelopoulos et al.³⁸ recommended the use of preoperative selective embolization therapy for the treatment of lesions with substantial soft-tissue expansion and for lesions measuring >5 cm to minimize intraoperative blood loss.

Radiation therapy also has been utilized in small series when surgical options have not been available. Of the thirty-six cysts that were treated with radiation therapy as reported in the literature^{6,11,15-21}, five (14%) recurred. As this treatment exposes the patient to the risks of radiation-induced sarcoma, physal arrest, and gonadal damage, it is not currently recommended for the treatment of aneurysmal bone cyst and is considered only when surgery is not possible^{11,17,21-24,38}. Radiation therapy also has been proposed as an adjuvant treatment after curettage and bone-grafting but carries the same risks^{11,16,17,19,21-24,38}.

Steroid injection was attempted by Scaglietti et al.³⁹ on the basis of the similarity of the aneurysmal bone cyst to the simple or unicameral bone cyst. Twelve aneurysmal bone cysts were treated with at least three successive injections over a period of eight months. None of the cysts showed signs of repair, but some showed signs of further development. All twelve patients subsequently underwent curettage and bone-grafting.

Calcitonin injection can result in partial healing of an aneurysmal bone cyst but has to be repeated frequently. Szendrői et al.³² reported on seven cysts that were treated with intralesional injection of calcitonin three times per week for a total of five weeks; cessation of growth was reported in six cases. The proposed mechanism of action of calcitonin is suppression of osteoclastic activity and promotion of the formation of new osseous trabeculae within the fibrous septa of the aneurysmal bone cyst³². Calcitonin also can be used in conjunction with methylprednisolone, but we are aware of only one report on such treatment; specifically, Gladden et al.³³ reported the case of a child who was managed with intralesional injection of calcitonin and methylprednisolone for the treatment of an aneurysmal bone cyst of the atlas.

Injection of Ethibloc (Ethicon/Johnson and Johnson, Norderstedt, Germany), an alcoholic solution of zein (corn protein) that has thrombogenic and fibrogenic properties, can result in complete or partial healing of an aneurysmal bone cyst³⁴⁻³⁶. Of the forty-three patients who were managed with percutaneous Ethibloc injection in previous reports, thirty-four demonstrated complete resolution of the lesion, six showed a partial response, and three had a recurrence³⁴⁻³⁶. Thirty-one of the forty-three patients underwent a single injection, and twelve underwent repeated injections³⁴⁻³⁶. Adamsbaum et al.³⁴ observed inflammatory reactions with local pain and fever in sixteen of seventeen patients and reported that three patients had development of a small cutaneous fistula.

The induction of healing with use of demineralized bone and autogenous bone marrow is a new approach. With

this technique, the cyst contents are not removed with curettage. As aneurysmal bone cyst can be considered as a reparative process with cells in the septa having an intrinsic potential for new-bone formation, it has been hypothesized that the presence of a bone inductor could convert the osteolytic process into an osteoblastic one^{5,14,40}. Demineralized bone matrix is an osteoinductive material, and its intramuscular or subcutaneous implantation in rodents has become an *in vivo* model for bone induction. The addition of autogenous bone marrow to the demineralized bone particles makes a consistent, workable paste that can be placed in a 2 or 5-mL syringe. The risk of bone-particle migration into the blood stream is minimized by the size of the particles and the consistency of the paste. The introduction of the material is easy and is compatible with a minimally invasive approach. Demineralized bone matrix is readily available in the United States and Europe.

We cannot positively demonstrate that the ossification resulted from an osteoinductive process as the demineralized bone powder was not assayed *in vitro* or in animal studies. Nevertheless, in a previous animal study, the same preparation was successful for achieving new-bone induction⁴⁰. It is likely that the observed ossification in the present series was the result of combined factors such as loss of cyst architecture, hemodynamic interference, and osteoinduction.

The recurrence rate in the present study (15%; two of thirteen) compares favorably with the rates in other series^{6,19,24,38}. However, as this was a case series without a control group, it cannot be inferred that this method is more effective than curettage and bone-grafting in terms of the rates of healing and recurrence.

The result of this technique generally can be seen after three months. If there is no peripheral shell by that time, recurrence should be considered likely. Conversely, the presence of an osseous shell around the cyst permits one to predict future healing, especially if local pain has resolved.

Our results encourage the further use of this minimally invasive method for the treatment of primary aneurysmal bone cysts. Its major advantage is to promote healing of the cyst without extensive surgery. As it is minimally invasive, it decreases the risk of infection and offers potential advantages for the treatment of cysts in poorly accessible locations such as the pelvis or spine, although we have no experience with spinal lesions. Another advantage is the hemostatic effect of the injected paste. Intraoperative bleeding is common and can be stopped by injecting the paste into the lesion. We believe that this method may offer several advantages for the patient and surgeon and that it is worth considering as an option for the treatment of an aneurysmal bone cyst.

Appendix

 A table presenting clinical details on all patients is available with the electronic versions of this article, on our web site at jbjs.org (go to the article citation and click on "Supplementary Material") and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM). ■

Pierre-Louis Docquier, MD
Christian Delloye, MD, PhD

Department of Orthopaedic Surgery, Cliniques Universitaires St-Luc, 10, avenue Hippocrate, B1200 Brussels, Belgium. E-mail address for C. Delloye: delloye@orto.ucl.ac.be

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