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ORIGINAL ARTICLE

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Induced healing of aneurysmal bone cysts by demineralized bone particles

A report of two cases

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Abstract Two cases of induced healing of aneurysmal bone cyst (ABC) following intralesional implantation of a bone paste made of autogeneic bone marrow and allogeneic bone powder are reported. The calcaneum in one case and the superior pubic ramus in the other were blown out by an ABC and would have required extensive surgery. Via a minimal exposure, the cyst was partially evacuated and filled with an admixture of a partially demineralized bone particles with bone marrow. Ossification of the peripheral shell was the first sign of healing and was observed within the first 3 postoperative months. Successful healing was observed in both cases. The rationale underlying this intralesional treatment was that the bone grafting material might reverse ABC expansion by promoting ossification through a bone induction mechanism. The concept of this treatment was to retain the ABC tissue, using its own intrinsic osteogenic potential to promote healing. By triggering intralesional new bone formation, the bone paste represented an effective means to reverse the expanding phase of ABC. The particulated bone allograft was easy to handle and to introduced in an irregular cavity. Moreover, as a complete cyst evacuation was not required, a minimal surgical approach could be used so that the risks and morbidity associated with an extensive approach were reduced. Its use is of particular interest in poorly accessible areas like the pelvis and spine.

Introduction

Aneurysmal bone cyst (ABC) is a benign lesion composed of cyst-like walls that are filled with blood [6, 21]. The course of ABC may be very perplexing. The growth of this pseudotumoral lesion can be impressive, with rapid expansion in the bone that will be progressively blown out. ABC may also recur after curettage and bone grafting. Conversely, cyst maturation with subsequent ossification may be observed either spontaneously or after incisional biopsy. Spontaneous healing of ABC has been reported by Malghem et al. [20] but is only rarely observed. Healing after biopsy alone was noted in 3% of the cases by Campanacci et al. [5]. Selective arterial embolization has also been reported to favour ABC maturation [5, 12, 22]. Recurrence occurred in about 12%–21% of the cases that were treated by curettage and bone grafting and in 22% of those treated by curettage and radiotherpay [5, 17]. The treatment of choice today remains complete curettage of the cyst or even an extraperiosteal excision of the lesion followed by bone grafting [5, 6, 9]. However, in poorly accessible locations like the pelvis and spine, preference is now given to arterial embolization [6, 12].

Although the true pathogenetic mechanism of ABC formation and evolution is unknown, most authors consider ABC as a reactional bone response to haemorrhage [6, 10, 21]. As some ABC exhibit a self-healing capacity, whether spontaneously or after biopsy, and the cystic-like walls contain spotty osteoid or woven bone trabeculae, meaning that ABC do have an intrinsic potential of new bone formation, we attempted in two difficult cases with a "blowout" lesion to promote ossification of ABC by the implantation of a partially demineralized bone powder that was supplemented with autogeneic bone marrow through a minimal surgical exposure. Successful healing was observed.

Case reports

Case 1

A 16-year-old girl had a 2-year history of left heel pain. The heel was dramatically enlarged, and she had not been able to wear shoes or bear weight in the 2 years since she was originally referred. Roentgenograms demonstrated a "blowout" calcaneum, suggesting an ABC that was confirmed by open biopsy (Fig. 1a). She had been treated for the past 2 years with 14 corticosteroid injections (80–120 mg of methylprednisolone acetate per injection)

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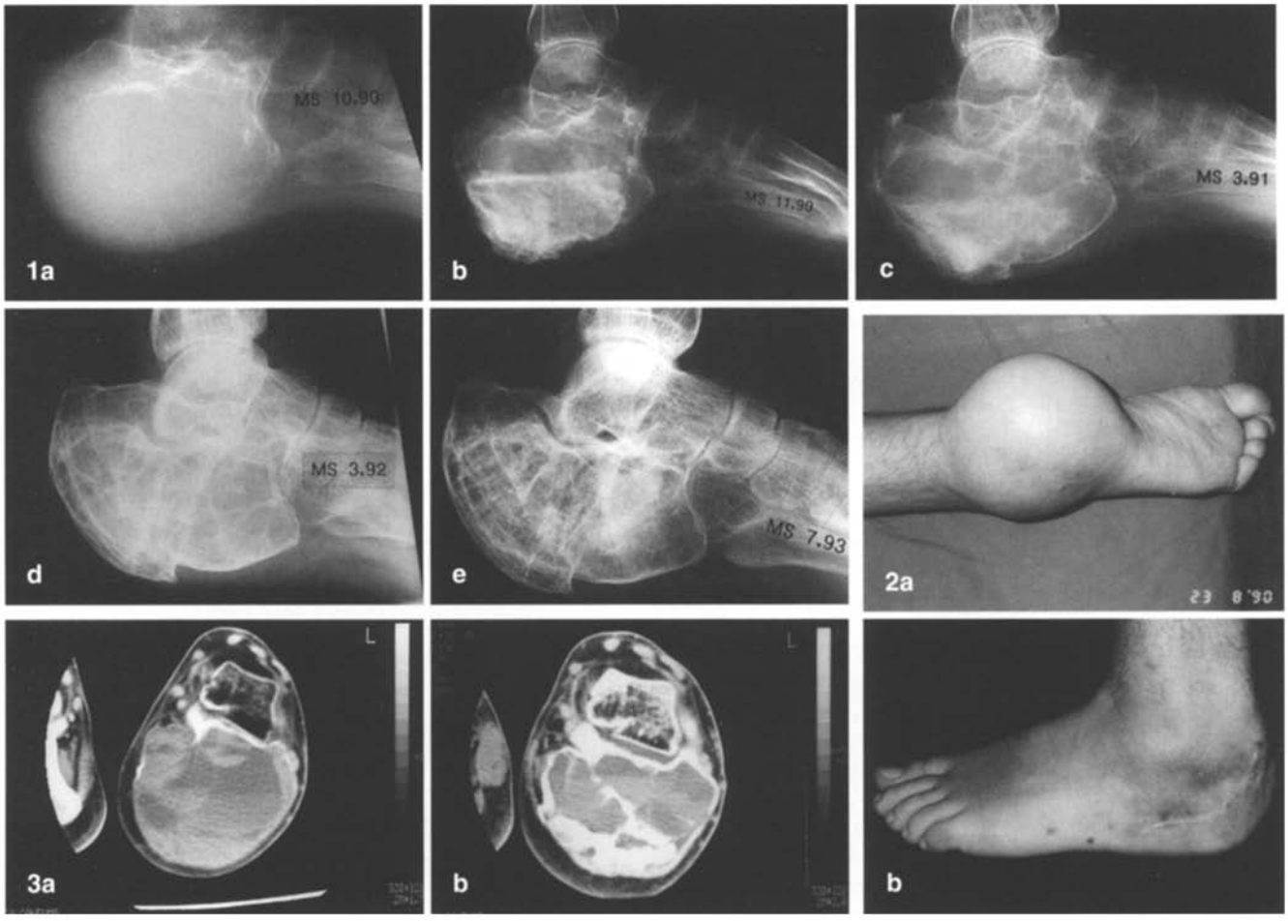

Fig. 1a–e Case 1. Lateral radiographs of the "blow out" calcaneum and the aneurysmal bone cyst (ABC) and its progressive healing after bone paste implantation. **a** Preoperative lateral radiograph of the calcaneum. **b** Immediate postoperative lateral radiograph showing the incomplete packing of the cyst by the partially demineralized bone particles. **c** Four-month aspect of the calcaneum on the lateral radiograph showing a well delineated peripheral shell of new bone. **d** Progressive development of an irregular ossification throughout the cavity at 16 months after surgery. **e** Lateral radiograph at 32 months after surgery showing the enlarged but fully ossified calcaneum which required surgical reduction twice to allow her to wear shoes

Fig. 2 Clinical aspects of the calcaneum (case 1): **a** preoperative aspect of the expanded calcaneum; **b** final aspect of the calcaneum after two surgical reductions of the bone mass

Fig. 3 **a** Preoperative computed tomogram (CT) of the ABC of the calcaneum. Typical "blowout" appearance with presence of a fluid-fluid level. **b** Four-month postoperative CT of the same calcaneum. Persistence of a faint fluid-fluid level. Presence of a distinct peripheral bony shell and internal septa

and cast immobilization without any effect. The calcaneum was laterally approached via a limited exposure, and the cyst was partially curetted. A bone paste obtained by mixing 10 cc of bone marrow with 16 g of partially demineralized bone powder was introduced through a syringe into the cavity, leading to only incomplete filling of the cyst (Fig. 1b). The postoperative course was uneventful. Roentgenograms showed that the whole cavity was not fully packed with the bone grafting material. Four months after surgery, the cyst was completely delineated by a thin shell of new bone (Fig. 1c). Intralesional osteogenesis became evident at 4–5 months with a meshwork of non-oriented trabecular bone. The implanted granular material was progressively embedded in new bone which was only formed within the original limits of the cyst. Ossification of the "blowout" calcaneum was progressively achieved (Fig. 1d). Twenty months later, the expanded bone mass was reduced and remodelled by surgical osteotomy, using the first approach. Two years after initial surgery, the bone volume was further reduced via a medial exposure (Fig. 1e). This two-step reduction of the ossified cyst allowed normal shoe wear and gave a satisfactory cosmetic appearance (Fig. 2). Computed tomograms in the first postoperative year demonstrated the persistence of aneurysmal tissue, with some typical horizontal fluid levels in the cystic spaces that were delineated by an irregular network of new trabecular bone (Fig. 3). Histological analysis of the healed bone retrieved at 20 and 28 months showed that some residual cavities of ABC separated by septa of fibrocellular and fibroadipose tissues were still present at 20 months (Fig. 4), whereas at 28 months, only dense fibrous tissue and adipose marrow could be found. The follow-up period is now 52 months.

Case 2

A 19-year-old girl was referred for a biopsy-proven ABC of the right superior pubic ramus that had caused pain in the groin for 3 months. In September 1991, she underwent a preoperative arterial embolization and immediately afterwards a curettage and bone grafting with freeze-dried bone allografts through an ilioinguinal approach. The ABC was confirmed at histology. On roentgenograms, the lesion progressed, with further enlargement of the expansile lytic process and resorption of the bone grafts (Fig. 5a).

Fig. 4 Section of a specimen taken from the calcaneum at the time of surgical reduction, 20 months after the initial surgery. Residual cavities of ABC separated by septa of fibrocellular and fibroadipose tissues are still present. (Haematoxylin and eosin; original magnification × 125)

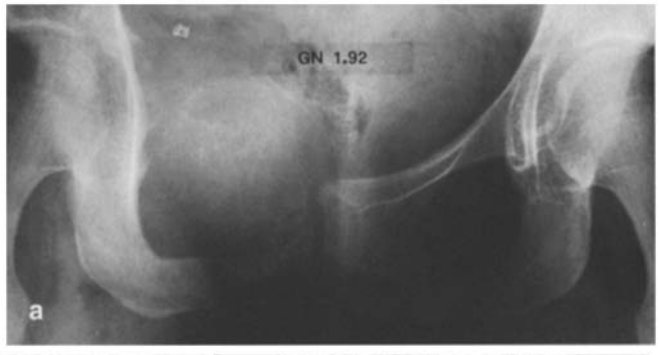

Fig. 5a–d Case 2. Destruction of a superior pubic ramus by an ABC and its induced healing. **a** Recurrent, aggressive ABC of the superior pubic ramus after arterial embolization, curettage and bone grafting. **b** Early postoperative anteroposterior radiographs, 2.5 months after surgery. The ABC is delineated by a bony shell. Incomplete packing of the cavity by the granular material can be seen. **c** Progressive ossification of the cyst at 5 months postoperatively. **d** Aspect of the ossified lesion on anteroposterior radiograph at 21 months after surgery

Through a limited incision at the pubis, the cyst was partially evacuated and curetted. Twenty milliliters of autologous bone marrow were aspirated from the iliac crest and mixed with 25 g of partially demineralized, freeze-dried bone particles to make a paste that was introduced as far as possible with the finger into the cavity. The postoperative course was uneventful, with rapid disappearance of the pain. Ossification of the peripheral shell was the first sign of cyst healing. The cyst reached the healing phase, characterized by gradual ossification and development of an irregular bony mass (Fig. 5). Partial weight-bearing was allowed at 6 weeks, while full weight-bearing was resumed at 4 months. The follow-up is now 38 months.

Materials

Bone particles were prepared as follows: sterilely procured lower limb bone diaphyses were selected from our bone bank. Selection of the donors was made according to the guidelines issued by the American Association of Tissue Banks (AATB) [1] and the European Association of Musculoskeletal Transplantation (EAMST) [14, 16]. They were kept frozen at –80° C until preparation. While still

Fig. 6 Partially demineralized and pulverized bone allograft is mixed with autogenous bone marrow to obtain a paste that will be introduced into the cavity

refrigerated, they were sawn into small pieces and milled to a powder of less than 1-mm particle size under running water (Retsch, Cross beater mill type SK1, Haan, Germany). The powder was sieved to retain the fraction between 200 and 800 μm. Defatting and dehydration were carried out with a 1:1 (v/v) chloroform-methanol solution for 3 h and rinsed in methanol for 1 h. Partial demineralization of the bone was achieved with 0.6 N hydrochloric acid (HCL) (15 ml/g of bone) for 15 h at 4° C. The powder was rinsed several times in water, freeze-dried and finally gamma-irradiated at a dose of 25 kGy [13]. Before being implanted, the powder was mixed with bone marrow to obtain a paste (Fig. 6).

Discussion

Treatment of a largely expanded ABC lesion may prove very perplexing and difficult. Firstly, in rare instances, spontaneous healing has been reported [20], while ABC regression has also been observed either after biopsy [5, 25] or therapeutic embolization [5, 12, 22]. Secondly, in sites such as the pelvis or spine, or when the size of the cyst is particularly large, the recommended surgical treatment of extraperiosteal excision and bone grafting makes surgery difficult and risky. Under such circumstances, being able to reverse the expansile activity of the cyst into the healing phase with minimal surgery would be extremely rewarding. Filling the ABC with bone powder proved to be successful, with subsequent healing and no recurrence of aggressive activity in these cases.

The rationale underlying this intralesional treatment was that the admixture of a partially HCl-demineralized bone powder with bone marrow might reverse the cyst expansion through a bone induction mechanism. It has been known for several years that intramuscular or subcutaneous implantation of completely demineralized bone matrix can promote a sequence of events leading to new bone formation [15, 23, 27, 28]. Whereas the induction phenomenon with this system is constant in rodents, the observed response remains inconstant and minimal in long-lived animals [3, 18, 24]. However, as new bone formation in dogs could be more consistently induced if partially instead of completely demineralized bone was used [13], the bone particles were only partially demineralized.

A successful osteoinduction requires not only an adequate release of bone morphogenetic proteins (BMP) but also the presence of responding cells. ABC represents a reactive repair tissue that has the intrinsic capacity of self-healing [6]. It is a common finding to observe in ABC spotty slivers of woven bone in the walls of the cyst which exhibit a fibroblastic or mesenchymal cellular exuberance. It was hypothesized that these cells would be able to respond to the osteoinductive bone particles. Supplementation of autologous bone marrow cells to bone matrix has been shown to increase osteogenesis by both its own bone-forming capacity and the supply of responding cells for BMP [2, 19, 26, 30]. Since demineralized bone matrix and bone marrow were used in combination, it is impossible to determine whether the effects were due to the inductive properties of the matrix or the introduction of osteogenic cells or growth factors contained in the marrow. Whether bone marrow alone would have been sufficient to reverse the osteolytic activity of the cyst cannot be answered by the present investigation. The aim of our treatment in these two dramatic clinical observations was an attempt to stimulate maturation of the tumour with a conservative approach to avoid extensive surgery that would have otherwise been necessary.

The final shape of the new bone will correspond to the one developed by the cyst at the time of surgery. The presence of aneurysmal tissue left in place by the incomplete curettage did not prevent the ossification process.

The first sign of healing was the early appearance of a complete peripheral shell of new bone which was observed within the first 3 months after surgery. A spontaneous healing of the cyst induced by the incomplete curettage appears unlikely as on preoperative roentgenograms both cysts were in the active growth phase, considered aggressive according to criteria developed by different authors [5, 11, 20, 29], and a surgical biopsy had already been done with a long observation period in the first case and arterial embolization and a failed bone grafting procedure for the second case.

This limited experience shows that the inductive material represents an effective means to reverse the expanding phase of an ABC lesion to its reparative phase with resultant ossification of the cyst. The particulated bone allograft can be easily manipulated for introduction into an irregular cavity. Such material could be substituted in the future by more purified osteogenic material such as recombinant human osteogenic protein [8] or bone morphogenetic proteins [7, 31]. Moreover, as only minimal surgical exposure is required to implant the powder, the risks and morbidity associated with an extensive approach are

avoided, particularly in areas when surgical access is difficult, like the pelvis and spine. It might therefore represent a potential improvement over conventional forms of surgical treatment, but further clinical series are required for confirmation.

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