Autologous, and combined autologous, and hydroxyapatite granules in the treatment of benign bone lesions in children

Badawi Ihab

Department of Orthopedic Surgery and Traumatology, Alexandria University, Alexandria, Egypt

Correspondence to Ihab Badawi, MD Orth, 5 Abdel Salam Aref Street, El Hedaya, Alexandria, Egypt. Tel: +20 102 000 7626/20 100 690 9751;
e-mail: ihabbadawi@yahoo.com

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Background

Despite all established treatments, large bone cysts in children remain an unsolved problem. Bone grafts are often necessary to fill the defect, provide support, and enhance biological repair. Autogenous cancellous bone grafts usually from the iliac crest have been considered the gold standard. However, the limited quantity of a bone graft especially in children may limit its use. Calcium phosphate ceramics can be used to fill bone defects. These materials act as an osteoconductive bone-void filler that completely gets resorbed as newly formed bone remodels and restores anatomic features and structural properties.

Aim of the work

This study was carried out to assess the results of treatment of benign bone lesions in children using autologous bone graft either alone or in combination with hydroxyapatite (HA) granules.

Patients and methods

The study included 18 children having benign bone lesions. Their age ranged from 5 to 15 years (mean, 8.2±1.59 years). The resultant defect was filled with autogenous iliac crest graft in five (27.8%) patients in group I, and a combination of autogenous bone graft and G-bone HA granules in 13 (72.2%) patients in group II. The defect size ranged from 6 to 17 cm^3 in group I (mean, 9.75±43.86 cm^3), and from 11.5 to 115.5 cm^3 in group II (mean, 43±33.92 cm^3). The patients were followed up clinically and radiologically for a period that ranged from 12 to 56 months (mean, 17±11.41 months).

Results

The overall success rates were 80% for group I (four out of five) and 92.3% for group II (12 out of 13). Recurrence was met in one (20%) of five patients in group I, and one (7.7%) of 13 patients in group II. At the final follow-up, four of five patients in group I (80%) were considered Neer class I, and one (20%) patient was considered Neer class IV. Ten (77%) of 13 patients in group II were considered Neer class I, two (15.3%) patients were Neer class II, and one (7.7%) was Neer class IV. The differences in the results of both groups were statistically insignificant.

Conclusion

The use of HA synthetic granules with autogenous bone graft is a safe and effective option for the situations when a large amount of graft is needed especially in children with large and recurrent benign bone lesions.

Keywords:
autologous, bone lesions in children, hydroxyapatite granules

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Introduction

Autologous bone grafts have osteogenic, osteoinductive, and osteoconductive properties. Autologous bone grafts have an excellent success rate, low risk of transmitting diseases, and histocompatibility. However, there is a limited quantity of autogenous bone graft especially in children [1,2].

Allografts are associated with a risk of transmitting infectious diseases. This limits its use to fill bone cysts, especially in children [1,2].

Calcium phosphate ceramics can be used to fill bone defects. These materials act as an osteoconductive bone-void filler that completely gets resorbed as newly formed bone remodels and restores anatomic features and structural properties [1,2].

This study was carried out to assess the results of treatment of benign bone lesions in children using autologous bone graft either alone or in combination with hydroxyapatite (HA) granules.

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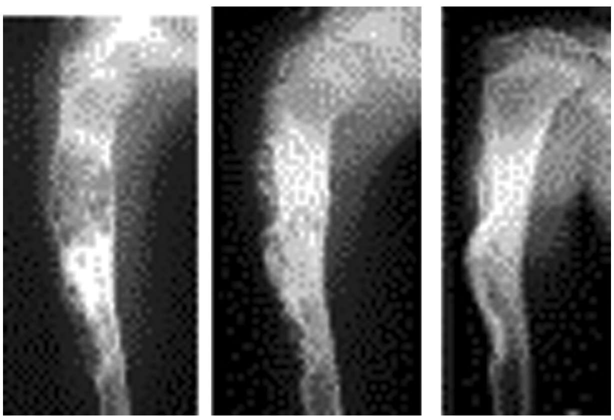
Patients and methods

Between January 2008 and January 2012, 18 children were diagnosed as having benign bone lesions. There were 10 boys and eight girls. Their age ranged from 5 to 15 years (mean, 8.2±1.59 years). The proximal metaphysis of the humerus was affected in seven (38.8%) patients, the distal humerus in one (5.6%) patient, the proximal femur in six (33.3%) patients, the distal femur in one (5.6%) patient, and the distal tibia in three (16.7%) patients. This study was approved by ethical committee of Department of Orthopedic Surgery and Traumatology, Alexandria University. All patients signed an informative consent form.

All procedures were done under general anesthesia. The surgical approach was chosen according to the site of the lesion to allow for adequate exposure. The lesions were thoroughly curetted. The tissues obtained were sent for histopathological study. The diagnosis was nonossifying fibroma in seven (38.9%) patients, aneurysmal bone cyst in four (22.2%) patients, recurrent aneurysmal bone cyst in two (11.1%) patients, fibrous dysplasia in two (11.1%) patients, eosinophilic granuloma in one (5.6%) patient, fracture through fibrous dysplasia in the femoral neck in one (5.6%) patient, and recurrent fibrous dysplasia with a malunited femoral neck fracture in one (5.6%) patient.

The resultant defect was filled with autogenous iliac crest graft in five (27.8%) patients, and a combination of autogenous iliac crest and G-bone HA granules in 12 (66.6%) patients. In one (5.6%) patient, a nonvascularized fibular graft was used together with the combination (Fig. 1).

Figure 1



(a) Preoperative radiography showing recurrent aneurismal bone cyst following two previous operations for grafting. (b) Combined autogenous iliac crest graft, fibular graft, and hydroxyapatite granules. (c) 30-month follow-up radiography showing healing with no recurrence.

G-bone is a synthetic multiphasic HA granule with 1.8–3 mm average particle size. It consists of synthetic calcium HA in low crystalline form. It is a mixture of HA, tricalcium phosphate (TCP), and other forms of calcium such as calcium carbonate and bicalcium phosphate [3].

Patients treated by autogenous iliac crest graft alone were considered as group I, and patients treated by a combination of HA granules and autogenous graft were considered as group II. One patient had aneurysmal bone cyst in the proximal femur and was treated by iliac crest graft and was included in group I. The lesion recurred and the graft was completely absorbed. He was considered as a failed case. Then he was treated using the combined technique and was included in group II (Fig. 2).

The mean age of patients in group I was 8±1.22, and in group was II 8.3±1.75. This difference was statistically insignificant (Table 1).

The defect size ranged from 6 to 17 cm^3 in group I (mean, 9.75±43.86 cm^3), and from 11.5 to 115.5 cm^3 in group II (mean, 43±33.92 cm^3). This difference was statistically significant (Table 1).

Internal fixation was used in two patients in group II. The first patient presented with fracture of the femoral neck through fibrous dysplasia. This patient was treated by internal fixation using plate and screws in addition to the combined technique, and a hip spica was applied for 2 months (Fig. 3).

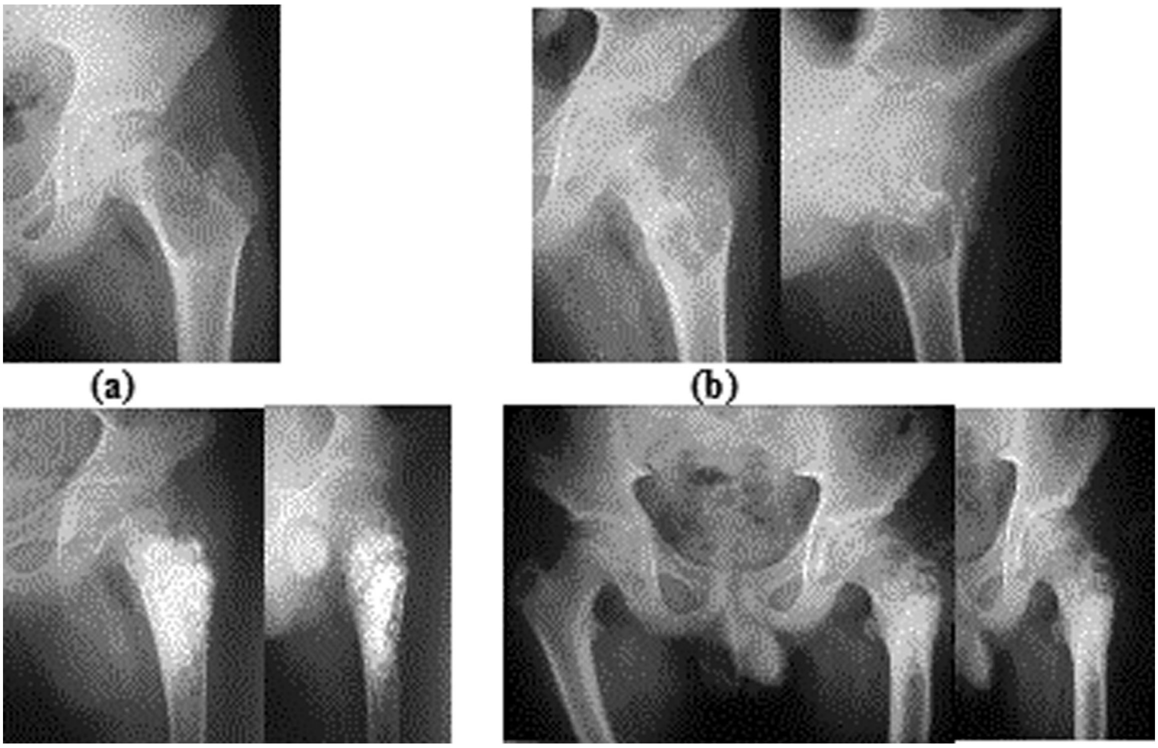
The second patient had recurrent fibrous dysplasia together with coxa vara deformity. This patient was primarily treated elsewhere by a bone graft and a hip spica to treat a pathological fracture through the femoral neck. The patient was treated by corrective osteotomy, dynamic hip screw fixation, and combined grafting (Fig. 4).

The physical activities were restricted until the radiography showed enough signs of bone healing. Thereafter, the physical activities were resumed gradually.

The patients were followed up clinically and radiologically for a period that ranged from 12 to 56 months (mean, 17±11.41 months). The mean follow-up period in patients in group I was 14.6±7.79, and in group II was 18.69±12.6. This difference was statistically insignificant (Table 1).

Radiological changes were evaluated according to the modified Neer classification system [4].

Figure 2



(a) Preoperative radiography showing aneurismal bone cyst in the proximal femur. (b) radiography showing recurrence and complete absorption of autogenous iliac crest graft at 3 months postoperatively. (c) Combined autogenous iliac graft and hydroxyapatite granules. (d) 26-month follow-up radiography showing no recurrence.

Table 1 Comparison between the mean age, size, and duration of follow-up between both groups

	Group I	Group II	*t*
Mean age	8±1.22	8.3±1075	0.295
Mean size	9.75±43.86	43±33.94	0.007*
Mean follow-up	14.6±7.79	18.69±12.6	0.499

Neer I: healed cyst filled with new bone with or without small radiolucent area less than 1 cm.
Neer II: healing cyst with a defect. Contains a radiolucent area less than 50% of the diameter of the bone with enough cortical thickening to prevent fracture.
Neer III: persistent cyst with a radiolucent area more than 50% of the diameter of the bone and with a thin cortical rim. No increase in the size of the cyst. Continued restriction of activity or repeated treatment is required.
Neer IV: recurrent cyst. The cyst reappears in a previously obliterated area, or a radiolucent area increases in size.

The procedure was considered successful if the lesion was completely healed or healed with a radiological defect. When evidence of consolidation of the lesion or cortical thickening was absent 6 months after the initial procedure or when recurrence occurred, the procedure was considered unsuccessful [4].

Results

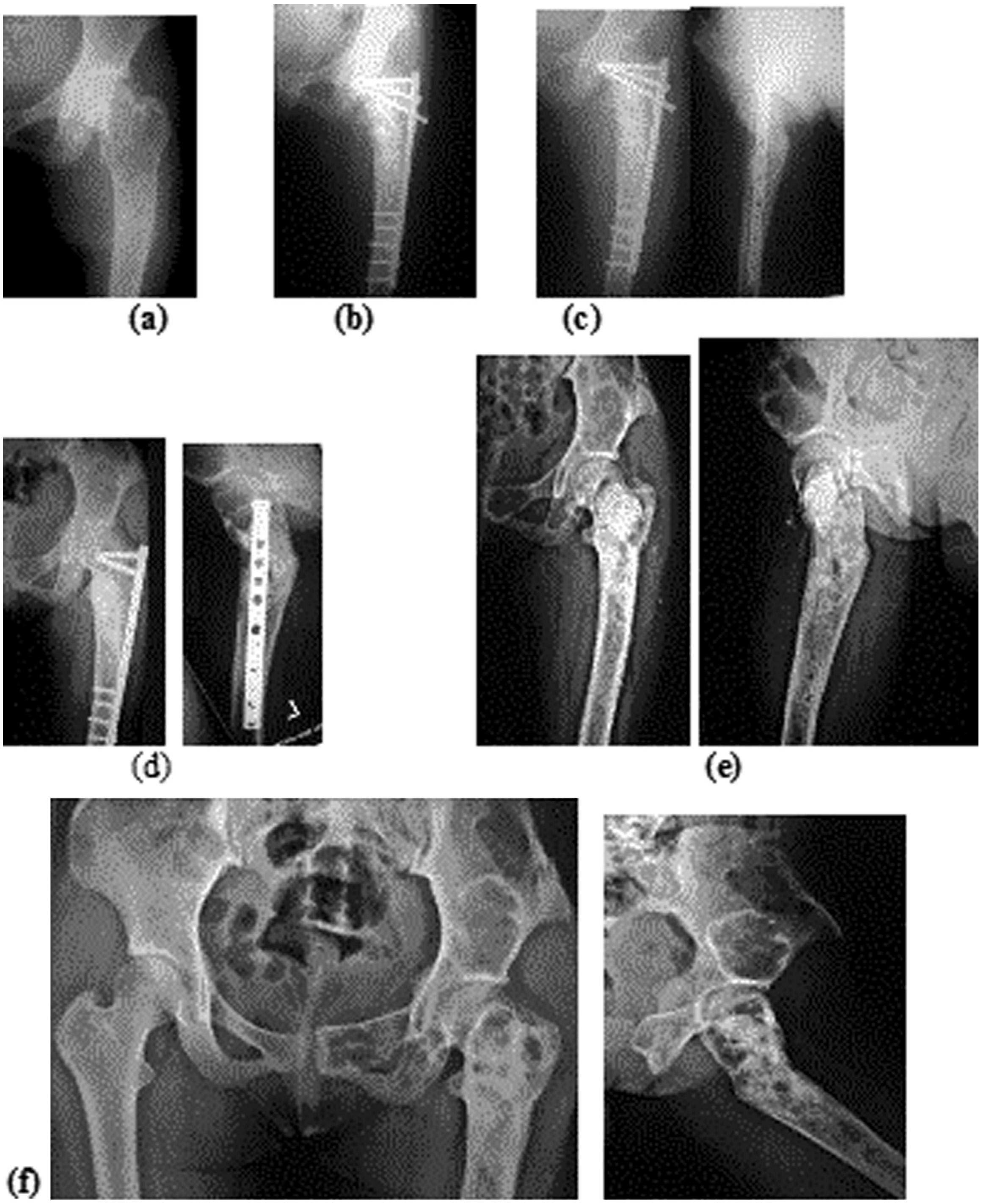
The overall success rates were 80% for group I (four out of five), and 92.3% for group II (one out of 13). This difference was statistically insignificant. χ^2: 0.554.

Recurrence was met in one of five (20%) patients in group I, and one (7.7%) of 13 patients in group II. This difference was statistically insignificant. χ^2: 3.04.

At the final follow-up, four of five (80%) patients in group I were considered Neer class I, and one (20%) patient was considered Neer class IV. Ten (77%) of 13 patients in group II were considered Neer class I, two (15.3%) patients were Neer class II, and one (7.7%) was Neer class IV. This difference was statistically insignificant (Table 2).

The patient who experienced recurrence in group I had recurrence after iliac crest grafting of an aneurysmal bone cyst in the proximal end of the femur. The graft was completely absorbed 3 months after grafting. The patient was retreated by the combined technique and was included in group II. The lesion healed, and there was no evidence of recurrence within 26 months of follow-up (Fig. 2).

Figure 3

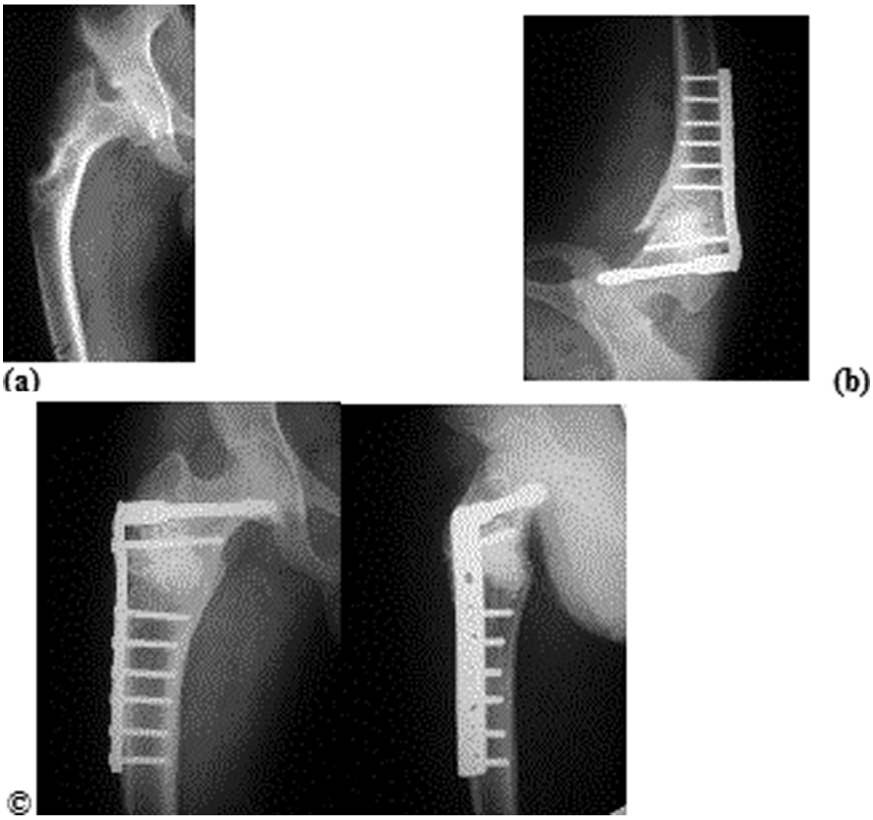


(a) Radiography showing fracture of the femoral neck through fibrous dysplasia of the proximal femur. (b) Postoperative radiography showing plate and screws fixation together with combined grafting. (c) Radiography 5 months postoperatively showing healing of the fracture and the defect. (d) Radiography 14 months postoperatively showing recurrence. (e) Radiography after removal of the metal work and re-grafting using hydroxyapatite granules. (f) 52-month follow-up radiography showing recurrence in the proximal femur together with the appearance of new lesions in the ipsilateral hemipelvis.

In addition to this patient, group II included two recurrent lesions that were treated somewhere else. One of them had an aneurysmal bone cyst that was treated by iliac crest graft 7 years before the definitive procedure. The lesion recurred and was treated again somewhere else using iliac and a nonvascularized fibular graft. Again the lesion recurred. The patient was treated using the combined technique together with a nonvascularized fibular graft. The lesion healed with no recurrence within 30 months of follow-up (Fig. 1).

The second patient had a recurrent fibrous dysplasia together with coxa vara deformity following previous

Figure 4



(a) Preoperative radiography showing recurrent fibrous dysplasia with severe coxa vara deformity. (b) Postoperative radiography showing corrective osteotomy, combined grafting, and DHS fixation. (c) 12-month postoperative radiography showing healing of the osteotomy and the defect with no recurrence.

Table 2 Neer class for both groups at the final follow-up

Neer I	Neer II	Neer III	Neer IV	Total
4	0	0	1	5
10	2	0	1	13
14	2	0	2	18

χ^2: 1.26 (not significant).

treatment somewhere else for fracture through the femoral neck through the lesion. He was treated primarily by bone graft and a hip spica. Unfortunately the lesion recurred and the fracture was malunited in coxa vara. The lesion was treated by the combined technique together with corrective osteotomy and dynamic hip screw (DHS) fixation. The deformity was corrected, the osteotomy healed and the lesion did not recur within 12 months of follow-up (Fig. 4).

Recurrence occurred in one patient in group II. This patient presented with a fracture through fibrous dysplasia in the femoral neck. She was treated by the combined technique together with internal fixation using plate and screws. The fracture and the cyst healed. However, the lesion recurred. Another surgery was done after 14 months for removal of the metal work and the recurrent lesion was curetted and regrafted using HA granules. Unfortunately the lesion recurred not only in the femoral neck, but also several lesions occurred in the pelvis. The follow-up period of this patient was 52 months. She is able to walk without any walking aids. She had attacks of severe pain that responded to bed rest and anti-inflammatory drugs. In addition, she has 2-cm shortening that is compensated for by a shoe lift (Fig. 3).

Discussion

Despite all established treatments, large bone cysts in children remain an unsolved problem [5]. Bone grafts are often necessary to fill the defect, provide support, and enhance biological repair [5,6].

Autogenous cancellous bone grafts usually from the iliac crest have been considered the gold standard because it is the only graft that provides osteointegration (the ability to chemically bond to the surface of bone without an intervening layer of fibrous tissue), osteoconduction (the ability to support the growth of bone over its surface), osteoinduction (the ability to induce differentiation of pluripotential stem cells from the surrounding tissues), and osteogenic potential (formation of new bone by osteoblasts and precursor cells within the graft material). In addition, they are histocompatible and lack any immunogenicity [6–9].

Cancellous bone grafts are more osteogenic than cortical grafts because of the presence of spaces allowing for diffusion of nutrients, and revascularization by micro-anastomosis of its circulating vessels [8,10].

This standard autograft has its own share of problems like inadequate amount, especially in children, donor site morbidity, and potential complications like pain, hematoma, and infection [6,7].

To overcome these problems, biological bioalternatives mainly allografts and xenografts have been processed and used. However the limitations of the ready availability, high cost of harvesting and appropriate testing, and problems of abnormal histology, infection, and immunogenicity have accelerated the search for other bone graft substitutes including growth factors, platelet-rich plasma, bone marrow injections, demineralized bone matrix, and synthetic bioinert materials as an alternative [6,7,10,11].

Demineralized bone matrix removes the mineral phase and exposes the underlying bone collagen and growth factors, most notably bone morphogenetic protein (BMP). These grafts have no structural capability but provide sufficient bone morphogenetic proteins to osteoinduce bone in osseous defects [10,12].

Bone marrow (BMI) has a substantial number of osteogenic cells that are capable of providing bone regeneration. It has been demonstrated that 150 cm^3 of bone marrow can successfully heal established tibial nonunions. Most researchers in the field of bone marrow urge the co-insertion of bone marrow with any of the bone graft alternatives [4,10].

Platelet-rich plasma contains growth factors such as platelet-derived growth factor, transforming growth factor beta, vascular endothelial growth factor, insulin-like growth factor, and many others. These factors play an important role in the early phase of fracture healing and may thus encourage healing of the cyst, and decrease the recurrence rate. However, platelet-rich plasma needs separation kit costing about $400 and a centrifuge [11].

The cost of growth factors and bone morphogenetic proteins restricts their use in clinical practice to a limited number of academic and reference centers [11].

The most commonly used synthetic bone grafts are calcium-based compounds including calcium sulfate, calcium phosphate, and HA. Those compounds can provide osteointegration, and osteoconduction [9]. In addition, they may have an osteoinductive potential by activating the release of stimulatory proteins by the local scaffold [7]. Moreover, these substances are biocompatible [7].

The acceptance of these substitutes by the host tissues is determined by two important features: pore size, and the porosity or interconnectivity [6]. Minimum pore size of 100 μm is optimal for bone ingrowth, whereas pore sizes more than 200 μm facilitate the development of mature osteon. Interconnectivity is essential because dead-end pockets limit vascular supply to the ingrowing bone [6].

The form whether blocks or granules can also determine the clinical utility as the size of the defect determines the appropriate size of the implant. In metaphyseal large voids, a block form actually provides better support [6].

Calcium sulfate is resorbed by a process of dissolution within 5–7 weeks. Its rapid reabsorption may be used to advantage in the context of osteomyelitis where antibiotic impregnated form could be used in place of gentamycin beads, thus alleviating the need for a second operation [9].

Calcium sulfate in its set form has a compressive strength greater than cancellous bone and a tensile strength slightly less than cancellous bone. Calcium sulfate, however, requires a dry environment to set, and if it is re-exposed to moisture, it tends to soften and fragment. For this reason, it has no reliable mechanical properties *in vivo*, and its application should be limited to a contained area [9].

Calcium sulfate is used with calcium phosphates in some preparations. Animal studies showed that calcium sulfate and calcium phosphate composites promoted significantly more new bone formation compared with autograft bone, calcium sulfate alone, or calcium phosphate alone [7].

B-TCP was one of the earliest calcium phosphate compounds to be used as a bone graft substitute. It is available in porous or solid forms as either granules or blocks. Structurally, porous B-TCP has a compressive strength and a tensile strength similar to cancellous bone. Like other calcium phosphate preparations, it has been found to be brittle and weak under tension and shear but resistant to compressive loads. Typically it has been used in its granular porous form. Porous granules tend to migrate less than solid granules owing to earlier fixation by fibrovascular ingrowth. B-TCP undergoes resorption via dissolution and fragmentation over a 16-18-month period [9].

Unfortunately, the replacement of B-TCP by bone does not occur in an equitable way. That is, there is always less bone volume produced than the volume of B-TCP reabsorbed. For this reason, the clinical use of B-TCP has been an adjunctive with other less absorbable bone graft substitutes or as an expander for autogenous bone grafts [9].

Synthetic HA comes in ceramic or nonceramic forms as porous or solid blocks or granules. Ceramic HA preparations are resistant to reabsorption *in vivo*, which occurs at a rate of 1–2% per year. Conversely, nonceramic HA is more readily reabsorbed *in vivo* and is also available in a self-setting cementable form [9].

Synthetic HA have good compressive strengths but are weak in torsion and shear. They are brittle and are fracture prone on shock loading. Synthetic HA in solid block form is difficult to shape, does not permit fibro-osseous ingrowth, and has a much higher modulus of elasticity than bone. Synthetic HA has been successfully used to cover implants to enhance osteointegration. Its porous granular form has been used alone or with bone grafts to fill voids [9].

Cho *et al.* [12] used demineralized bone matrix to fill the defect after decompression of unicameral bone cysts in 25 patients. Nineteen lesions completely consolidated in a single procedure. Four had incomplete healing but had enough cortical thickness to prevent fracture. Two required a second intervention. Both had healing after 10 additional months.

Lokiec *et al.* [13] used autologous marrow to treat 10 unicameral bone cysts. All cysts healed after one injection.

Cho *et al.* [4] used bone marrow injections to treat 28 unicameral bone cysts. The overall success rate was 92%. The recurrence rate was 13.3% after the initial procedure.

Wright *et al*. [14] reported 23% overall success rate using bone marrow injection to treat 28 unicameral bone cysts compared with 42% success rate after steroid injection.

Kanellopoulos *et al.* [15] used a combination of demineralized bone matrix and autogenous bone marrow to treat 19 unicameral bone cysts. Two required a second injection. All patients were asymptomatic at the last follow-up.

Pedzisz *et al.* [11] treated nine unicameral bone cysts using allograft mixed with platelet-rich plasma. All cysts healed after 2 months with no recurrence within 19.5 months of mean follow-up.

Saikia *et al.* [6] treated 24 benign bone tumors. A total of 20 lesions were treated with HA granules or blocks. In four of them, iliac crest grafts were used. Four lesions were treated by TCP and fibular struts. They had complete incorporation and no recurrence after 6–18 months of follow-up.

Uchida *et al*. [16] used HA blocks and granules to fill defects in 60 cases of benign bone tumors after resection. The implants were well incorporated into the host bone in all cases.

Evaniew *et al.* [7] treated 24 benign bone tumors with intralesional curettage followed by reconstruction with calcium sulfate and calcium phosphate composite. Recurrence occurred in two cases, and deep infection in four cases.

In this study, we used cancellous bone grafts either alone (group I) or combined with G-bone HA granules (group II) to fill defects resulting from curettage of benign bone lesions in children. G-bone is a synthetic HA. It is made up of multiphasic calcium HA in low crystalline form. It is derived from chemical synthesis. It is a mixture of HA, TCP, and other forms of calcium such as calcium carbonate, and bicalcium phosphate. We used the SHAG 4 G-bone granules with an average particle size of 1.8–3 mm [3].

Bone grafts only were used in small size defects (group I), and the combined technique was used in large defects or recurrent cases after bone grafting alone. Our results showed that there were no statistically significant differences in the results of both groups in spite of the fact that the mean size of the defect was significantly smaller in the graft-only group. The graft-only group had one recurrence out of five cases, and the combined graft group had one recurrence of 13 cases.

In addition, three patients included in the combined graft group were recurrent cases after autogenous grafting. All three cases healed with no evidence of recurrence during follow-up.Recurrence occurred in group one in a case of aneurysmal bone cyst. The study included six aneurysmal bone cysts; two of them were recurrent cases. This makes the incidence of recurrence after treatment of aneurysmal bone cysts in this study 16.7%. In fact, this is comparable to the 20% incidence of recurrence reported by Mankin and colleagues after reviewing 150 cases of aneurysmal bone cysts treated over 20 years. They treated their cases by biopsy, followed by curettage, and implantation of allograft bone chips or polymethylmethacrylate. They used autografts in patients with large lesions or after failure of the primary procedure [17].

The recurrence in the combined group occurred in a patient with fibrous dysplasia making the recurrence rate one (25%) out of four cases of fibrous dysplasia included in this series. The recurrence occurred in the only case of poloystotic fibrous dysplasia included in this study. We were obliged to do bone grafting because she presented with a transcervical femoral neck fracture through a large lesion. It is known that in fibrous dysplasia, bone grafting may be indicated for selected patients with monostotic disease. Allograft is preferred to autograft in these cases to eliminate donor site morbidity. In fact bone grafting for patients with polyostotic fibrous dysplasia is not useful. Attempts to completely remove polyostotic disease with curettage and bone grafting are rarely successful. Such surgery results in significant blood loss, and the fibrous dysplasia lesions typically remodel the grafts over time. There may be a limited indication for the use of allograft in conjunction with internal fixation for selected cases where the graft material provides temporary augmentation for the internal fixation [18].

Conclusion

The results of this series indicate that the use of HA synthetic granules with autogenous bone graft is a safe and effective option for the situations when a large amount of graft is needed especially in children with large and recurrent benign bone lesions.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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