



USE OF ALLOGENIC BONE GRAFT IN TREATMENT OF BENIGN OSTEOLYTIC LESIONS

Oncology

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ABSTRACT

In management of osteolytic lesions of bone definitive treatment involve intralesional excision and filling of the bone defect.^{1,2} Various material such as autologous bone graft³, allogenic bone graft^{4,5}, synthetic materials including calcium phosphate⁶, calcium hydroxy apatite⁷, have been used with variable results. Allogenic Bone Graft (ABG) have got distinct advantage of being available in sufficient quantity without the risk of donor site morbidity and doesn't warrant a second surgery for removal. From 2011 to 2013, 8 consecutive benign osteolytic lesions (3 cases each of aneurysmal and simple bone cysts and 2 cases of Giant Cell Tumour) were treated by intralesional curettage and bone grafting using deep freeze gamma irradiated allogenic bone graft either alone or in combination with autogenic bone graft/ bone marrow aspirate. All the patients were randomly allocated to either vancomycin impregnated allogenic bone graft group (n=5) or simple allogenic bone graft group (n=3). The age range of studied patients was from 14 to 43 years. Vancomycin impregnated allogenic bone graft appears to be a safe & effective filler, without any systemic local and adverse effects, for bone defects secondary to benign osteolytic lesions. None of the patients develop postoperative infection. All the eight osteolytic lesions in the study healed with the use of allogenic bone graft.

KEYWORDS

Introduction

Management of benign osteolytic lesions of bone involve intralesional excision and filling of the bone defect.^{1,2} Various material such as autologous bone graft³, allogenic bone graft^{4,5}, synthetic materials including calcium phosphate⁶, calcium hydroxy apatite⁷, have been used with variable results. Allogenic Bone Graft (ABG) have got distinct advantage of being available in sufficient quantity without the risk of donor site morbidity and doesn't warrant a second surgery for removal. However, high risk of infection has been reported by Tuli SM et al⁸ and Goyal SC et al⁹ using decalcified allograft for benign cystic lesions. Allogenic bone graft (BG) also has limitation that it can serve only as a scaffold and lacks osteoinductive potential¹⁰. Therefore the present study was undertaken to address these shortcomings associated with use of Allogenic Bone Graft (ABG). In order to address the problem of infection associated with the use of allogenic bone graft, gamma sterilization of the graft was carried out prior to use in all patients and vancomycin impregnation of the graft material was carried out. This deep freeze gamma irradiated allogenic bone graft was combined with osteogenic potentiators either Bone Marrow Aspirate(BMA) or Autologous Bone Graft and the results were evaluated in terms of healing of lesion, osteointegration and infection.

Material & Methods

The study was approved by institutional ethical committee and all patients were fully informed and agreed to participate in the study. The inclusion criteria were histological confirmation of benign osteolytic bone lesion either by aspiration or incisional biopsy and having a minimum follow up period of six months. Exclusion criteria were patients having any active osteoarticular infection at the concerned site and patients with any medical contradiction to the use of vancomycin. From 2011 to 2013, 8 consecutive benign osteolytic lesions (3 cases each of aneurysmal and simple bone cysts and 2 cases of Giant Cell Tumour) were treated by intralesional curettage and bone grafting using deep freeze gamma irradiated allogenic bone graft either alone or in combination with autogenic bone graft/ bone marrow aspirate. All the patients were randomly allocated to either vancomycin impregnated allogenic bone graft group (n=5) or simple allogenic bone graft group (n=3). The age range of studied patients was from 14 to 43 years.

The institutional bone bank had bone grafts procured from consenting patients having undergone total hip and knee arthroplasty at the institute and stored them at -76 degree Celsius for minimum of three months before use. The gamma irradiation was achieved by giving a dose of 25 grays of radiation at an accredited centre. The graft was

manually morcelized to fragment size of 0.4-0.6 cms and washed with plenty of sterile saline. The bacterial culture of the allograft was taken before implantation to ascertain sterility. were all negative. In randomly selected 3 out of 8 cases in which antibiotic impregnated graft was used, the morcellized bone graft was kept in 20ml distilled water solution consisting of vancomycin 50mg/ml for a period of one hour.

Patients were seen at 5 days for 1st wound check, then 2 weeks postoperatively for suture removal and again at 6 and 12 weeks. Particular attention was given to infection / local signs of active inflammation. Radiographs were done every four weeks for initial four months and then at every two months till completion of follow up. A minimum followup of six months was there. Results were assessed in terms of cyst healing as defined by the Neer's criteria¹² (Table 1), rate of osteointegration using criteria given by Sloof et al¹³ (Table 2) and occurrence of infection according to the WHO Surgical Site Infection (SSI) guidelines¹⁴.

Table 1. — Neer's classification system for radiographic evaluation of cyst healing

Stage I	100% cyst filling with new bone
Stage II	Partial cyst filling, increased cortical thickness
Stage III	Recurrence, cortical thinning, osteolytic areas > 3 cm
Stage IV	No response to treatment

Table 2. — Sloof's criteria for assessing osteointegration of allogenic bone grafts

- (i) Presence/Absence of progressive lucent lines between the preexisting bone and the graft,
- (ii) absence of resorption of graft
- (iii) radiographic homogeneity of the graft.

Statistical analysis was performed using computer software. Continuous variables were compared with Student's t tests. Binary variables were compared with chi square tests.

Results & Conclusions

All the eight patients could be followed for more than one year. The maximum followup period was of 18 months. None of the patients showed clinical or histological evidence of any immunological reaction.

Graft incorporation and healing

The earliest radiological sign of incorporation of allograft material was

seen at about ten weeks. Initially the graft material was seen as having different radiodensity as compared to the host bone bed but later progressive homogeneity of the graft material with filling of the cavity and obliteration of margins of the original lesion was seen. In this study, the time of healing and consolidation of Benign osteolytic lesion and adequate osteointegration closely followed each other and varied according to the nature of lesion. In simple bone cysts all the three cases showed incorporation of bone allograft within 4 months. In aneurysmal bone cysts all the three cases showed graft incorporation but the time period varied within a range of 7-10 months while both cases of giant cell tumour showed adequate osteointegration within 9-11 months. For all these benign osteolytic lesions the mean time of osteointegration in the study group was 7.20 ± 1.64 months and in the control group was slightly lesser at 5.33 ± 2.08 months but there was no statistical difference with p value of 0.206.

Vancomycin impregnated allogenic bone graft appears to be safe and effective filler, without any systemic and local adverse effects, for bone defects secondary to benign osteolytic lesions

Infection

Surgical Site Infection guideline was used to identify postoperative infection. None of the patients developed postoperative infection. Any extraosseously placed allogenic bone graft, that is graft material placed out of the cystic cavity in lytic lesions and outside the bone defect in cases of fractures, inevitably got resorbed in both the study and control groups in an average time period of 9 weeks. Allogenic bone graft appears to carry a little, if any, risk of getting converted to sequestrum vulnerable to infection in the future. Thus allogenic bone grafts impregnated with antibiotics may also be used in active osteoarticular infection as there are less chances of the remaining graft serving as dead necrotic bone aiding in persistence of infection.

Recurrence

All the 8 cystic lesions in the study healed with the use of allogenic bone graft. Thus no difference in terms of healing of Benign osteolytic lesions (Simple Bone Cyst, Aneurysmal Bone Cyst and Giant Cell Tumour) was noted in the study. Thus vancomycin impregnated allogenic bone graft can serve as an excellent filler for augmenting healing in Benign osteolytic lesions of bone.

Discussion

Earliest use of bone allografts for reconstruction have been practiced by Aubigne RM⁵ since 1966. In most experimental models, fresh allografts are associated with a rigorous inflammatory response as well as a specific immune response. However, deep frozen allografts are associated with decreased immunogenicity and no demonstrable change in initial mechanical properties as reported by Friedlander G¹⁶ in 1987.

Spence et al⁴ in 1969 implanted freeze dried cancellous allografts in solitary bone cysts and obtained adequate healing in 55% of cases with partial healing in 9% and recurrence in 36% of cases. Kakiuchi et al⁷ performed 75 implantations using decalcified human bone matrix gelatin and achieved complete healing in 68 cases with seven cases having recurrence of benign tumour. Tuli SM et al⁸ in 1992 used decalcified allogenic bone graft in giant cell tumour, simple and aneurysmal bone cysts, fibrous dysplasia and achieved complete healing in 65% of cases with recurrence rate of 6%. Similarly Goel SC et al⁹, 1992, reported successful allograft incorporation in 30 out of total 35 cases of cystic bone lesions with one failure and four recurrences. Finkemeier CG et al¹⁷ in 2002 used morselized bone grafting in bone defects such as bone cysts, infective non unions and other reconstructive procedures.

The period of incorporation varied within reasonable limits among different studies. Spence et al⁴ reported a mean healing time of approximately 1 year. Kakiuchi et al⁷ reported a time of 3-15 months in their series. Tuli SM et al⁸ found age as an important factor in time of incorporation of graft and found that in children the incorporation occurred relatively earlier at 6-9 months while incorporation occurred at a period of 9-15 months in adults. Goel SC et al⁹ pointed towards variation in incorporation depending upon the type of lesion with simple bone cysts having graft incorporation of around 3 months, aneurysmal bone cysts between 3-6 months and giant cell tumours between 6-9 months. Spence KF¹⁸ (1976) in separate study involving treatment of simple bone cyst by using freeze dried cortical allograft reported that inadequate filling of the lesion also adversely affected graft incorporation.

Almost all studies reported some recurrence rates after curettage and bone grafting. Age of the patient, size and type of lesion lesion and

adequacy of cavity filling by allograft are the factors seemingly affecting the recurrence rates. Glancy et al¹⁹ in a study on cystic lesions in children, reported complete healing in 80% of small volume cysts and 38% in large volume cavities. Spence et al⁴ reported recurrence rate of 36 % in adult patients. Tuli SM et al⁸ also concluded that small size cavities had better healing rates as compared to larger lesions. . Goel SC et al⁹ also reported a similar conclusion regarding size of lesion and recurrence rates. In locally aggressive lesions, such as giant cell tumours, recurrence rates vary from 27% to as high as 45%.

Surgical site infection associated with use of allogenic bone graft merits concern as shown by Ketonis C et al²⁰ in who carried out a study assessing bacteriological colonization of allogenic bone grafts and found a high risk of graft being colonized by microorganisms. . Goel SC et al⁹ found a higher rate (10.9%) of infection in benign cystic osseous lesions treated by curettage along with decalcified allogenic bone grafting as opposed to infection rate (9.5%) series done by Campanacci et al²¹ where treatment alone by curettage was done. The incorporation of antibiotic loaded bone graft was first studied by Gudmundson C²² 1971 who showed that the presence of tetracycline locally markedly inhibited bone graft incorporation. Cancellous bone as a carrier for vancomycin has been studied in vitro by Witso E et al¹¹ in 1999. Use of vancomycin is favoured because of its physiochemical properties of hydrophilicity, heat stability and efficacy against *Staphylococcus* species which is most common cause of osteoarticular infection. Buttaro MA et al²³ in 2003 showed in an in-vitro study that vancomycin if used in appropriate concentration (1 gram dry vancomycin powder for 300 grams of bone graft.) will not affect osteointegration of allogenic bone graft as the peak levels attained locally by such a use were higher than Minimum Inhibitory Concentration (MIC) value of vancomycin for most susceptible organisms, but were 2000 times lower than the levels (10,000 µg/ml) associated with death of osteoblasts.

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