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Restoration of long bone defects treated with the induced membrane technique: protocol and outcomes

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KEYWORDS

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ABSTRACT

This prospective study was undertaken at a regional tertiary referral centre to evaluate the results of treatment of bone defects managed with the induced membrane (IM) technique. Inclusion criteria were patients with bone defects secondary to septic non-union, chronic osteomyelitis and acute fracture with bone loss. Pathological fractures with bone loss were excluded. Data collection included patient demographics, pathology, previous surgical intervention, size of bone defect, type of graft implanted, time-to-union and complications/re-interventions. The minimum time of follow up was 12 months. Forty-three patients (32 males) met the inclusion criteria with a mean age of 47.9 years (range 18–80 years). 22 patients had an acute traumatic bone loss associated with open fracture and 21 presented with an infected non-union or underlying osteomyelitis requiring bone excision. The most common microorganisms grown were staphylcoccous aureus and coagulase negative staphylococcous. The mean length of the bone defect area was 4.2 cm (range 2–12 cm). All patients were managed with the two stage technique receiving composited grafting (Autologous bone graft (Iliac crest/RIA), graft expander as required, osteoprogenitor cells, growth factor) during the second stage. There was one failure (humeral infected non-union) in a previous background of bone radiation that necessitated reconstruction with a free fibula vascularized graft. One patient had a fall and sustained implant failure (humeral defect) 3 months after reconstruction and following re-plating progressed to union 4 months later. Two patients required re-grafting due to failure of healing in one of the defect sides. One patient presented with a discharging sinus 2 years after successful healing of a tibial defect that was treated successfully with soft tissue and bone debridement without necessitating further interventions. One patient despite union (distal 1/3 tibia) underwent a below knee amputation due to a dysfunctional ankle/foot (previous foot compartment syndrome- regional pain syndrome). Of those patients, with lower limb injuries, 4 patients had leg length discrepancies of 1 cm, 1.5 cm, 2 cm (two patients) respectively. The mean time to radiological union was 5.4 months (range 2–12 months). The average time of healing of 1 cm bone defect was 1.24 months. Patients with upper limb reconstruction recovered earlier than those with lower limb injuries. At the latest follow up all patients were able to mobilize full weight bearing without residual pain.

The induced membrane technique appears to be an alternative good option for the management of large bone defects secondary to acute bone loss or infected non-unions. The incidence of re-interventions was low in this challenging cohort of patients. The technique should be considered in the surgeon's armamentarium as it is effective and is associated with a low rate of complications.

Introduction

Critical size bone defects are defined as defects exceeding 2–2.5 times the diameter of the affected bone [1,2]. Their treatment continues to be challenging despite the latest advances in surgical techniques and tissue regeneration procedures [3]. Their incidence is variable ranging between 0.4% and 11.4% [4].

Treatment modalities include such techniques as bone transport (distraction osteogenesis), vascularised bone free transfer, massive cancellous autograft or allograft, titanium cages, replacement of the defect with megaprosthesis and the last resort being amputation of the affected extremity [5–14]. Each one of the above techniques has limitations and the results of treatment are variable in regards to each technique's effectiveness.

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During the last 2 decades, the induced membrane (Masquelet) technique was introduced as a complementary option for the management of bone defects [15]. The technique consists of two stages. During the first stage a PMMA cement is implanted at the bone defect area and acts not only as a spacer to maintain the length of the affected limb but also facilitates the production of a pseudo membrane which has been shown to contain osteoprogenitor cells and has the ability to release inductive molecules (growth factors) capable of stimulating osteogenesis [16,17]. At the second stage, 6–8 weeks later, after incision of the membrane, the cement spacer is removed and autologous bone grafting is implanted in the defect area facilitating a positive osseous healing response. Healing of defects as lengthy as 25 cm have been treated effectively with this technique [18].

The aim of the current study is to present our institutional experience of applying this technique in a series of patients that were managed in our institution with bone defects. We wished to determine the incidence of success rate (osseous healing) and the number of complications encountered.

Patients and methods

Between January 2008 and December 2014, all consecutive patients who presented in our unit with bone defects either as a result of traumatic injury or developed bone loss as a result of infection requiring radical bone debridement were eligible to participate. Main inclusion criteria were: acute fracture with bone loss, septic nonunion and chronic osteomyelitis associated with bone loss secondary to radical bone debridement. Patients with pathological fracture resulting in bone loss or patients treated with another surgical technique (i.e. bone transport) were excluded.

Prospective data documented included patient demographics, mechanism of injury, type of injury and presence of associated injuries; open or closed injury, anatomical region involved, type of surgery, time elapsed between the 2 stages of the technique, graft material implanted, type of pathogen isolated in the cases where infection was the causative factor, complications and mortality. All patients were managed by fellowship trained consultant grade surgeons according the protocol designed by the senior author.

Assessment and management

Patients were assessed and managed as the previously developed algorithm by the senior author (Figure 1). This was designed with an aim to standardize the assessment and treatment of patients. The surgical management consisted of 2 stages as previously described [18]. In summary, stage 1 surgery consisted of the following standardized surgical steps in each case:

1. Debridement of the soft tissue in case of open fracture (acute setting) or sinus secondary to chronic infection, debridement of the devascularised or infected bony segment.
2. Insertion of a PMMA cement spacer (PALACOS® Bone Cements mixed with 2grams of Vancomycin)
3. Reconstruction of the soft tissue envelope as needed (rotational muscle flap, free muscle flap, skin grafting)
4. Temporary (external fixator) or permanent skeletal stabilization (open fractures) depending on the skeletal and local soft tissue conditions.
5. Prescription of appropriate pathogen specific antibiotics when necessary (infected cases) for a period of minimum of 6 weeks as guided by the local microbiology guidelines.

Stage one lasted between 6 and 8 weeks, (average 7 weeks). Stage 2 consisted of the following standardized steps:

1. Autologous bone graft was harvested from intramedullary cavity of femur/iliac crest as indicated, pending on the volume of graft needed. Concentrated bone marrow aspirate to increase the cellularity of the graft material was aspirated from the iliac crest. Bone harvesting from the femoral canal was carried out using the RIA device – Reamer Irrigator Aspirator (Depuy- Synthes, West Chester, PA, USA) either from the contralateral and/or ipsilateral femur as it was indicated. In cases that the volume of graft was not adequate, Orthos scaffold (Geistlich, Wolhusen, Switzerland) was used as a graft expander.
2. Removal of external fixator – pin site irrigation /debridement.
3. Cement spacer removal following incision and preservation of the membrane formed.
4. Further inspection of the bone defect area. Tissue biopsies for microbiology. If suspicion that any bone area is non-viable, tissue removed.
5. Definitive surgical stabilization of the fracture with plate fixation or intramedullary nail as indicated.
6. Implantation in the defect area of the composite graft (autologous bone graft, BMP-7 (Olympus Biotek) and BMA (bone marrow aspirate- concentrated osteoprogenitor cells)
7. Closure of the membrane, creating a closed compartment.
8. Wound closure without using a surgical drain.

Post-operatively all patients except those with upper limb surgery received thromboprophylaxis (low molecular weight heparin subcutaneously (Tinzaparin 4.500 IU)) for 6 weeks. Patients with lower limb injuries were mobilized toe touch weight bearing initially using either a zimmer frame or crutches for 6–8 weeks and thereafter progressed from partial to full weight bearing. Outpatient follow-up with both clinical and radiographic assessment was carried out at 2 weeks for wound inspection and at 6 weeks, followed by a 3, 4, 5, 6, 8, 12 months or until radiological signs of union and pain free mobilization. Radiologically union was defined when 3 out of 4 cortices showed callus formation (bridging).

Broad spectrum empirical antibiotic therapy (Augmentin 1.2 g) was given after obtaining tissue samples at the time of debridement. The empirical antimicrobial regimen was either continued or modified according to the culture results and local microbiology guidance. The duration and the route of administration of the antibiotics were dependent on the patients systemic and local wound response.

All infected patients were treated systemically with a course of antibiotics based on the local microbiology tissue sensitivities for a minimum period of 6 weeks and were discontinued only after the haematological biomarkers were normalised.

This study was approved by the institutional review board. The minimum follow-up period was 12 months.

Results

Forty-three patients (32 males) with bone loss after debridement of a septic non-union or after an acute fracture were eligible to participate during the specified period of the study. The mean age was 47.9 years (range 18–80 years). Patient's characteristics are shown in Table 1.

Overall, 22 patients had an acute traumatic bone loss associated with open fracture. Out of the twenty-one patients with infected non-union, 11 had a previous open fracture. One patient developed infection as a result of wound contamination following leaking of the ileostomy on to the hip wound after gamma nail fixation of the subtrochanteric femur fracture. A patient with Lisfranc injury had a successful open reduction internal fixation but subsequently developed wound infection and deep sepsis requiring removal of metal work and bone debridement leading to a bone defect of the medial cuneiform. The most common microorganisms grown were staphylcoccous aureus and coagulase negative staphylococcous and all patients had 6–8 weeks of systemic antibiotic except of one patient who continued for 3 months, Table 2. The mean length of the bone