TECHNICAL NOTE

Epithelialization Over a Scaffold of Antibiotic-Impregnated PMMA Beads: A Salvage Technique for Open Tibial Fractures with Bone and Soft Tissue Loss When all Else Fails

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Abstract

The management of soft tissue defects in tibial fractures is essential for limb preservation. Current techniques are not without complications and may lead to poor functional outcomes. A salvage method is described using three illustrative cases whereby a combination of flaps and antibiotic-impregnated polymethylmethacrylate beads are employed to fill the bony defect, fight the infection, and provide a surface for epithelial regeneration and secondary wound closure. This was performed after the partial failure of all other options. All patients were fully ambulatory with no clinical, radiographic or laboratory sign of infection at their most recent follow-up. Although our findings are encouraging, this is the first report of epithelialization of the skin on a polymethylmethacrylate scaffold. Further studies investigating the use of this technique are warranted.

Keywords: Infection, Open tibial fracture, Polymethylmethacrylate, Soft tissue defect

Introduction

Fractures of the tibia are often complicated by soft tissue defects that increase the risk of infection and amputation (1-3). The management of these soft tissue defects, therefore, is essential in limb reconstruction. Improvements in surgical skills and techniques of soft tissue coverage have vastly contributed to the increased success of limb preservation in these patients.

The reconstructive ladder, which starts from skin grafts, to rotational muscular flaps, and free microvascular tissue transfer provides surgeons with the necessary armamentarium in their attempt to salvage the mangled extremity. Nevertheless, the failure rate of these complex surgeries is not negligible, and the complications of these injuries may lead to poor functional outcomes, even with the achievement of bony union (4-6).

In this report we present three patients with a limited area of soft tissue defect overlying an infected fracture site after partial failure of previous attempts to reconstruct the soft tissue envelope. Partial failure meant that there was a persistent uncovered area despite attempts at reconstruction. A salvage method is described using antibiotic-impregnated polymethylmethacrylate (PMMA) beads to fill the bony defect, fight the infection, and provide a surface for epithelial regeneration and secondary wound closure.

Case 1

A 58-year-old male epileptic patient fell from a height and sustained an open comminuted proximal left tibia fracture (Gustilo-Anderson Type IIIC) complicated with a deep wound infection and extensive skin and soft tissue necrosis following vascular repair. After extensive debridement of the wound, a microvascular rectus abdominus muscle transfer was attempted but was unsuccessful. Acute shortening was performed (7cm) with an Ilizarov fixator and a soleus flap was rotated to cover most of the defect. There was a persistent uncovered area measuring 3*2 cm just distal to the fracture.

Over the two weeks that followed, there was failure of secondary healing with a stable defect size, persistent purulent discharge, and complete absence of any healthy granulation tissue. Wound cultures grew *Escherichia*

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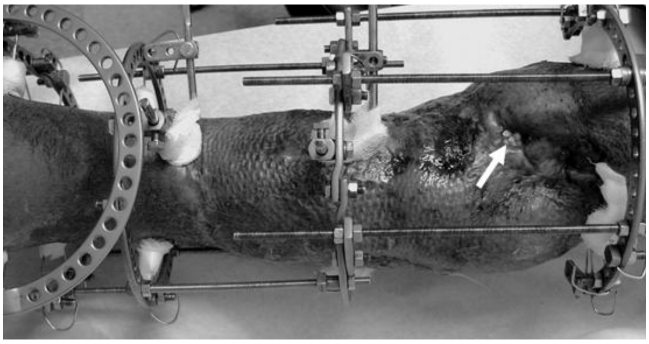

Figure 1a. Clinical image of the leg of Case 1 demonstrating the proximal soft tissue defect filled with cement pellets (white arrow) after reconstruction with a rotational flap and split thickness skin graft.

coli. The patient was taken back to the operating room where limited debridement of the anterior cortex was performed, leaving only the posterior cortex intact. The defect was packed with PMMA (Stryker, Kalamazoo, MI, USA) pellets measuring 1cm in diameter mixed with 1 gram of vancomycin. The pellets were placed in order to fight the infection and provide a scaffold over which epithelialization and wound closure could take place. A distal corticotomy was performed for gradual lengthening to restore leg length [Figure 1A, B]. Daily wound care involved cleaning with saline solution and application of wet-to-dry dressings.

Over the next six weeks, the wound reduced in size with healthy granulation tissue covering the PMMA pellets, followed by epithelialization and complete closure of the defect with no discharge [Figure 2]. Three months later, the pellets were retrieved through small stab wounds away from the area of epithelialization, and autogenous cancellous iliac bone graft was used to fill the defect. At six months, radiographs showed complete healing of the fracture site as well as the regenerate, and the fixator was removed [Figure 3]. At 5-year follow-up, the patient was fully ambulatory with no clinical, radiographic or laboratory signs of infection.

Case 2

A 25-year-old male presented with a mangled right leg secondary to a landmine explosion (Gustilo-Anderson Type IIIC). There was significant bone and soft tissue loss. After vascular repair, extensive debridement of the wound was performed along with acute shortening (3cm), and the tibia was fixed with an Ilizarov apparatus. A soleus flap was used to close the wound. Five days later,

Figure 2. Clinical image showing the final result with secondary skin closure.

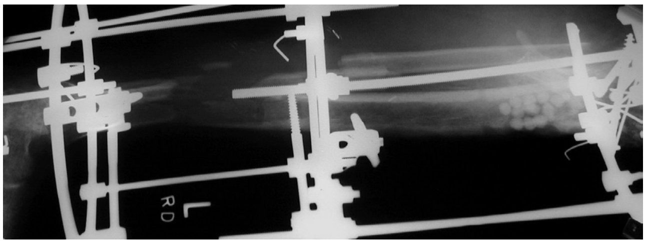

Figure 1b. A plain radiograph of the same patient showing the anterior bony defect filled with cement pellets.

there was drainage from the fracture site with partial failure of the flap. The patient was taken to the operating room where the bone was debrided and PMMA pellets measuring one cm, mixed with one gram of vancomycin, were placed into the defect [Figure 4]. Wound swab cultures grew *Acinetobacter baumanii* and *Klebsiella pneumoniae*.

Three weeks later, a distal corticotomy was performed for gradual lengthening. Daily wound care, as described above, was performed. Over the next six weeks, the wound reduced in size with healthy granulation tissue covering the PMMA pellets, followed by epithelialization and complete closure of the defect with no discharge [Figure 5]. At four months, the PMMA pellets were retrieved and calcium sulfate pellets (Stimulan Kit, Biocomposites Inc., Wilmington, NC, USA) impregnated with one gram of vancomycin were used to fill the defect. Two months later, radiographs showed complete healing of the fracture site as well as the regenerate, and the fixator was removed. At two-year follow-up, the patient was fully ambulatory with no clinical, radiographic or laboratory signs of infection.

Case 3

A 60-year-old male patient sustained a shrapnel injury to his right leg and foot (Gustilo-Anderson Type IIIC). He was managed acutely with vascular repair, skeletal traction, and extensive debridement. After debridement

Figure 3. A plain radiograph showing bone healing after substituting the pellets with bone graft.

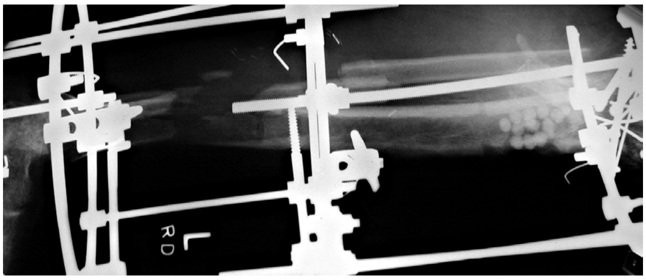

Figure 4. A plain radiograph showing distal tibial shaft bone defect along with the defect filled with cement pellets.

Figure 5. Clinical image showing the final result with closure of the proximal wound.

of the bone and soft-tissue in the leg and foot, an Ilizarov frame was applied and split thickness skin grafts were used to cover the leg wounds. A microvascular tissue transfer was considered inappropriate because of the poor general condition of the patient. The foot wounds were judged to be too contaminated for coverage. Wound swab cultures grew *Acinetobacter baumanii* and *Klebsiella pneumoniae.* The skin graft was subsequently lost over the medial side of the distal tibia fracture site.

A second debridement was performed two weeks later. The tibia fracture was exposed, the cuboid was exposed laterally, and the proximal lateral metatarsals dorsally [Figure 6]. PMMA pellets measuring one cm in diameter, mixed with one gram of vancomycin, were placed deep inside the lateral and dorsal foot wounds as well as at the fracture site. With daily wound care, filling of the skin defect and secondary closure of the wound was observed over a period of six weeks. The cement pellets were then removed through stab wounds at bedside. The distal tibia fracture was then compressed by modification of the external fixator. At nine months, the fractures were healed on radiographs, after which the fixator was removed [Figure 7]. The patient was ambulating freely, with no radiographic or clinical signs of infection at 18 months follow-up.

Discussion

Osteomyelitis is a devastating complication in musculoskeletal trauma. When associated with segmental instability of bone, it can jeopardize survival of the limb (1, 7). The classic treatment of an infected nonunion includes radical debridement of dead bone and necrotic tissue, rigid skeletal fixation, reconstruction of the soft tissue envelope and appropriate antibiotic therapy. Soft tissue coverage plays an essential role in the treatment of bone infections. A vascularized soft tissue envelope will optimize the milieu for systemic antibiotic therapy and bone healing (8, 9).

In combination with microsurgical transplants, the Ilizarov method may provide the best reconstructive option for extremity reconstruction (10). The combined versatility of modern free-tissue transplantation and distraction osteogenesis techniques has taken limb salvage to the next level and improved the salvage rate of the mangled extremity with high rates of success (10, 11). However, these techniques are not free of complications which may lead to undesirable functional outcomes or amputation. The most serious complication is the loss of softtissue coverage with the persistence or recurrence of infection. Our experience in microvascular transfer has previously been reported in the treatment of osteomyelitis and infected segmental osseous defects (10). In the three patients of this series the free flap option was considered risky, either due to the general condition of the patient or the presence of a single vessel in the injured limb. All three patients had local flaps after extensive debridement with partial dehiscence over the infected segmental defect and persistent drainage with positive cultures despite receiving systemic antibiotic therapy.

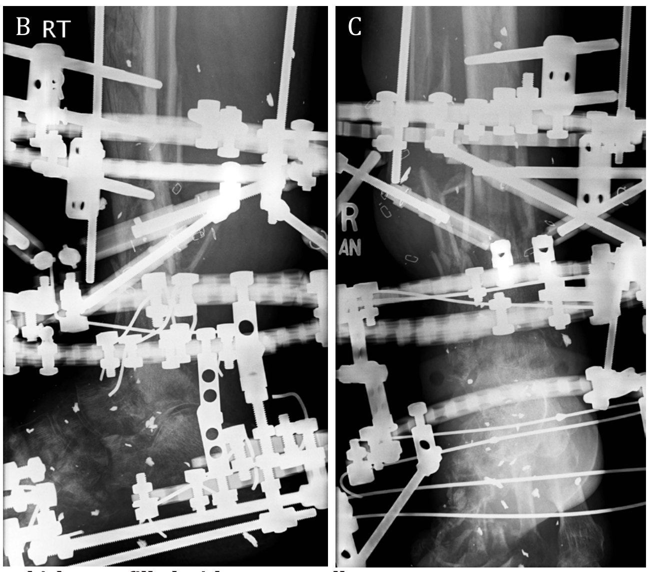

Figure 6a, b, c. Intraoperative image showing the open lateral foot wounds which were filled with cement pellets.

Figure 7. Clinical image after removal of the fixator and secondary closure of the foot wounds.

PMMA beads impregnated with antibiotics have been used over the past 40 years (12). It has been shown that they are efficient in increasing antibiotic delivery to bone with a chance for cure (13, 14). In our first patient, we considered filling the anterior tibial defect by PMMA beads to accomplish three goals: [1] attempt to fill the defect, [2] deliver local antibiotics and eradicate the infection, and [3] prevent further shortening of the leg. In the weeks that followed, we observed the epithelialization which took place and secondary wound closure. Subsequently, we used the same technique in our two remaining patients. Although a decrease in soft tissue swelling may partially explain the decrease in wound size, there was a clear area of granulation followed by epithelialization overlying the beads. This may not have been possible without an underlying scaffold. A recent animal model study suggests that the use of a bio absorbable gel may provide enhanced antibiotic delivery with lower infection rates when compared to PMMA beads, however this would not provide an adequate scaffold over which epithelialization could take place (15). Regarding soft tissue coverage over PMMA beads, rabbit model studies with mandible and oral mucosa defects showed that using limited porosity PMMA implants resulted in a fibrous capsule as opposed to persistence of the mucosal defect with solid PMMA implants (16, 17).

In the technique described by Masquelet in 2000, a “pseudo synovial membrane” was formed between the spacer and native bone, which was hypothesized to prevent resorption of the graft and improve vascularity (18). This ‘bio membrane’ has subsequently been studied and found to have a pluripotent stem cell population that provides a favorable environment for osteointegration of bone grafts and union by secreting growth factors (19-21). Potentially, these same pluripotent stem cell populations were involved in the epithelialization over the PMMA beads in our patients. Harvesting, and molecular analysis of these cells is needed to further elucidate the nature of these cell populations.

Synthetic high purity calcium sulfate is used in the form of an injectable and moldable paste which sets and is remodeled by new bone. It allows for the local delivery of both powder and liquidantibiotics; and since it is an osteoconductive biodegradable material, it obviates the need for cement removal or the use of a bone graft.These qualities made it highly effective in our second patient who benefited from continued local antibiotic therapy, while preventing the need for a second procedure to remove the cement or undergo bone graft harvesting.

Although our findings are encouraging, this is the first report of epithelialization of the skin on a PMMA scaffold and is limited to three patients. These are the only patients in whom we have attempted this technique. This is a salvage technique to be reserved for patients who have a persistent localized osteocutaneous defect after total or partial failure of the standard techniques of soft tissue coverage. Further studies investigating the use of this technique are warranted.

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