Treatment of Complex Infected Non-union of Bone of the Upper Extremity by a Staged Approach: Debridement and Antibiotic Cement Followed by a Vascularized Free Fibula Flap

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Abstract: *Background:* Infected non-union of bone of the upper extremity remains a difficult problem to treat with limited options. Management must address chronic osteomyelitis and skeletal instability caused by the non-union. We present our experience with a staged approach in five patients.

Methods: The study cohort consisted of five males with an average age of 38 years and 4 prior procedures for infected non-union of the humerus (1) radius(1), ulna(1), ulna and radius(1) and metacarpal(1). The first stage consisted of aggressive debridement of all infected devitalized bone, bone cultures, removal of hardware, placement of antibiotic impregnated cement and stabilization with an external fixator (4 of 5 patients) followed by culture specific antibiotics. This was followed by definitive reconstruction using a free vascularized fibular flap and a course of post-operative antibiotics.

Results: The average bony defect measured 8.6 cm. All flaps survived, one required re-exploration for venous thrombosis 72 hrs post-operatively and was successfully salvaged with a re-do anastomosis using a vein graft. The average time to bony union was 14 weeks. There was one hypertrophic non-union from proximal hardware failure which required repeat surgical intervention. At an average of 5.1 years follow-up all patients remain infection free and were working.

Conclusions: A stage approach to the treatment of infected non-union of bone consisting of aggressive debridement, antibiotic cement, culture specific antibiotic followed by a vascularized fibular transfer is an effective treatment to a complex problem with limited alternatives.

Keywords: Infected non-union of bone, Osteomyelitis, Microsurgery, Antibiotic cement, Free vascularized fibula flap.

INTRODUCTION

Treatment of infected unstable segmental upper extremity defects remains a reconstructive challenge. Osteomyelitis by definition is an infection of bone. When osteomyelitis occurs at a fracture site that has not gone on to achieve bony union it is referred to as an infected non-union of bone. The management must address the problems of osteomyelitis and skeletal instability. Common treatment options for upper extremity instability such as functional bracing and activity modification, internal or external fixation with conventional bone grafting, structural grafts of allogenic or autogenous cortical bone, large volume autogenous cancellous bone grafts, or distraction osteogenesis may be inadequate [1-10]. Often, infected non-unions of bone and long bone defects are refractory to these conventional approaches. Although amputation remains an option, poor results of upper extremity prosthetics are well known, and even more so in these patients who often have functional hands [11-13].

There has been several papers on the use of the vascularized free fibula in the treatment of upper extremity long bone defects most of these have been limited case series addressing a mixed bag of upper extremity defects including tumor resection, aseptic non-union and infected non-union of bone [14-25]. None have addressed solely the treatment of infected non-union of bone with particular reference to the surgical technique and outcome in detail. In this article we report our experience with five complicated infected non-union of long bones in the upper extremity that had failed multiple conventional approaches to obtain bony healing. We described our staged approach, timing for reconstruction, surgical technique and long-term outcomes.

MATERIALS AND METHODS

A retrospective chart review was carried out of the author's microsurgery database between 1995-2017.

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Of a total of 79 free vascularized fibula flap 9 were performed for upper extremity segmental defects, 5 for infected (osteomyelitis) non-union of bone and 3 for aseptic non-union of bone and 1 for a failed cemented total wrist arthroplasty. The 3 free fibula flap for aseptic non-union of bone and 1 for a failed total wrist arthroplasty went on to bony healing without any significant complications and are not subject of this current study. Of the 5 vascularized fibula flaps used for infected non-union of bone they were used for 1 humerus, 1 radius, 1 ulna, 1 radius and ulna, 1 metacarpal infected bone non - union.

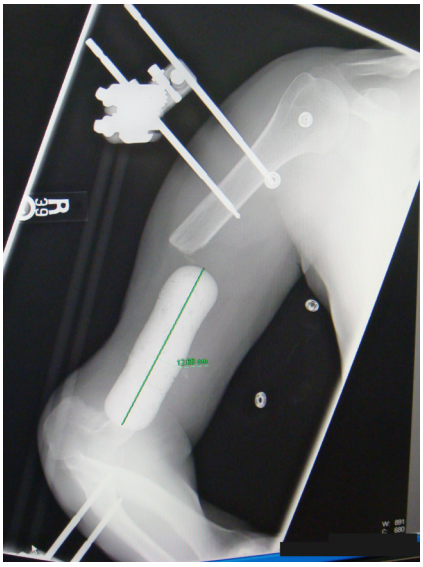
The average age of the patients with an infected bony non-union was 38 years (range 17 – 64 years). All were male with 4 out 5 being chronic smokers, none were diabetic, malnourished, and immunocompromised or had other major medical conditions. The injuries were from a close range shotgun in 1, fall in 1, industrial crush injury in 1, iliac crest bone grafted osteotomy complicated by osteomyelitis in 1, and motor vehicle accident in 1.

All patients had failed conventional methods to obtain bony healing and had an average of 4 operations (range 2 - 6) prior to presenting for staged microsurgical salvage. The average defect was 8.6 cm (range 3.5 – 15cm). The time of initial injury to the time of presentation for staged microsurgical salvage was 3 years and 2 months (range 2 months – 7.5 years). Three of five patients had sustained significant soft tissue injuries with 2 having had previous skin grafts and one a prior fasciocutaneous free flap. At the time of presentation initial cultures grew out Pseudomonas Aeruginosa in 1, Clostridium and Staphylococcus Aureus in 1, Serratia Marcenscens in 1, Methicillin Resistant Staphylococcus Aureus in 1, and Staphylococcus Epidermidis in 1 patient (Table **1**).

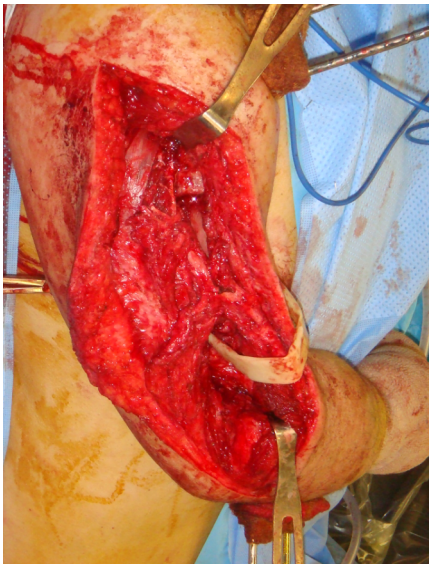
The patients with infected non-unions of bone were managed by a staged surgical approach. The first staged consisted of aggressive debridement of devitalized soft tissues, removal of any hardware in the wound, and en-block resection of the segments of infected bone to clinically healthy well vascularized bone with bleeding in the cancellous ends. In general, an external fixator was applied for skeletal stabilization (1 radius and ulna, 1 ulna, 1 radius, 1 humerus defect) unless the unstable bony segment could be stabilized with casting (1 metacarpal defect). Bone and wound Gram stains, and cultures and sensitivities were obtained. An antibiotic cement spacer was placed and the wound closed. The antibiotic cement spacer was fabricated at the time of surgery by taking a package of polymethylmethacrylate cement (Surgical Simplex P Radiopaque Bone Cement Stryker Orthpaedics; Limerick, Ireland) and mixing it one gram of Vancomycin powder and 2.4 grams of Tobramycin powder [26]. (Figure **1**)

Table 1: Patients History Prior to Reconstruction

Case	Gender, Age (years)	Type of Skeletal Defect and Microbiology at Presentation	Initial Treatment
1	M, 64	Shotgun wound to L. forearm complicated by infected non-union of radius and ulna Pseudomonas	Multiple I and D, fasciotomy for compartment syndrome, external fixation, skin grafting
2	M, 17	Open Left both bone forearm fracture complicated by osteomyelitis of ulna Clostridium and Staphylococcus Aureus	ORIF, multiple I and D
3	M, 30	Mangled R. hand complicated by osteomyelitis of 4th MC Serratia Marcenscens	Multiple I and D, ORIF, lateral arm free flap
4	M, 34	Distal Radius Osteotomy with tricancellous iliac crest graft complicated by osteomyelitis Methicillin Resistant Staphylococcus Aureus	Iliac crest bone graft, I and D
5	M, 47	Open fracture right humerus complicated by Osteomyelitis Staphylococcus Epidermidis	Multiple I and Ds and ORIF



(A)



(B)

Figure 1: (A) Patient status post irrigation and debridement with removal of internal hardware, placement of an external fixator and antibiotic cement for infected non-union of the humerus. (**B**) Humerus bony defect at time of reconstruction with free fibula flap.

The patients received culture specific intravenous antibiotics. The second stage was delayed for an average of 9 weeks and 5 days (range 2 – 22 weeks) until the WBC, ESR and CRP had returned to normal and there was no clinical or laboratory evidence of infection. If there was evidence of ongoing infection a repeat irrigation and debridement as above was performed prior to proceeding with definitive reconstruction. Three patients required only one debridement and two required two debridements before definitive reconstruction with a vascularized free fibula flap. All patients underwent pre-operative angiograms of the involved upper extremity and lower extremities for surgical planning.

At the second stage the free fibula osteoseptocutaneous flap was elevated using standard technique with some minor modifications as previously described by us [25]. The wound bed was prepared, and the antibiotic cement and external fixator removed. The fibula was inset, and a bony trough was created in the recipient bone site whenever possible to maximize the bony contact. Corticocancellous crushed fibular bone was packed around the osteosynthesis site to aid in bone healing. Standard rigid fixation was used in 4 patients adhering to AO principles and K - wires in one patient (metacarpal). The patients were immobilized in a cast or splint until bony union was achieved. The patients received at least 6 weeks of intravenous antibiotics post-operatively. (Figures **2** and **3**)

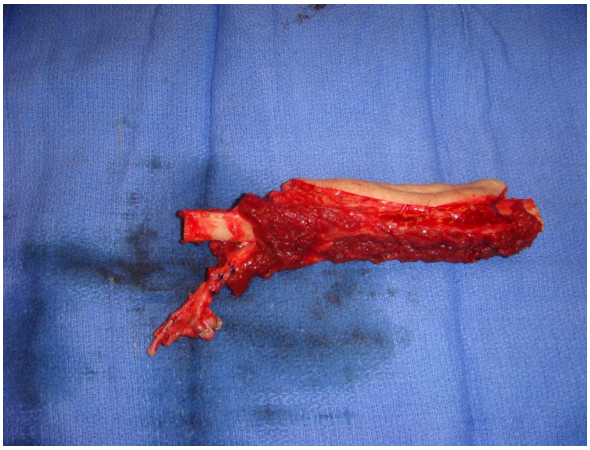


Figure 2: Free fibula flap.

RESULTS

All 5 vascularized fibula free flaps survived. The patients were given Heparin 5000 units subcutaneous q8h for the first 7days and aspirin 81 mg for 6 weeks post-operatively. Three patients had an end to side arterial repair and two an end to end repair. Three patients had two venous anastomosis one to a recipient vena comitantes and another to a superficial vein (cephalic or basilic vein) two patients had one venous repair both to the cephalic vein. One flap which had only one venous repair had an acute venous thrombosis at 72 hours that was detected clinically and on the laser probe monitor. It was successfully

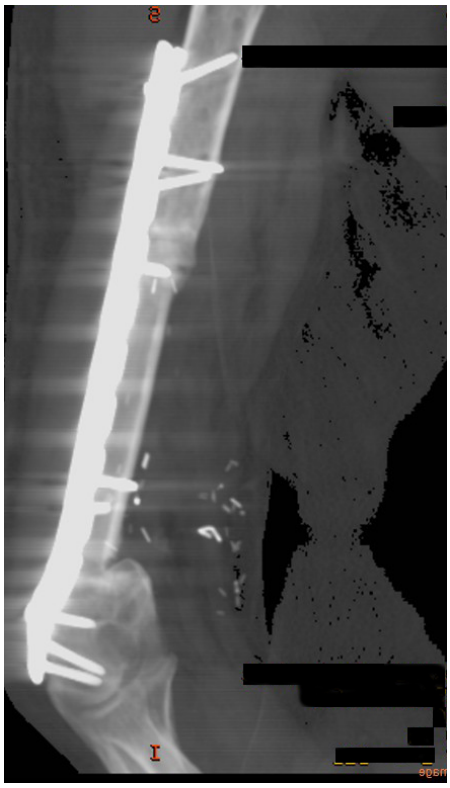


Figure 3: CT Scan showing bony union with bridging callus.

salvaged with a vein graft. The average length of fibular bone was 10.2 cm (range 4 – 16 cm). The average skin paddle size was 7.6 x 3.8 cm (range 4 x 3 to 10 x 4 cm). In 2 patients the skin paddle was not necessary for closure and thus it was trimmed to a small piece of skin used for monitoring. Primary bony union both clinically and on X-rays was achieved at 9 of the 10 osteosynthesis sites at an average of 14 weeks (range 10 – 21 weeks). One patient had distal bony union of the ulna but developed proximal hardware failure, the plate fractured at the proximal ulna fibula osteosynthesis site prior to bony union. This was complicated by a proximal hypertrophic bony non-union. The hardware was replaced 9 months later his post-operated course was complicated by a bout of pseudomembranous colitis and a secondary infection requiring removal of the proximal hardware. This went on to heal with a fibrous hypertrophic bony non-union that was asymptomatic. The patient declined further surgery thereafter and at 17 year follow up when he was seen for an unrelated condition. One patient requested removal of the fibula flap skin paddle for cosmetic reasons one year post reconstruction. The skin flap and the hardware were removed uneventfully at this juncture. There were no significant donor site complications. All patients returned to their preinjury employment. At an average of follow up of 5.1 years (range 8 months – 17 years) patients remained infection free. (Table **2**)

DISCUSSION

Chronic unstable upper extremity bone defects remain a difficult problem to treat. In the setting of osteomyelitis simpler methods such us limited debridement followed by open reduction and internal fixation with autogenous bone graft are often unsuccessful as it was in three of the five patients referred to us. The vascularized free fibula flap allows for immediate structural support of large defects with vascularized bone that heals by primary osteogenesis rather than creeping substitution as in autologous non-vascularized bone [27]. It has the potential for graft

Table 2: Operative Reconstruction and Outcome

Case	Graft length	Dimensions of Cutaneous Paddle	Proximal and Distal Fixation	Proximal/Distal Union	Additional Operations
1	14 cm	7 x 4 cm	Plate	Yes/yes	None
2	16 cm	9 x 4 cm	Plate	No/Yes	Revision graft fixation-proximal plating, I and D and removal of hardware
3	4 cm	4 x 3 cm	K-Wire	Yes/Yes	Revision venous anastomosis with vein graft
4	4.1 cm	8 x 4	Plate	Yes/Yes	Removal of hardware and Skin paddle for cosmetic reasons 13 months post reconstruction
5	12.8 cm	10 x 4	Plate	Yes/yes	None

hypertrophy. It does not rely on the surrounding soft tissue envelope for incorporation and its retained blood supply also allows for a better humoral response and penetration of antibiotics to the area. The soft tissue deficits can be addressed by an inclusion of a skin paddle with the vascularized fibular flap. The skin paddle also allows for a simple way to monitor the flap. Our current indications for the use of a vascularized fibula include a segmental bone defect greater than 6 cm, where conventional methods have failed, or in a previously infected or radiated site.

Bone infections are difficult to eradicate and in the face of a nonunion of the bone this is compounded by instability of the extremity. Radical debridement, antibiotics, and trying to achieve bony union are the cornerstone of treatment of bone infections with non-unions. The use of antibiotic beads provides high local concentrations of antibiotics, well above the minimum inhibitory concentration for most pathogens, while limiting systemic levels of drugs to safe values. Local antibiotic concentrations can reach levels 20 times higher than the therapeutic serum concentrations from parenteral therapy, while serum and urine concentrations from beads are 10-20 times lower [28, 29]. They have shown to be both safe and effective since Buckholz described their usage in 1970. Past work demonstrates that antibiotic beads and cement greatly decrease the bacterial count in wounds when compared to parenteral antibiotic therapy [28-30].

Hurst *et al*. in 1982 reported the first case in the literature of treatment of an upper extremity infected bone nonunion with a vascularized fibula that of an infected loss of the ulna [31]. Since that case report there have been several small case series on the use of the free vascularized fibula for upper extremity defects [15-24]. In general, these have addressed the use of free vascularized fibula for reconstruction of skeletal defects after a multitude of etiologies including tumor defects, segmental nonunion of bone, infected nonunion of bone, failed allograft reconstruction, bone loss after trauma. As these studies addressed the skeletal reconstruction there has been little or no mention of the specific treatment of the infected bone non-unions. In Han *et al*. series of 160 patients managed for a skeletal defect with a free vascularized fibula or iliac crest only 6 patients had an infected upper extremity bony defect [14]. Of these 6 it is not clear what type of vascularized bone graft was performed and what was the outcome. In their total of 60 infected bone defects of which 90% were femur and tibia they were able to achieve primary union in 29 after the vascularized bone transfer and 17 after a second procedure for an overall success rate of 77%. In Muramatsu *et al*. series of 23 recalcitrant post-traumatic nonunion of the humerus reconstructed with a vascularized bone graft only one of the four patients with an infected bone non-union was reconstructed with a free fibula. This one patient failed to achieve union of his humerus [20]. In Jupiter *et al*. series of 9 patients with segmental forearm bone defects 6 had an infected bony nonunion and 4 were actively infected at the time of presentation [15]. They were treated with sequential debridements with the specifics lacking followed by a free vascularized fibula. They had 1 failure of union and 2 venous thrombosis that were successfully salvaged. In Yajima *et al*. series of 20 free vascularized fibula in upper extremity only 3 had osteomyelitis including one infected bone non-union all 3 went on to heal without recurrent infection [22]. In Noaman's series of 16 vascularized osteoseptocutaneous fibular bone graft in where there were 9 infected bone non-union [24]. All but one patient with a flap failure in this series achieved bony union. In Heitmann *et al*. series of 15 humerus defect 6 had a history of a prior infection that was quiescent at the time of presentation [16]. These 6 patients were treated with a free vascularized fibula 2 developed a proximal bone non-union and one a distal bone non-union and three had a venous thrombosis that were successfully revised.

Our results with our staged technique compares favorably to the above studies. Although the use of antibiotic cement is not new nor the use of a free fibula vascularized graft we could not find any case series in our extensive literature search of the use of this combination in the treatment of large segmental infected bony defects of the upper extremity. The use of a staged approach with strict adherence to orthopaedic and plastic surgery principles resulted in successful bony union in 4 out of 5 patients and distal bony union with a proximal asymptomatic non-union in one patient with no long-term recurrence of the bone infection. This staged approach consisting of aggressive debridement, removal of hardware, application of an external fixator, antibiotic impregnated polymetylmethacrylate cement and culture specific antibiotics followed by free vascularized fibula should be considered for any upper extremity infected non-union that has failed conventional management.

FINANCIAL DISCLOSURES

None

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