Use of Topical Resorbable Antibiotic Cement and Synthetic Extracellular Matrix Dressings in the Treatment of an Infected, Dehisced, Transmetatarsal Amputation in a Vascularly Compromised Patient: A Case Study

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Abstract

Adequacy of perfusion directly correlates to the penetration and effectiveness of oral and parenteral antibiotics in the treatment of lower extremity wounds. Stimulan® Biocomposites® (Wilmington, North Caroline) is a resorbable, calcium sulfate matrix that can be used to deliver sustained antibiotic therapy into a bone void or defect. Synthetic extracellular matrices are artificial polymers that are elongated and deposited as a matrix of nanofibers which mimic the native extracellular matrix. RenovoDerm® Anthem™ Wound Matrix (Columbus, Ohio) is comprised of polyglycolic acid and poly (L-lactide-co-caprolactone) which degrade by hydrolysis into a-hydroxy and fatty acids, lowering the pH and promoting regenerative cellular activity including angiogenesis. Limited research exists for the off-label use of antibiotic impregnated calcium sulfate matrix applied topically to wounds and presently no studies have been performed to see what effect combining these two wound care modalities will have. The aim of this case study was to highlight the novel use of resorbable antibiotic cement as a topical antibacterial agent and synthetic extracellular matrix dressings to heal an infected transmetatarsal amputation in a vascularly compromised patient.

Introduction

Delivery of antibiotics can be to the site of infection via intravenous, intramuscular, or oral administration is severely impaired when perfusion is poor. Poly(methyl methacrylate) (PMMA) is a commonly used cement that can be mixed with antibiotics to deliver antibiotic therapy directly to an infected site, by passing the need for vascular transport. The use of PMMA bone cement has disadvantages however which include the release methyl methacrylate (MMA), high exothermic temperature during the polymerization of PMMA, which can cause thermal necrosis, it is not resorbable and therefore requires a second surgery for removal, and it can become a nidus for infection if colonized by bacteria. [1,2,4] Resorbable bone cements, such as calcium sulfate, have the advantage of being completely resorbable therefore they do not require additional surgery to remove and do not act a nidus for infection [3]. A wide range of antibiotics can be loaded into antibiotic cement depending on the target organism, including Vancomycin and Gentamycin [1].

Stimulan® Biocomposites® Rapid Cure is manufactured from medical grade calcium sulfate and its intended use is as a bone void filler for voids or gaps that are not intrinsic to the stability of the bony structure [3]. When used in bone voids, it provides a bone graft substitute that is resorbed and replaced with bone during the healing process [3]. It is engineered through a DRy26™ recrystallization method which is a multiple step process beginning with pharmaceutical grade precursors and takes over six weeks to complete [5]. It contains no hydroxyapatite, PMMA, or insoluble impurities [3] and is completely absorbable [3, 6-11]. It has been demonstrated to not act as a nidus for infection [3,11].

The design and engineering of Anthem™ Wound Matrix provides a consistent microporous scaffold for cellular migration, infiltration and proliferation of regenerative cells [12-13]. It is composed of Polyglycolic Acid and Poly(L-Lactide-co-caprolactone) which naturally degrade providing sustained release of glycolic, caproic, and lactic acid into the wound microbiome. This creates an inhospitable environment for bacteria by lowering the pH of the wound. It has been demonstrated that lowing the pH of a wound decreases microbial infection rates, bacterial virulence, and biofilm formation [13-21].

We propose that when used in combination therapy, synthetic extracellular matrix dressings and antibiotic loaded resorbable bone cement complement each other and work synergistically to eradicate infection and promote wound healing.

Case Report

We present the case of a 73-year-old male patient with past medical history of adult-onset diabetes mellitus, peripheral neuropathy, and peripheral vascular disease. The patient had undergone right lower extremity angiogram with posterior tibial artery angioplasty in August 2022 and right transmetatarsal amputation secondary to right foot ulcerations with osteomyelitis in June 2023. In February of 2024 the patient developed an ulceration of the left hallux with progressed to osteomyelitis and ischemic changes of the left forefoot began to occur. In March of 2024 the patient underwent left lower extremity angiogram with peroneal artery angioplasty. Unfortunately, the patient's ulceration, infection, and ischemic changes continued to worsen and a transmetatarsal amputation of the left foot was performed May 2024 by a community surgeon. The patient was lost to follow up with the community surgeon and returned to our care in July 2024 eight weeks postoperatively fully dehisced and grossly infected.

During the initial visit a thorough history was obtained which was comprised of their past medical history, current medications, allergies, surgical history, and social history. A complete review of systems was performed, and a lower extremity focused exam was conducted which included vascular, dermatologic, neurologic, and musculoskeletal. Radiographs were obtained of the lower extremity and blood tests were performed including glycosylated hemoglobin levels. A wound swab was then collected from the dehisced incision and sent for culture/sensitivity testing.

The patient had no known drug allergies and was on long-term anticoagulation therapy. The patient had no history of tobacco use. Physical exam demonstrated absent pedal pulses, diminished protective sensation, and no gross deformity of the foot or lower extremity except for bilateral transmetatarsal amputations. The posterior tibial artery pulse was monophasic on doppler exam and the dorsalis pedis artery was not detected.

The dehisced transmetatarsal amputation incision of the left foot measured 15.0cm x 2.5cm x 1.2cm with exposed fourth and fifth metatarsal shaft remnants. the duration of treatment.

Figure 1 Initial Presentation of Wound

The patient reported intense pain from the incision site. The incision flaps were poorly perfused. The periwound skin was erythematous and fragile. The wound was malodorous and had sanguinopurulent drainage. The lower leg and foot were edematous. The wound bed was 40% granular and 50% fibrotic and 10% necrotic tissue. Radiographs revealed demonstrated possible osteomyelitis of the fifth metatarsal but were negative for soft tissue emphysema or other concerning findings.

Glycosylated hemoglobin had a reported value 7.8. Wound swab was obtained and sent for culture and sensitivity testing which showed methicillin resistant staphylococcus aureus. Patient was started on oral antibiotic therapy which was continued throughout the duration of treatment. See figure 1.

At the initial visit, local anesthesia was obtained about the left foot using an ankle block. The foot was then scrubbed with Provodone-Iodine using a sponge brush, rinsed clean with sterile saline, and allowed to air dry. Sharp debridement was performed removing all non-viable tissue. Chlorhexidine was then applied with an applicator to the peri-wound skin and allowed to air dry. Using bone cutters and sterile technique, the distal remnants of the metatarsal shafts were resected, passed from the surgical field, and sent for surgical pathology and culture/sensitivity testing. Hemostasis was achieved with resorbable oxidized cellulose.

Figure 2 Anthem™ Wound Matrix was then applied directly to the wound bed after being cut to size and soaked in sterile saline.

Figure 3 Retention sutures were placed to begin reapproximating the incision flaps and heal the incision by secondary intention.

Figure 4 Topical application of resorbable antibiotic cement pellets mixed with Gentamicin and Vancomycin was then performed.

Anthem™ Wound Matrix was then applied directly to the wound bed after being cut to size and soaked in sterile saline. Topical application of resorbable antibiotic cement pellets mixed with Gentamicin and Vancomycin was then performed. This was followed by application of benzoin tincture to the periwound skin. Utilizing coaptive film and a non-adherent dressing, the synthetic extracellular matrix dressings and antibiotic loaded resorbable cement pellets were secured in place. Retention sutures were placed to begin reapproximating the incision flaps and heal the incision by secondary intention. The patient's left foot was appropriately offloaded, and dry sterile non-compressive outer dressings were used. The bone segments sent for surgical pathology and culture/sensitivity confirmed osteomyelitis with the causative organism of methicillin resistant staphylococcus aureus.

The following protocol was followed at each of the subsequent seven visits, each spaced two weeks apart. The left lower leg and foot was scrubbed with Provodone-Iodine using a sponge brush, rinsed clean with sterile saline, and allowed to air dry.

Figure 5 Wound Closure

Any remaining antibiotic pellets were flushed from the incision using sterile saline. Sharp debridement was performed removing all non-viable tissue. Wound size measurements were record at each visit. Would size was calculated as the product of the length, width, and depth in cubic centimeters (cm^3). Chlorhexidine was then applied with an applicator to the peri-wound skin and allowed to air dry. This was followed by application of benzoin tincture to the periwound skin. Anthem™ Wound Matrix was then applied directly to the wound bed after being cut to size and soaked in sterile saline. Topical application of resorbable antibiotic cement pellets mixed with Gentamicin and Vancomycin was then performed. Previous retention sutures were removed, and new retention sutures were placed, progressively bringing the incision flaps closer together. Utilizing coaptive film and a non-adherent dressing, the synthetic extracellular matrix dressings and antibiotic loaded resorbable cement pellets were secured in place.

The patient's left foot was appropriately offloaded, and dry sterile non-compressive outer dressings were used. Local signs of infection improved with each successive visit, as did the patient's reported pain, and progressive healing of the wound was observed.

At the ninth and final visit, the wound was found to be fully healed with no residual signs of infection and no pain reported. The patient was transitioned to regular shoe gear with a toe filler insert and resumed normal activity.

Discussion

Fourteen weeks of combination therapy using antibiotic loaded resorbable bone cement and synthetic extracellular matrix arrested the active infection in the dehisced and poorly perfused transmetatarsal amputation site. The patient's functional use of the lower extremity was restored, the wound pain level was resolved, and complete closure of the transmetatarsal amputation site was achieved.

The decrease in pH within the wound bed provided by the natural degradation of the Polyglycolic Acid and Poly(L-Lactide-co-caprolactone) into glycolic, caproic, and lactic acid from the synthetic extracellular matrix dressings combined with local antibiotic delivery from the topically applied resorbable cement prevented biofilm formation, eradicated the infection, and facilitated complete wound healing. This case study demonstrates the use of topically applied antibiotic loaded cement to deliver antibiotics directly to the site of infection in poorly perfused wounds and the value of the pH modulating effects of synthetic extracellular matrix dressings in fighting wound infection, and it exemplifies the synergism when these two modalities are used in combination.

It is important to note that this case was performed at the Southern Arizona Veteran Affairs Health Care System, therefore cost and reimbursement were not factors in determining treatment. Anthem™ Wound Matrix is branded specifically for the Department of Veteran Affairs. In private and commercial, it is branded as Phoenix™ Wound Matrix. Antibiotic loaded resorbable cement pellets and synthetic extracellular matrices are all reimbursable through Medicare and private insurance and have their own designated HCPCS codes. The cost to benefit ratio would need to be assessed on an individual provider and patient basis. All pricing of the wound care products used in this case are available to the public through the Department of Veteran Affairs Federal Supply Schedule.

Conclusion

When presented with this case our goals of therapy were to prevent a more proximal amputation, eradicate the infection, minimize patient discomfort, restore function of the limb, and achieve complete wound closure. The outcome of this case supports the topical use of antibiotic loaded resorbable bone cement in the treatment of lower extremity infected wounds, particularly in the setting of poor perfusion, in combination with synthetic extracellular matrix dressings to manage infection and promote healing. The wound achieved completed closure after fourteen weeks of combination therapy using topically applied antibiotic loaded resorbable bone cement and synthetic extracellular matrix dressings. Radiographs obtained at the end of therapeutic period demonstrated no new osseous erosions concerning for osteomyelitis and throughout the course of the therapy no new soft tissue infections occurred. Proximal amputation was prevented, full resolution of pain was accomplished, and restoration of full function to the limb was attained.

Conflict of Interest Statement

The authors of this article declare no conflict of interest. The companies involved had no role in the design of the study; in the collection, analyses, or interpretation of date; in the writing of the manuscript, or in the decision to publish the results.

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