Comprehensive Care and Management of Foot Infection in an Immunocompromised Patient: A Case Report

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INTRODUCTION

An immunocompromised patient is one who has the inability to respond normally to an infection due to an impaired and/or weakened immune system. The inability to fight infection can be caused by a number of conditions including illness, disease, malnutrition, or drugs. Wound healing in this patient population can be problematic due to a decreased resistance to infection. Infection in this patient population poses major diagnostic challenges. Infection of the soft tissues may occur as part of a broader systemic infection, and immune deficiency can obscure clinical findings, such as laboratory values and vital signs. We will present a report of a 62-year-old man who underwent pancreas and bilateral renal transplantation and was on immunosuppressive drug therapy as a result. A non-healing great toe ulcer was found upon initial presentation from which a multitude of infections, surgeries, amputations, grafts and complications ensued over the next 18 months. This case presents various, staged treatment modalities for serial soft tissue and bone infections in an immunocompromised patient.

CASE REPORT

The patient is a 62-year old man with a complex history resulting in an immunocompromised status. The patient underwent a bilateral renal transplant 14 years prior, followed by a pancreas transplant the following year. The patient has peripheral vascular disease, which he was revascularized for in 2014, underwent previous stenting for coronary artery disease, and currently has hypertension, hyperlipidemia, gastroesophageal reflux disease (GERD), and diabetes mellitus. The patient has had multiple surgical soft tissue and bone debridements, graft applications, and has bilateral transmetatarsal amputations. The right foot transmetatarsal amputation was performed in 2008 and transmetatarsal amputation of the left foot, which is the focus of this case report, was performed in August 2015. Current medications include omeprazole, enalapril, and pravastatin for GERD, hypertension, and hyperlipidemia, respectively.

Immunosuppressant-related medications include dapsone (an anti-infective) folic acid to restore folate depletions, methylprednisolone for induction of remission and prevention of organ rejection, mycophenolate mofetil for kidney immunosuppression, and tacrolimus for organ rejection. In early 2015, the patient presented with a plantar left great toe ulcer. He received conventional wound care and eventually had a total contact cast applied. Total contact casting reduces plantar peak pressures better than many other offloading modalities (1). Off-loading to prevent causative pressures and shear friction is pivotal to the healing of neuropathic wounds (2). Due to the chronicity of the wound, a bovine xenograft was applied and a gastrocnemius recession performed to reduce plantar pressures and correct equinus deformity. This acellular dermal scaffold contains bovine collagen and shark-derived chondroitin for partial and full-thickness wounds (3). Equinus deformities make preexisting deformities worse and negatively alter gait mechanics (4). The left hallux ulcer resolved, but the patient subsequently developed an ulcer to the plantar medial aspect of the left first metatarsophalangeal joint. The mainstay of post-debridement wound care at this time included the use of a cadexomer iodine pad and a dry sterile dressing.

OPEN TRANSMETATARSAL AMPUTATION WITH DELAYED PRIMARY CLOSURE (AUGUST 2015)

Upon return from a two-week work trip, the patient noticed acute changes to the open wound with increasing drainage, odor, skin changes, and discoloration overlying the great toe. Three days later, when he presented to the emergency room, radiographs revealed extensive soft tissue emphysema to the left foot consistent with gas gangrene (Figures 1-4). Gangrene caused by a bacterial infection in a dysvascular and anoxic environment can quickly disseminate and cause rapid death of tissue and structures if not treated emergently (4). He was febrile with a temperature maximum of 102.3 degrees Fahrenheit, a white blood cell count within normal

Figure 1. Anterior-posterior view of soft tissue emphysema.

Figure 2. Lateral view of soft tissue emphysema.

Figure 3. Clinical view at admission.

Figure 4. Clinical view of gas gangrene at admission.

limits at 8.8, and anemia with a hemoglobin of 7.3. Arterial ultrasound did not reveal any significant acute hemodynamic stenosis. The goals of emergent surgical care are to free any and all necrotic and nonviable tissue and stimulate formation of healthy granulation tissue (2). Removing such necrotic soft tissue and osseous structures provides a healing environment for a higher probability of a salvageable and functional limb (4).

Emergent incision and drainage with an open transmetatarsal amputation was performed and extensive soft tissue necrosis with abscess formation with gangrenous changes were found (Figures 5-7). Transmetatarsal amputations eliminate pathologic invasive local infection, prevent septicemia, and ultimately salvages the affected limb (4). A successful attempt was made to create a viable plantar flap with adequate dermal thickness for delayed closure. Primary closure by a healthy plantar flap is ideal due to its vast arterial supply from the plantar artery (4). Only when the foot is free of infection, can a wound be closed successfully (2). Five days later, a debridement of metatarsals one through

Figure 5. Postoperative anterio-posterior view of open transmetatarsal amputation.

Figure 6. Postoperative lateral view of open transmetatarsal amputation.

five with delayed primary closure was performed. This procedure collectively eliminated a diseased portion of the lower extremity with the goal of maintaining ambulation, function, and limb viability. The patient was seen thereafter in clinic for surgical follow-up and was referred to a pedorthist for custom molded shoe therapy.

PARTIAL FIFTH RAY RESECTION, APPLICATION OF NEGATIVE PRESSURE WOUND THERAPY WITH INSTILLATION AND ALLOGRAFT APPLICATION (OCTOBER/NOVEMBER 2015)

Several months later, the patient was admitted for an infected left foot ulcer with cellulitis (Figure 8). He was brought into the operating room for an extensive soft tissue debridement, a fifth metatarsal bone biopsy and application of a wound vacuum-assisted closure device (VAC). Aggressive debridement down to the level of bone and tendon was necessary and the wound measured 10.0 x 6.0 x 0.5 cm. Two days postoperatively, a wound VAC with instillation of normal saline was applied to the left foot at bedside (Figure 9). The VAC with instillation was left intact and set to the manufacturer's setting for the instillation phase, soak phase, and negative pressure wound therapy (NPWT) phase. Although NPWT with instillation was only implemented for 3 days, the wound appeared well-granulated without fibrotic tissue, necrotic tissue, or slough

Figure 7. Postoperative view of open transmetatarsal amputation.

(Figure 10). There was minimal periwound maceration noted. A study by Lessing et al on porcine wounds revealed a 43% increase in granulation tissue of wounds treated with NPWT with instillation compared to NPWT without instillation after 1 week of treatment (5).

The left foot wound was surgically debrided in preparation for application of a cadaveric allograft 3 days later (Figure 11). A more proximal resection of the fifth metatarsal was also performed due to the diseased clinical appearance of the bone. The patient was discharged with home health care and a home wound VAC device and continued 6 weeks of intravenous antibiotic therapy. The patient was seen weekly for local wound care.

Figure 8. Clinical view of left foot upon admission, October 2015.

Figure 9. Application of VAC with instillation 2 days post debridement.

Figure 10. After 3 days of NPWT with instillation. Wound bed is granular with exposed fifth metatarsal and tendons.

Figure 11. Application of a cadaveric allograft following debridement and a more proximal fifth metatarsal resection.

APPLICATION OF SPLIT-THICKNESS SKIN GRAFT (DECEMBER 2015)

Negative pressure therapy was continued until granulation tissue covered the exposed tendon and bone. With an uninfected, well perfused and healthy granular wound bed present, the next line of treatment planned was the harvest and application of a split-thickness skin graft (STSG). Contraindications for the use of STSG include an infected wound, or exposed bone, tendon, or joint capsule (6). The wound was surgically debrided in preparation for the STSG. The harvest site healed without any complications and weekly local wound care was implemented.

A wound VAC was placed on the STSG to control drainage, continue promotion of perfusion to the wound bed, provide consistent and uniform pressure on the graft, as well as immobilize the graft. Literature has shown a higher rate of graft take, fewer repeated graft harvest and applications, and less complications and graft failure when the STSG was coupled with NPWT versus conventional therapy using a bolster dressing (7). The rate of complications and failure vary in literature. Anderson et al utilized conventional therapy with their STSG on diabetic wounds and had a low 2.8% complication rate with an average healing time of 5.1 weeks, despite multiple comorbidities present with their patients (6). Since the application of the STSG, the patient underwent multiple sharp aseptic debridements in the clinic with utilization of advanced wound care modalities, including human amniotic grafts. The wound was progressively decreasing in size (Figure 14) and superficial soft tissue infection was controlled with oral antibiotics.

Figure 12. Postoperative radiograph of more proximal fifth metatarsal resection.

Figure 13. Follow-up visit after application of cadaveric allograft.

Figure 14. Progression of wound status after split-thickness skin graft.

STAGED SOFT TISSUE AND BONE DEBRIDEMENT WITH THE PLACEMENT OF ANTIBIOTIC BEADS AND DELAYED PRIMARY CLOSURE (AUGUST 2016)

The patient was admitted for an acute infection of the left foot after presenting to the clinic with a small dorsolateral foot ulceration with a fibrogranular wound bed measuring 0.3 x 0.5 x 0.5 cm with erythema and periwound edema, purulent discharge, and a positive probe to bone (Figure 15). Imaging studies, including a magnetic resonance image without contrast and a WBC-labeled nuclear medicine scan, confirmed osteomyelitis of the residual metatarsals and cuboid (Figures 16, 17). As expected, the wound culture revealed methicillin sensitive staphylococcus aureus (MRSA). It was decided that the best approach for limb salvage was staging debridements with application of antibiotic beads and delayed primary closure.

The first stage of limb salvage included resection of the fourth and fifth metatarsal remnants and sharp debridement of all devitalized soft tissue (Figure 18). A curvilinear incision was fashioned in layers over the dorsolateral aspect of the foot, incorporating excision of the ulcer in toto. The remnant of the fifth metatarsal was highly fragmented and eroded (Figure 16). Resection of the fifth metatarsal remnant was performed in a piecemeal fashion due to the amount of fibrotic soft tissue incorporating the bone fragments. Intraoperative fluoroscopy was used to verify that the bony fragments from the fifth metatarsal were all excised. The fourth metatarsal remnant was disarticulated at its metatarsocuneiform joint. Both bone specimens were sent to pathology and the report showed acute and chronic osteomyelitis without malignancy.

The second stage of limb salvage was performed 4 days later with the goal of delayed primary closure. The distal portion of the cuboid was found to be soft and diseased. Partial resection of the diseased cuboid was performed with a sagittal saw. A more proximal portion of the cuboid was resected and sent as a bone biopsy. The remaining cuboid appeared to healthy with strong cortical bone and bleeding noted within the bone marrow. The operative site was irrigated and resorbable antibiotic beads were placed into the wound. Delayed primary closure was achieved (Figures 19, 20). The patient was placed in a well-padded posterior splint in order to minimize tension at the incision site.

The patient was discharged 2 days later with the recommendation of approximately 5 more weeks of intravenous vancomycin due to the confirmation of acute and chronic osteomyelitis on the last surgical pathology report. The patient was kept nonweight-bearing with a well-padded posterior splint. Eight days prior to this hospital admission, the wound on the left foot was epithelialized without signs of infection. We believe the presence of biofilm complicated the wound healing process, in addition to the patient's immunocompromised status. Debridement down to bone was necessary to remove as much biofilm as possible, along with the appropriate long-term antibiotic therapy to address the underlying osteomyelitis.

Figure 15. Clinical view of right lateral foot with acute signs of infection.

Figure 16. Radiograph of the left foot. In comparison to Figure 12, there has been extensive erosive changes noted to the fifth metatarsal remnant.

Figure 17. **(Left)**. Magnetic resonance image showing increased T2 and STIR signal and decreased T1 signal within the remaining metatarsals, cuboid, cuneiforms, and mild heterogeneous signal within the navicular bone and distal calcaneus. **(Right)**. Ceretec scan showing increased uptake within residual metatarsals and cuboid of the left foot suggesting osteomyelitis and minimal increased uptake within the distal third and fourth metatarsals of the right foot.

Figure 18. **(Left)**. Radiograph of the left foot after resection of the fifth and fourth metatarsal with cuboid bone biopsy. **(Right)**. Clinical view of the left foot after wide excisional debridement.

Figure 19. Radiograph of the left foot showing partial resection of the cuboid and application of resorbable mini antibiotic beads.

Figure 20. Clinical postoperative view.

More research is being published regarding the role of biofilm produced by bacteria in chronic and recalcitrant wounds. Even after adequate sharp debridements, biofilm has the ability to reform rapidly within days, making it difficult to manage (8). Additionally, a recent article by Mottola et al suggests that there is an increasing tolerance to antibiotics, especially seen in Staphylococcus aureus biofilm, and as a result, the clinical application of antimicrobial susceptibility testing cannot be effectively used in the guidance of the appropriate antibiotic therapy (9).

APPLICATION OF CRYOPRESERVED HUMAN AMNIOTIC GRAFT ON SURGICAL WOUND DEHISCENCE (SEPTEMBER 2016)

The distal portion of the incision site showed dehiscence with extravasation of some antibiotic beads at the first postoperative clinic follow-up. Local wound care was implemented. At a subsequent follow-up visit, a repeat primary closure of the centralized wound dehiscence

Figure 21. Clinical picture of epithelialized wound 21 days after application of a cryopreserved human amniotic graft.

was performed without success. Local wound care with sharp debridements to reduce bioburden, contaminants, and senescent cells was performed to maintain a healthy, granular wound bed. One month postoperatively, a cryopreserved human amniotic graft was applied to the granular wound bed that measured 3.6 x 0.5 x 0.3 cm. This graft is nonvascular consisting of epithelial cells, reticular fibers of the basement membrane, a thick compact layer, and a fibroblastic layer and contains cell-anchoring collagen (10). Amnion has been shown to positively influence all 3 phases of wound healing and provide a matrix for successful cellular migration, cellular proliferation and create a natural biologic barrier (10). The patient was transitioned into a CAM boot with instructions to weight bear as minimally as possible. The wound continued to progress without any complications and at the last follow-up visit, which was 21 days after application of the cryopreserved human amniotic graft, the wound was completely epithelialized (Figure 21).

CONCLUSION

The case study showed that the immunocompromised patient can be challenging, and the clinician must be aggressive in treatment for ultimate limb salvage. One also cannot rely solely on laboratory results, such as white blood cell counts and vital signs because this patient had normal laboratory values and vitals upon multiple admissions and office visits. Infections in compromised hosts pose major diagnostic challenges because the infections can be caused by organisms not ordinarily considered to be pathogens in an otherwise healthy host. Infection of the soft tissues may occur as part of a broader systemic infection and the degree and type of immune deficiency can obscure clinical findings. One advanced wound care modality, such as applying amniotic allografts on a chronic wound in a patient undergoing immunosuppressive therapy, has shown a reduction in pain and facilitation of wound healing (11). We would like to further investigate and illustrate the pitfalls of treatment in the immunocompromised patient, the effect on wound healing by immunosuppressive drugs, and the role of biofilm in chronic infections and wound recidivism. A well-planned strategy for prompt diagnosis, including biopsy and aggressive treatment protocols is essential for recalcitrant wounds in an immunocompromised patient.

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