Efficacy of a Urinary Bladder Matrix for Treating Wound Dehiscence With Hardware Exposure in a Patient With Rheumatoid Arthritis

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ABSTRACT

Objective. This case report explores an effective treatment modality in a medically complicated patient, with considerable wound dehiscence refractory to treatment with negative pressure wound therapy (NPWT). **Case Report.** A 35-year-old woman with a past medical history of hypothyroidism, osteoporosis, and rheumatoid arthritis treated with tumor necrosis factor (TNF) alpha inhibitors and disease-modifying antirheumatic drugs presented to the clinic following right great toe arthrodesis, metatarsal neck osteotomies, extensor tendon lengthening, and capsulotomy of the second, third, fourth, and fifth toes 2 weeks prior, with wound dehiscence of the right great toe and subsequent exposure of surgical hardware, complicated by infection. At the 2-week postop, a urinary bladder matrix was placed on the wound following failed NPWT, which was in place for 10 days. At the 3-month follow-up, the wound was closed and without any drainage. Patient reported a significant reduction in pain (visual analogue scale: 3) with adherence to weight-bearing restrictions. **Conclusions.** Wound healing was accomplished without removal of the exposed deep hardware in a patient with comorbidities and post-surgical wound dehiscence.

KEY WORDS

hardware exposure, infection, rheumatoid arthritis, urinary bladder matrix, wound dehiscence

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Surgical wound dehiscence is a known postoperative complication that involves the breaking open of a surgical incision along the suture. Wound healing is reliant on a series of interactions among cells and cell mediators; any disruption to this cascade of interactions will cause impairment of the normal physiologic response to insult and increase the likelihood of wound dehiscence.[1] Treatment is further complicated in patients with rheumatoid arthritis (RA), a chronic, erosive inflammatory disease that has been known to impede wound healing and increase baseline risk for infection.[2,3] In addition, the exposure of orthopedic hardware from surgery acts as a nidus for microbes, further increasing the incidence of infection and impeding healing.[4] Consequently, the traditional management of postoperative wound infection with hardware exposure has been serial irrigation and debridement, intravenous antibiotics, and likely removal of hardware.[5] The authors report the case of a patient with RA with an open, infected surgical wound of the right great toe with exposed hardware following right great toe arthrodesis successfully treated without removal of exposed hardware and use of an epithelial matrix graft.

CASE REPORT

A 35-year-old woman with a past medical history of hypothyroidism, osteoporosis, and RA presented to the clinic at the University of Texas Medical Branch following right great toe arthrodesis, metatarsal neck osteotomies, extensor tendon lengthening, and capsulotomy of the second, third, fourth, and fifth toes 2 weeks prior, with wound dehiscence of the right great toe and subsequent exposure of surgical hardware complicated by infection. She reported a 9 on the visual analogue scale (VAS), and the open wound was malodorous and erythematous with purulent discharge (**Figure 1**). Erythrocyte sedimentation rate and C-reactive protein were elevated at 49 mm/HR and 5.8 mg/dL, respectively, but these would have been potentially poor surrogates for inflammation secondary to infection due to the patient's chronic RA. The patient reported being unable to use her walker and crutches due to her debilitating RA. When the patient had to use them, she accidentally stepped onto

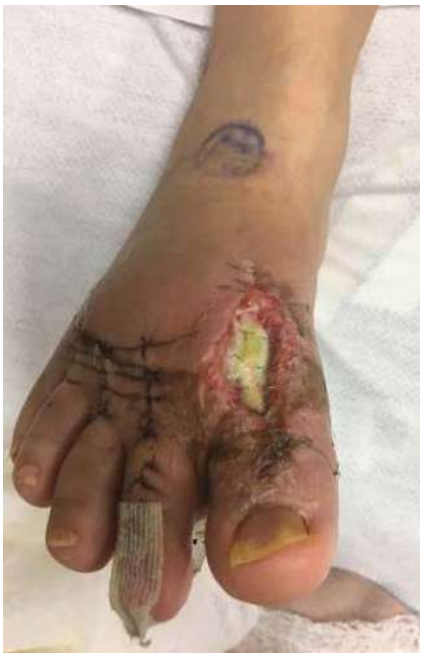

Figure 1. Dehisced right hallux with hardware exposure.

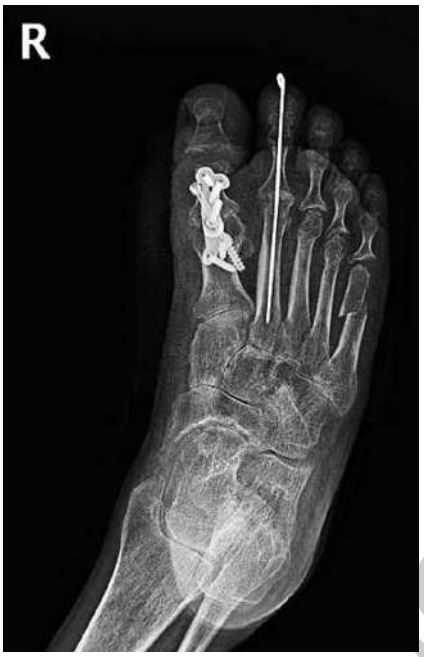

Figure 2. X-ray of right foot.

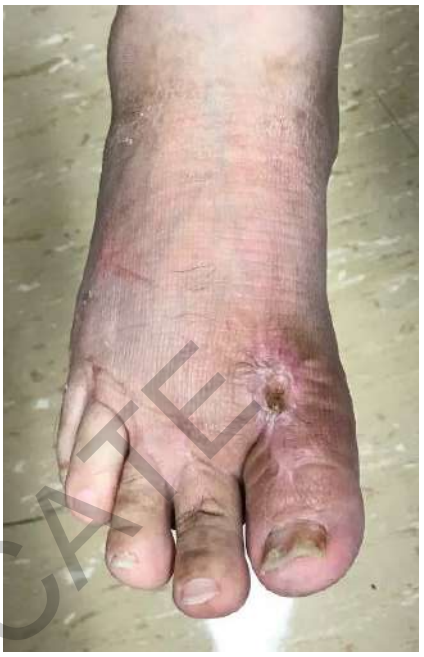

Figure 3. At 3-month follow-up, wound closure achieved with urinary bladder matrix.

her foot and the sutures came out. She reported no fever or chills.

Treatment course

Despite negative methicillin-resistant *Staphylococcus aureus* (MRSA)/methicillin-sensitive *S aureus* polymerase chain reaction (PCR) of nares, treatment was initiated with prompt administration of intravenous vancomycin 1000 mg every 12 hours for 7 days. She was seen by rheumatology, who recommended adalimumab and methotrexate (MTX) be discontinued until the right foot became clear of infection to facilitate wound healing. Plaquenil (hydroxychloroquine; Concordia Pharmaceuticals Inc) was recommended as an alternative, but the patient was not amenable to trying the drug. Wound care involved twice daily Dakin's solution (sodium hypochlorite; Century Pharmaceuticals, Inc) dressing changes. The wound improved after 5 days of antibiotics, at which time the transitioned to oral trimethoprim/sulfamethoxazole (TMP/SMX) 400/80 mg twice daily. The decision was made to use negative pressure wound therapy (NPWT; V.A.C. Therapy; 3M+KCI) on the wound to expedite healing and closure. The NPWT device, which consisted of an open-pore polyurethane ether foam sponge, adhesive cover, fluid collection reservoir, and a suction pump, was employed. A week into admission, an X-ray of the foot showed moderate soft-tissue swelling of the great toe with soft-tissue emphysema consistent with cellulitis (**Figure 2**). No acute hardware complications were noted.

After noticeable clinical improvement, including increased range of motion of toes and diminished swelling and erythema, NPWT was discontinued after 10 days due to poor suction caused by the location and irregular contour of the wound. The wound was still open and extremely susceptible to major infection. Ultimately, a Cytal 1-Layer Wound Matrix graft (ACell) was placed on the wound. While biological materials composed of extracellular matrix may be harvested from a wide variety of tissues and organs, the porcine urinary bladder matrix (UBM) has a unique bimodal surface that consists of an intact basement membrane and organized connective tissue comprised of urinary bladder lamina propria. This serves as a robust scaffold for cell infiltration and expedited wound healing. In addition, the prefenestrated design is conformable to irregular wound beds and optimizes fluid management. The conformability of the UBM was the reason why treatment was sought with this matrix following discontinuation of NPWT.

The UBM graft was in place for 7 days before the patient was discharged. The patient was instructed to keep the dressing clean, dry, and intact for 2 weeks. Following that, the dressing was changed every other day; the patient was instructed to remove the elastic bandage, gauze dressing, and gauze pad using the following instruction. The yellow Xeroform layer (Xeroform Occlusive Dressing; Cardinal Health) was to be taken off with care; with clean gloves and a tongue depressor, a generous amount of SURGI-gel (Orion Laboratories Pty Ltd) was to be applied to the UBM graft. Subsequently, the wound was to be recovered with a Xeroform, gauze pad, Kerlix (Cardinal Health), and elastic bandage. The patient was instructed to do so every other day for 1 week until the follow-up appointment with orthopedic surgery. At that point in time, the patient was stable for discharge and scheduled to be seen for follow-up in 1 week at the clinic. At discharge, adalimumab was held and MTX was restarted to prevent disease progression of RA. The patient was

discharged on Bactrim (trimethoprim/sulfamethoxazole; Roche) 80 mg twice daily.

Outcomes

At the 1-week follow-up from discharge, the patient reported feeling much better with an improvement in pain. The UBM graft on the patient's right great toe stayed intact and had been kept clean. Physical examination revealed that the patient could move her toes more freely, and sensation was returning as well. The dehisced right great toe incision had no evidence of purulence, was minimally odorous, and had mild erythema. The patient did not report any fever or chills but endorsed dorsal toe numbness that was chronic. At the 2-month follow-up, the patient reported doing much better. Despite restarting the previous regimen of MTX 2.5 mg tablets, 8 tablets per week, the wound was healing very nicely and was devoid of any drainage or odor. At the 3-month follow-up, the patient reported a significant improvement in pain with a VAS of 3, and with adherence to weight-bearing restrictions. The wound was closed and without any drainage (**Figure 3**). There was no sign of infection related to the implant at that time, and further follow-up was unnecessary.

DISCUSSION

Wound dehiscence is typically managed with debridement, antibiotic therapy, and resuturing or implementing another type of wound closure device to facilitate healing by secondary intention. Negative pressure wound therapy is a treatment modality that has been a useful adjunct in the treatment of several wound types following foot and ankle surgery.[6] This negative pressure technique removes chronic edema fluid, which in turn decreases afterload to blood flow, facilitating increased perfusion of the damaged tissue and enhancing formation of granulation tissue.[6] Mendonca et al[6] ascertained NPWT use in foot and ankle surgery leads to wound closure more quickly, and, in most patients, circumvents the need for further surgery. In the present case, wound care was initially started with NPWT, but eventually NPWT was discontinued due to its inability to hold suction well because of the location of the wound.

The management of an infected, dehisced wound is one of the greatest challenges an orthopedic surgeon must face. Viol et al[5] proposed an algorithm to determine whether hardware retention was possible after wound dehiscence. They suggested that within 2 weeks of wound dehiscence, it was reasonable to retain the hardware.[5] The present authors believe their patient's prompt presentation and eventual coverage with the UBM graft made hardware retention possible.

The ideal matrix for wound healing would be amenable to cell infiltration and proliferation, while serving as a viable scaffold for the deposition of fibrous connective tissue and epithelial layer.[7] The UBM shows a bimodal growth pattern — cell infiltration on 1 surface of the scaffold and development of a monolayer of cells on the other surface. The biocompatible constitution of the UBM consists of a motley of multiple types of carbohydrates, collagens, proteins, and other components, further augmenting its clinical utility in the context of wound dehiscence.[8] The UBM product's MatriStem UBM (ACell) technology platform is based on an extracellular matrix derived from porcine bladder. The UBM is composed of an intact basement membrane and lamina propria opposing surface. A randomized controlled trial by Alvarez et al[7] comparing the effectiveness of treatment of diabetic foot ulcers with UBM plus offloading with a total contact cast (TCC) versus standard care (nonadherent dressing with TCC) revealed a significantly reduced healing time and diminished rate of ulcer occurrence. The literature documents a marked efficacy in rapid healing of severe, recalcitrant wounds that were unresponsive to conventional wound therapy.[8-10]

There is often concern about the influence of disease-modifying agents on wound healing and infection rates in surgical patients. Theoretically, the mechanism of action of tumor necrosis factor (TNF) alpha inhibitors and antimetabolites (eg, MTX) would lead to compromised wound healing. In vitro and animal studies have shown the process of wound healing can be completely arrested when inflammation or cellular proliferation are suppressed or removed from the healing cascade.[11] However, there is a paucity of clinical evidence corroborating the hindering effect MTX has on wound healing and very little evidence suggesting low-dose MTX in patients who undergo orthopedic surgery should be discontinued.[11] The clinical data on the effect of biologic TNF blockade on risk of surgical site infection are conflicting. While certain meta-analyses and observational studies have demonstrated treatment with TNF antagonists is associated with an increased risk of developing serious infection and resultant healing complication,[12-14] another national prospective observational study of 7664 anti-TNF-treated and 1354 disease-modifying anti-rheumatic drugs-treated patients with severe RA from the British Society for Rheumatology Biologics Register showed contrary results.[15] Therefore, the widely adopted discontinuation of TNF inhibitors, such as adalimumab, is often predicated on caution and experience rather than adherence to compelling literature.[16]

CONCLUSIONS

While the utility of the proprietary UBM graft has been demonstrated in the literature,[7,8] there is a dearth of studies showing its efficacy in the context of wound dehiscence involving exposed hardware in patients with RAs. The placement of the UBM in this patient with impediments to wound healing facilitated closure of the irregularly contoured wound without having to remove the exposed hardware.

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Disclosure: Dr. Panchbhavi is a consultant for Stryker Orthopaedics as well as an editor for Lippincott Williams and Wilkins Publishing.

REFERENCES

1. Janis JE, Harrison B. Wound healing: part I. Basic science. *Plast Reconstr Surg*. 2014;133(2):199e–207e. doi:10.1097/01.prs.0000437224.02985.f9
2. Ishie S, Ito H, Azukizawa M, et al. Delayed wound healing after forefoot surgery in patients with rheumatoid arthritis. *Mod Rheumatol*. 2015;25(3):367–372. doi:10.3109/14397595.2014.966975
3. Pappas DA, Giles JT. Do antitumor necrosis factor agents increase the risk of postoperative orthopedic infections? *Curr Opin Rheumatol*. 2008;20(4):450–456. doi:10.1097/BOR.0b013e3282fcc345
4. Meaike JD, Kaufman MG, Izaddoost SA. Orthopedic prosthetic infections: plastic surgery management. *Semin Plast Surg*. 2016;30(2):73–77. doi:10.1055/s-0036-1580728
5. Viol A, Pradka SP, Baumeister SP, et al. Soft-tissue defects and exposed hardware: a review of indications for soft-tissue reconstruction and hardware preservation. *Plast Reconstr Surg*. 2009;123(4):1256–1263. doi:10.1097/PRS.0b013e31819f2b5e
6. Mendonca DA, Cosker T, Makwana NK. Vacuum-assisted closure to aid wound healing in foot and ankle surgery. *Foot Ankle Int*. 2005;26(9):761–766. doi:10.1177/107110070502600915
7. Alvarez OM, Smith T, Gilbert TW, et al. Diabetic foot ulcers treated with porcine urinary bladder extracellular matrix and total contact cast: interim analysis of a randomized, controlled trial. *Wounds*. 2017;29(5):140–146.
8. Brown B, Lindberg K, Reing J, Stolz DB, Badylak SF. The basement membrane component of biologic scaffolds derived from extracellular matrix. *Tissue Eng*. 2006;12(3):519–526.
9. Lecheminant J, Field C. Porcine urinary bladder matrix: a retrospective study and establishment of protocol. *J Wound Care*. 2012;21(10):476, 478–480, 482.
10. Kimmel H, Rahn M, Gilbert TW. The clinical effectiveness in wound healing with extracellular matrix derived from porcine urinary bladder matrix: a case series on severe chronic wounds. *J Am Col Certif Wound Spec*. 2010;2(3):55–59.
11. Pountos I, Giannoudis PV. Effect of methotrexate on bone and wound healing. *Expert Opin Drug Saf*. 2017;16(5):535–545. doi:10.1080/14740338.2017.1310839
12. Listing J, Strangfeld A, Kary S, et al. Infections in patients with rheumatoid arthritis treated with biologic agents. *Arthritis Rheum*. 2005;52(11):3403–3412.
13. Bongartz T, Sutton AJ, Sweeting MJ, Buchan I, Matteson EL, Montori V. Anti-TNF antibody therapy in rheumatoid arthritis and the risk of serious infections and malignancies: systematic review and meta-analysis of rare harmful effects in randomized controlled trials. *JAMA*. 2006;295(19):2275–2285.
14. Leombruno JP, Einarson TR, Keystone EC. The safety of anti-tumour necrosis factor treatments in rheumatoid arthritis: meta and exposure-adjusted pooled analyses of serious adverse events. *Ann Rheum Dis*. 2009;68(7):1136–1145. doi:10.1136/ard.2008.091025
15. Dixon WG, Watson K, Lunt M, et al; British Society of Rheumatology Biologics Register. Rates of serious infection, including site-specific and bacterial intracellular infection, in rheumatoid arthritis patients receiving anti-tumor necrosis factor therapy: results from the British Society for Rheumatology Biologics Register. *Arthritis Rheum*. 2006;54(8):2368–2376.
16. Berthold E, Geborek P, Gülfe A. Continuation of TNF blockade in patients with inflammatory rheumatic disease. An observational study on surgical site infections in 1,596 elective orthopedic and hand surgery procedures. *Acta Orthop*. 2013;84(5):495–501. doi:10.3109/1745367 4.2013.842431