Use of Antibiotic-Impregnated Absorbable Beads and Tissue Coverage of Complex Wounds

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The treatment of complex wounds is commonplace for plastic surgeons. Standard management is debridement of infected and devitalized tissue and systemic antibiotic therapy. In cases where vital structures are exposed within the wound, coverage is obtained with the use of vascularized tissue using both muscle and fasciocutaneous flaps. The use of nondissolving polymethylmethacrylate and absorbable antibiotic-impregnated beads has been shown to deliver high concentrations of antibiotics with low systemic levels of the same antibiotic. We present a multicenter retrospective review of all cases that used absorbable antibiotic-impregnated beads for complex wound management from 2003 to 2013. A total of 104 cases were investigated, flap coverage was used in 97 cases (93.3%). Overall, 15 patients (14.4%) required reoperation with the highest groups involving orthopedic wounds and sternal wounds. The advantages of using absorbable antibiotic-impregnated beads in complex infected wounds have been demonstrated with minimal disadvantages. The utilization of these beads is expanding to a variety of complex infectious wounds requiring high concentrations of local antibiotics.

THE TREATMENT OF complex wounds is commonplace for plastic surgeons. A multitude of circumstances exist that contribute to developing acute or chronic complex wounds which include trauma with exposed bone, osteomyelitis, exposed orthopedic hardware, wound dehiscence, and infected grafts. Standard management of the infected wound is debridement of infected and devitalized tissue and antibiotic therapy.

In cases where vital structures are exposed within the wound, coverage is obtained with the use of vascularized tissue using both muscle and fasciocutaneous flaps.[1–4] In addition to systemic antibiotic therapy, the use of nondissolving polymethylmethacrylate (PMMA) beads and absorbable antibiotic-impregnated beads have been shown to deliver high concentrations of antibiotics with low systemic levels of the same antibiotic.[5] These devices elute therapeutic concentrations of antibiotic for weeks.[5] The theoretical advantage of local delivery is high concentrations of antibiotic and low systemic levels. When the systemic antibiotic levels are low, this could avoid concentration-associated side effects. The use of absorbable antibiotic beads is preferred, as they do not require an additional operation for removal.[6]

The treatment of extracavitary prosthetic vascular graft infections with initial placement of PMMA beads in the wound has been described with adequate wound sterilization and graft preservation.[7, 8] This has also been described in the salvage of infected left ventricular assist devices (LVAD).[9]

In many complex wounds, critical structures may be involved that may either have limited blood supply or may be associated with prosthetic materials not allowing extensive debridement or removal. Antibiotic-impregnated beads have exhibited the capability of locally sterilizing wounds and reducing reinfection rates in a variety of wounds, but not enough evidence exist to make its usage the standard of care. After a review of current literature, a study was determined necessary to assess the efficacy of absorbable antibiotic beads in the management of complex infected wounds and reconstructive surgery.

Methods

A multicenter retrospective review of all cases that used absorbable antibiotic-impregnated beads for complex wound management from 2003 to 2013. Prior to data collection, the study was submitted to the Institutional

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TABLE 1. *Types of Wounds*

	Entire Cohort Number = 104 (%)	Flap Coverage Number = 97 (%)	Reoperation for Reinfection Number = 15 (%)
Orthopedic wounds	44 (42.3)	43 (97.7)	9 (20.5)
Mediastinitis	19 (18.3)	19 (100.0)	3 (15.8)
Vascular wounds	20 (19.2)	18 (90.0)	1 (5.0)
Other soft tissue Wounds	21 (20.2)	17 (81.0)	2 (9.5)

Review Board and approved. The case database was compiled from two institutions including Dartmouth-Hitchcock Medical Center and Staten Island University Hospital from January 2003 to August 2010 and September 2010 to May 2013, respectively.

The cases were separated into groups that met our criteria for the types of complex wounds being evaluated, which included the following: vascular graft infections, orthopedic wounds, mediastinitis, and other soft tissue wounds that included all other infected or nonhealing wounds not included in the primary categories. The orthopedic group included wounds with infected hardware, traumatic open fractures, and wounds with exposed bone. Our primary endpoint was the necessity for reoperation for infection within 30 days.

For all cases that were evaluated, the Osteoset® calcium sulfate absorbable bead kit or Stimulan® absorbable bead kit was used. Beads were impregnated with vancomycin, tobramycin or gentamicin powder, or combination during creation. An evaluation for the utilization of flaps for wound coverage within the cases was instituted. The necessity for reoperation for infection within 30 days was determined. Overall, these groups were small and do not lend themselves to robust statistical analysis.

Results

A total of 104 cases were investigated that are shown in Table 1. Flap coverage was used in 97 cases (93.3%). Overall, 15 patients (14.4%) required reoperation for infection with the highest group requiring reoperation involving orthopedic wounds. Within the subset of patients with mediastinitis, all were treated with pectoralis muscle flaps in conjunction with antibiotic bead placement. We had 19 patients with 3 (15.8%) requiring reoperation.

The 30-day mortality was zero per cent (0%) in all wound types.

Case Presentation

A 55-year-old male with a history of T2N1 squamous cell carcinoma of the hypopharynx underwent chemoradiation therapy. He had completed therapy seven months before presentation. On examination, he had recurrence at the level of the hypopharynx. The extent of recurrence necessitated a total laryngopharyngectomy.

FIG. 1. Exposed carotid after failed IMA fasciocutaneous perforator flap.

The defect was reconstructed at that time with a tubed anterolateral thigh free tissue transfer. At the initial operation, a monitoring paddle was placed as well as a salivary bypass tube. These were removed on postoperative day 6. A high-output pharyngocutaneous fistula then developed that was conservatively managed but persisted.

Two months after the initial operation, he developed skin loss and infection associated with the fistula, as well as an exposed carotid artery on the right side of the neck. After judicious debridement, an internal mammary artery fasciocutaneous perforator flap was rotated to cover the defect. The fistula healed but unfortunately necrosis of the distal aspect of this flap occurred, re-exposing the carotid artery on the right side (Figure 1). On evaluation of the wound, postradiation changes were present with a necrotic and fibrotic wound bed.

The patient was again taken to the operating room for debridement and planned pectoralis flap for wound coverage. In the process of debridement, safe removal of all contaminated tissue was unable to be performed due to the presence of the common carotid artery, the internal jugular vein and nerve structures in the base of the wound (Figure 2). Wound cultures were positive for methicillin-resistant staph aureus and few Serratia species.

The decision was made to use antibiotic-impregnated beads with vancomycin and tobramycin. The beads were partially crushed due to concerns of pressure erosion to the great vessels (Figure 3). The pectoralis muscle flap was placed over the wound, and a split thickness skin graft over the surface (Figure 4). In 13 months of follow-up, the wound healed with no further breakdown or evidence of a fistula (Figure 5).

Discussion

The treatment of complex wounds with critical structures or prosthetic devices presents a unique challenge to the surgeon treating these patients. For most cases, the standard treatment is debridement of infected or necrotic tissue with removal of the underlying prosthetic material, if present. This can significantly increase morbidity. Antibiotic-impregnated beads have been proven to sterilize infected wounds leading to decreased reinfection rates and increased preservation of vascular grafts and orthopedic prosthetics resulting in a decrease in morbidity and mortality.[10, 11, 12]

Stone et al. in 2006 described 34 patients treated for vascular surgical site infections (VSSi) involving 36 prosthetic lower extremity arterial bypasses using antibiotic-loaded PMMA beads and culture-specific parenteral antibiotics for four to six weeks. PMMA powder was polymerized with an antibiotic (vancomycin, daptomycin, or tobramycin/gentamicin, or a combination), molded into a chain of beads, and implanted adjacent to the infected graft after debridement and pulsed-spray antibacterial lavage. All wounds were closed primarily. Vancomycin PMMA beads were implanted in 29 of 36 VSSi at the first procedure; daptomycin (n = 4) or tobramycin (n = 3) beads were implanted in the rest. Repeat VSSi exploration and culture revealed an average of 2.5 antibiotic bead replacements before definitive treatment. A sterile (no growth on tissue culture) VSSi was achieved in 87 per cent of cases before a graft preservation (n = 16) or *in situ* replacement of an infected graft (n = 20) procedure. No patient deaths were reported. Early and late limb salvage was 100 per cent. Infection reoccurred in four (11%) VSSi during a mean 23-month follow-up period.[7] In our cohort of vascular patients, we had 20 patients with a reoperation rate for infection of 5 per cent with 30-day follow-up.

Stone et al. in 2012 describes 40 patients who developed 42 extracavitary lower extremity VSSi. Exploration and culture results led to an average of 1.4 bead replacements before definitive treatment. Final treatment strategy included graft preservation of patent bypasses in 28 patients partial graft excision with *in situ* replacement in eight patients, graft removal only with residual graft remaining at implant site (*i.e.*, incorporated anastomotic conduit, 11.9%) in five patients,

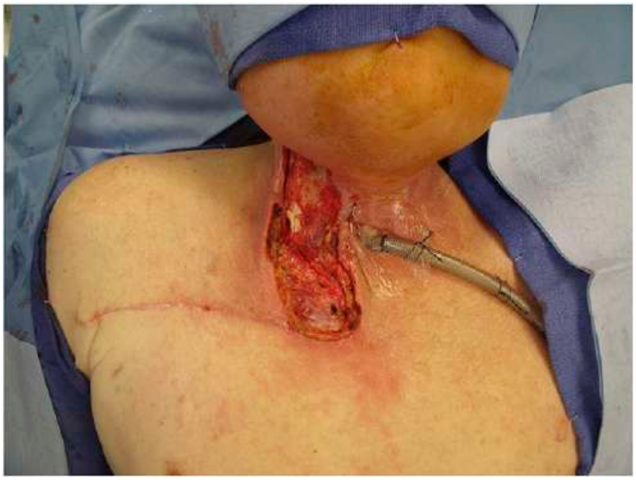

FIG. 2. Wound after debridement with exposed common carotid artery and internal jugular vein in preparation for pectoralis flap.

FIG. 3. Wound during placement of crushed vancomycin and tobramycin absorbable antibiotic-impregnated beads.

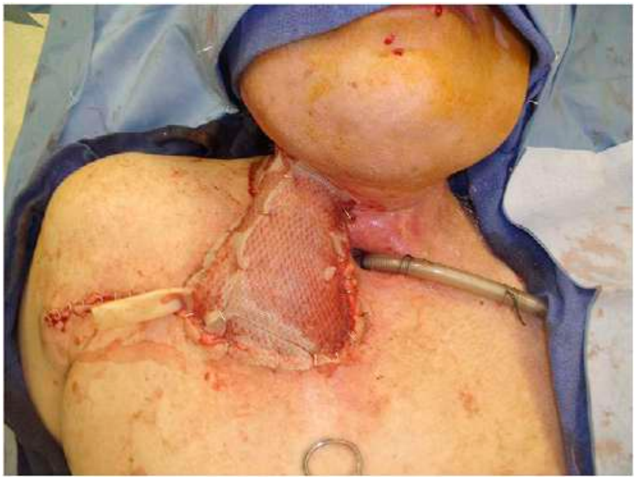

FIG. 4. Wound after pectoralis flap and split thickness skin graft.

FIG. 5. Follow-up after 13 months with no evidence of infection, wound breakdown, or fistula.

and extra-anatomic reconstruction in one. Sartorius muscle flap was performed in 14 groin infections (37.8%). The 30-day mortality was 0 per cent, and limb loss was 7.1 per cent (n = 3). At the median follow-up of 17 months, the limb loss was 21.4 per cent and the recurrent infection rate was 19.4 per cent (7 of 36) in those with attempted graft preservation or *in situ* replacement.[8] In our cohort of vascular patients, we had 20 patients with a reoperation rate for infection of 5 per cent with 30-day follow-up. Flap coverage was used in 18 patients (90%) with 30-day follow-up.

Poi et al. described 31 patients with 37 vascular graft infections. After multiple debridements and washouts, cultures were sent and PMMA beads were impregnated for five to seven days with vancomycin, gentamicin, and/or tobramycin. The PMMA beads were used in 37 of 37 (100%) graft infections. Also, flap coverage was used in all patients. They describe wound sterilization in 32 of 34 wounds (94.1%). Graft preservation was attempted in 32 cases (86.5%) with limb salvage achieved in 28 of the 32 preserved graft cases (87.5%) at a mean follow-up of 26 months (6 to 51 months). Of the patients, four presented with recurrent graft infection and occlusion, causing acute limb ischemia, and resulting in major amputation. The reinfection rate was 12.5 per cent in the graft-preservation group and 11.4 per cent in both the graft-preserved and the *in situ* replacement groups.[9] Comparatively, in our cohort we had 20 patients with a reoperation rate for infection of 5 per cent with 30-day follow-up. Also, we used flap coverage in 90 per cent of cases compared with 100 per cent in the Poi cohort.

Kretlow et al. reported 17 of 26 (65%) patients had resolution of LVAD infection after serial debridement and placement of antibiotic-impregnated beads. The beads were placed in a variety of wounds ranging from superficial infections to deeper pocket infections. Of those that cleared infection 10 of 17 (59%) underwent flap coverage.[10] Comparatively, we used flap coverage in 93 per cent of our total cohort of patients. However, we did not encounter any LVAD in our cohort.

Tintle et al. described nine patients with deep joint infections treated successfully with PMMA beads. Each patient underwent serial irrigation and debridements, interval placement and exchange of intra-articular tobramycin/vancomycin-impregnated PMMA beads and six weeks of intravenous antibiotics. The primary outcome measures were evidence of recurrent prosthetic infection or revision total joint arthroplasty for any reason. At a mean follow-up of 37 months (range, 23–41 months), all infections were eradicated while retaining prosthetic components.[11] In our study, we had 44 patients with orthopedic wounds with a reoperation for infection rate of 20 per cent.

Diageler et al. described 69 patients with mediastinitis treated with pectoralis flaps, in which long-term follow-up demonstrated a need for reoperation in 36.2 per cent of these patients.[12] Chiu et al. described two patients with deep sternal osteomyelitis that were treated with single-stage aggressive debridement followed by placement of gentamicin-impregnated PMMA antibiotic beads within the deep sternal space. Neither of these patients needed reoperation, and notably did not have their PMMA beads removed.[13] In comparison to these historical controls, our study yielded 3 of 19 patients (15.8%) requiring reoperation for infection in those patients treated for mediastinitis. The follow-up was not as long ranging, from three months to greater than four years.

Limitations of our study would be threefold. First, it is relatively low level of evidence due to its retrospective nature. However, we have concerns about a prospective study due to our ongoing experience that demonstrates such good results. Second, our sample size is relatively small with approximately 100 patients. To increase the power, a larger sample would be ideal. And third, our follow-up was limited to 30 days *versus* 5 to 10 years for some of the papers in the literature describing use of PMMA beads. There is a clear advantage of using the antibiotic beads in terms of reduction of need for reoperation for infection and mortality. Use of the absorbable beads only further improves on the efficacy of the PMMA beads by decreasing the need for another separate procedure to remove them.

The advantages of using absorbable antibiotic-impregnated beads in complex infected wounds have been demonstrated with minimal disadvantages. The utilization of these beads is expanding to a variety of complex infectious wounds requiring high concentrations of local antibiotics. Even with all the evidence that currently exists, an adequate randomized prospective study ascertaining the efficacy of antibiotic-impregnated beads is still warranted in order to standardize the treatment.

Conclusion

The treatment of complex wounds with critical structures or prosthetic devices presents a unique challenge to the surgeon treating these patients. For most cases, the standard treatment is debridement of infected or necrotic tissue with removal of the underlying prosthetic material, if present. Antibiotic-impregnated beads have been proven to sterilize infected wounds leading to decreased reinfection rates and increased preservation of vascular grafts and orthopedic prosthetics resulting in a decrease in morbidity and mortality. Even with all the evidence that currently exists, an adequate randomized prospective study ascertaining the efficacy of antibiotic-impregnated beads is still warranted in order to standardize the treatment.

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