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ORIGINAL ARTICLE

Successful Management of Infected Intramedullary Nailing With Reaming, Lavage, and Insertion of Antibiotic-Impregnated Cement Rods

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Background: Intramedullary nailing is widely accepted as the gold standard for most metaphyseal fractures of the long bones. Infections after intramedullary nailing have increased and cause recalcitrant metaphyseal osteomyelitis. Usually, multiple surgeries combined with adjuvant administration of local and systemic antibiotics are required to achieve infection control. The recurrence rate is still high and often causes poor limb function. Enhancement of local antibiotic concentrations through different delivery systems has been developed as an effective solution for eliminating musculoskeletal infections. Our study was conducted to evaluate the efficacy of antibiotic-loaded acrylic cement rods in managing infected intramedullary nailing.

Methods: Twelve patients with metaphyseal osteomyelitis following intramedullary nailing were enrolled. The causative organisms were identified in eight patients, including six methicillin-resistant *Staphylococcus aureus*, one methicillin-susceptible *S aureus*, and one methicillin-resistant *S aureus* and *Prevotella intermedia* mixed infection. All patients were treated with radical reaming debridement, copious intramedullary lavage, insertion of an impregnated acrylic cement rod, and systemic antibiotic administration.

Results: The average follow-up duration was 59.1 months. None of the 12 patients showed a relapse of infections. Four patients had nonunion of the old fracture site and received subsequent revisional internal fixation and bone grafting. All of them achieved solid bony union within 18 weeks.

Conclusions: Insertion of antibiotic-loaded acrylic cement rods combined with adequate debridement, lavage, and systemic antibiotic administration significantly contribute to infection control after intramedullary nailing.

1. Introduction

Locked intramedullary nailing has been in clinical practice for metaphyseal fractures of long bones since the early 1970s and has long enjoyed general acceptance. Because of refined surgical techniques and improved implant design, the practice of intramedullary nailing is increasing and its use has been extended to open fractures.[1,2] Thus, infections after intramedullary nailing are increasing and remain a challenge to orthopedic surgeons.[3,4] The tenuous local blood supply after trauma and intramedullary reaming, the presence of sequestra, and the high degree of soft-tissue damage caused by multiple surgeries often interfere with antibiotic penetration into the infected area. The consequences of these infections are often devastating and difficult to eliminate. Patients have to undergo repeated extensive debridement and long-term antimicrobial therapy. Unfortunately, the rate of recurrent infection is high and often causes impaired limb function.[5,6]

The adjunctive administration of local antibiotics is effective in managing recalcitrant skeletal infections.[7,8] The concept of local delivery of antibiotics to manage osteomyelitis was developed in the early 20th century in an effort to increase local antibiotic concentrations.[9] Various delivery vehicles for antibiotics are currently available, including polymethylmethacrylate (PMMA) cement and several types of biodegradable bone fillers. PMMA cement, however, is the most commonly used[10] and cost-effective

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delivery material. After being mixed into the PMMA cement, antibiotics are steadily released from the cement's surface and from cracks and voids in the cement.[11] In one study evaluating antibiotic concentration of the joint fluid in total hip arthroplasties fixed with antibiotic-loaded PMMA cement, the authors showed that, although most antibiotic release occurred within the first 9 weeks, a slow liberation through cracks was found to persist for 10 years after the original procedure.[12]

Using PMMA as an antibiotic delivery material is widely practiced by orthopedic surgeons in the reconstruction surgery of septic joint replacement and in tumor surgery to prevent infection.[11,13] Generally, the procedure is as follows. After meticulous debridement and removal of the endoprosthesis, the antibiotic-impregnated PMMA cement spacer is temporarily placed to fill the bony defect. After the infection is controlled by replacing the cement block with definite arthroplastic implants, staged revisional arthroplasty is performed. In the past two decades, more than 100 septic joint reconstructions were successfully treated by this method at the corresponding author's institute. The idea of placing antibiotic-loaded cement rods into the medullary canal for managing metaphyseal infection was proposed by Paley and Herzenberg[14] in 2001, who had gained success in treating nine intramedullary infections after long bone nailing. A more recent study showed that combining reaming and lavage with antibiotic-loaded cement rod insertion was also effective in the treatment of chronic osteomyelitis in pediatric patients.[15]

Since first being isolated and reported on in 1961,[16] the rate of methicillin-resistant *Staphylococcus aureus* (MRSA) infection has risen dramatically and is currently the leading pathogen of skeletal infections.[17–19] Among those antibiotics effective in treating MRSA-related infection, vancomycin is considered the standard agent.[20] Consequently, more orthopedic surgeons use vancomycin against MRSA before identifying the causative organism.

2. Purpose

To achieve control of *S aureus*-related osteomyelitis, the effect of the insertion of vancomycin-embedded acrylic cement rods was studied. These rods were also used to treat those infections associated with intramedullary nailing that were caused by no definite causative pathogen. After reaming debridement and lavage of the medullary canal, the hand-made vancomycin-impregnated PMMA rod was inserted into the canal. The clinical results of this method for infection control were studied.

3. Methods

This study comprised 12 consecutive cases of osteomyelitis after intramedullary nailing treated at two institutes between April 2003 and October 2007. The indication for the original procedure (intramedullary nailing) was fixation for metaphyseal long bone fracture over the lower extremities and included three patients with open fractures. Four females and eight males participated in the study. The average age at the index procedure (reaming debridement of the intramedullary canal, lavage, sequestrectomy, and implantation of a vancomycin-loaded PMMA cement rod) was 45.9 (range, 20–81) years. Locations of the infection included the tibia in nine patients and the femur in three patients. The average time interval between the original and the index procedure was 10.8 (range, 3–36) months. Comorbid diseases were present in two patients, including one with diabetes and one elderly patient with congestive heart failure. Six of the 12 patients had received surgical debridement and saucerization before the index procedure, and the intramedullary hardware had been removed in five patients.

Diagnoses of osteomyelitis in the six patients without previous surgical intervention were based on an apparent cloaca directly communicating with the involved bone in five patients and purulent discharge from the fracture site during a bone grafting procedure in one patient with tibial nonunion. For the six patients who had had previous operations that had failed, diagnoses of osteomyelitis were made from the preceding pathological reports. Four of the six patients presented a discharging sinus, and the remaining 2 patients suffered from persistent erythematous swelling of the wounds. Definite final pathological diagnoses of the surgical specimens were obtained in all patients after the index procedure. The causative pathogens ultimately identified included six MRSA, one methicillin-susceptible *S aureus*, and one MRSA and *Prevotella intermedia* mixed infection. In the remaining four patients, the causative pathogens were not identified during the treatment protocol.

All patients signed an informed consent form before the operation. The surgical procedures were all similar. Briefly, all patients received removal of any intramedullary fixation devices present as well as a thorough removal of the devitalized soft tissue and sequestra in the medullary canal. The medullary canal was then reamed systematically to about 2 mm larger than the original nail size and until no infected tissue could be grossly identified. Versatile intramedullary irrigation with 10,000 mL of normal saline was performed with the Pulsavac Plus wound debridement system (Pulsavac; Zimmer, Warsaw, IN) to wash out the necrotic tissue and blood clots.

Intramedullary cultures were taken from all patients, and the removed devitalized bone was forwarded for pathological diagnosis. Vancomycin-containing cement was prepared by adding 4.0 g of vancomycin to each 40.0 g PMMA cement pack (Simplex; Howmedica, Rutherford, NJ). The powder of the cement was gently stirred to ensure uniform distribution of the vancomycin within the cement. The powdered polymer was then mixed with the liquid monomer, and a vancomycin-loaded cement rod was made with a smooth 3.2 mm Steinmann pin placed in the center. The proximal end of the Steinmann was bended to avoid migration of the cement rod into the canal. The cement rod was then molded to ensure easy insertion into the canal. The rod was put in place, and the wounds were all primarily closed with one or more drainage tubes inserted. After the index surgery, adjuvant antimicrobial therapy with intravenous antibiotics was prescribed according to the recommendation of infectious disease physicians who were guided by the culture data. Intravenous antibiotics were given for 2 weeks, and the patients were discharged. Oral antibiotics were given to substitute for the intravenous medication for another 4 weeks for patients with a normal preoperative C-reactive protein (CRP) level ($<$0.5 mg/dL). For patients whose CRP level had not returned to normal after these 4 weeks, antibiotics were given until a normal CRP level was reached. All patients subsequently received regular follow-ups at a 2-week intervals for at least 1 3 months, then at a 3-month interval for 2 years, and, after that, yearly.

The serum level of CRP was recorded before the operation. For patients with an elevated preoperative CRP level, their CRP level was monitored at every visit until at least two continuous normal values were obtained. Radiographs of the lesion site were taken before the operation, immediately after the operation, and then monthly for at least 3 months in all patients. The wound conditions and the roentgenographs were evaluated by the same orthopedic surgeon. Failure of treatment was defined as infection occurring again at the same site. No control group was enrolled in this study because of the relative small case number.

4. Results

At the beginning of treatment, six patients had an elevated CRP level, and nine patients presented with a chronic discharging sinus

in the infected area. After an average follow-up duration of 59.1 (range, 30–83) months, the infection had improved after the treatment protocol without relapse in any of the patients. Table 1 lists patient data and the radiograph for one patient with femoral osteomyelitis. Figure 1 shows a photograph of a vancomycin-loaded cement rod. In the latest follow-up, five patients had developed mild irritation over the entry point of the cement rod. No other surgery-related complications were recorded in this series. Complete wound healing was observed in these 12 patients without any signs of recurrent infection.

A normal CRP level (<0.5 mg/dL) was obtained after a mean duration of 6.8 (range, 2–14) weeks in the 6 patients with an elevated preoperative CRP level. The low incidence of elevated CRP levels in this series may have been because of multiple previous treatments. No detectable progression of the osteolytic lesions was found on the follow-up plain radiographs in any of these 12 patients.

Four of the 12 patients had nonunion of the old fracture site. The cement rod was, subsequently, removed; and, after the infections had cleared, revisional intramedullary fixation to stabilize the fracture and bone graft into the bony defect were carried out.

Intramedullary cultures were obtained on removal of the rods and the results showed no bacterial growth. All of the rods achieved solid bony union within 18 weeks (range, 12–18).

5. Discussion

Osteomyelitis is not a rare problem, and most cases are because of surgical infections or subsequent antecedent open fractures. Managing recalcitrant osteomylitis often requires the combination of local and systemic treatments. The ultimate goals of management are to eradicate infection, prevent recurrence, and maintain optimal limb function. The literature on osteomyelitis treatment emphasizes the importance of extensive surgical debridement in eliminating these infections.[21,22] However, surgical debridement and systemic antibiotic treatment without local antibiotic augmentation is associated with a higher rate of recurrence and subsequent operations.[22] Repeated surgeries often deteriorate the already compromised condition of the soft tissue and local blood supply, which may diminish the level of antibiotic penetration. A higher complication rate and poor limb function usually jeopardize such limb-salvaging procedures.

Currently, most orthopedic surgeons treat prosthetic infections with staged surgeries by the contemporary placement of an antibiotic-loaded PMMA cement block. In this study, we extended this concept to manage infected intramedullary nailing with a modification of Paley's method.[14] Insertion of a vancomycin-impregnated cement rod after meticulous debridement and pulsatile lavage was effective in eliminating intramedullary osteomyelitis after a single surgery. The benefit of fewer surgical interventions cannot be overemphasized. Complications from repeated anesthesia use were avoided and better limb function was also preserved.

In our series, after radical sequestrectomy and removal of the hardware, the intramedullary canals were filled with PMMA cement rods as an antibiotic carrier. After eradication of the infection was obtained, bone-grafting procedures over nonunion sites were conducted in four patients, all of whom finally achieved a solid union. An additional procedure to remove the cement rod might not have been necessary for the remaining patients because the *in situ* cement rod may, to some degree, contribute to the bony strength. Vancomycin-containing cement beads have also been widely used for orthopedic infections. The difficulty in inserting them into the canals and the hazard of breaking the chain during subsequent removal limits their practicality in treating medullary osteomyelitis.

Some newly developed biodegradable materials are undoubtedly promising bone-void fillers that could also be used for delivering antibiotics.[23–26] The most significant benefit of such materials is that no extra procedure is needed to remove the implanted fillers. However, most of these fillers are still under investigation and are expensive. A major concern is that these bone substitutes may be absorbed before the infection is controlled. More clinical studies on these new fillings are, therefore, required.

In our series, the treatment efficacy of osteomyelitis was monitored through radiographs and clinical wound observations. No radiographic progression of the osteolytic area was noted, and all patients had complete wound healing. For a patient with diagnosed osteomyelitis, evaluation of the condition of the wound and radiographs should be sufficient in determining the efficacy of the osteomyelitis treatment.[27] In this study, an elevated preoperative CRP level was detected in 6 of the 12 patients, subsequent CRP levels were measured to monitor treatment efficacy in these patients. For the other six patients having normality in CRP levels, the success of their treatment was monitored with clinical and radiographic evaluations. An normal CRP level is not conflict with the diagnosis of osteomyelitis as reported by many authors,[28,29] maybe because of long-term antibiotic therapy or multiple surgeries.

Table 1 Patient data

Number	Age (yr)/ gender	Involved bone	Previous surgical debridement (number of times)	Interval between the original and the index procedure (mo)	Pathogen	Follow-up period (mo)	Additional surgery
1	68/M	Right tibia	4	36	N/A	83	Revisional fixation + BG
2	81/M	Left tibia	0	10	MRSA	79	None
3	33/F	Left femur (open fracture, Type IIIA*)	4	7	N/A	76	None
4	52/M	Right tibia	2	4	MRSA	67	None
5	20/F	Left femur (open fracture, Type II)	1	3	MRSA	64	Revisional fixation + BG
6	32/M	Left tibia	0	5	MRSA	63	Revisional fixation + BG
7	55/M	Left tibia	2	6	MRSA and *Prevotella intermedia*	56	None
8	46/M	Right tibia	0	8	MSSA	56	None
9	77/M	Right tibia	0	12	MRSA	52	None
10	51/F	Right tibia	1	18	MRSA	51	None
11	25/M	Right femur	0	16	N/A	32	None
12	33/M	Left tibia	0	5	N/A	30	Revisional fixation + BG

* The Gustilo classification.

BG = bone grafting; MRSA = methicillin-resistant *Staphylococcus aureus*; N/A = not available.

Figure 1 (A) Radiograph of right femur of a 25-year-old male with intramedullary osteomyelitis. He had received bone grafting and removal of the proximal locking screw for delayed union 6 months after the original surgery and acquired the infection. (B) A chronic discharging sinus extending from the wound of distal screws was found. (C) Photograph of the vancomycin-impregnated cement rod. A 3.2 mm Steinmann was placed in the center. (D) Postoperative plain film. The vancomycin-embedded cement rod was inserted into the medullary canal.

To some degree, the routine use of vancomycin in treating osteomyelitis may increase the bacterial resistance to antibiotics. In our series, seven patients were proven to have MRSA-related infection. In four patients without an established causative organism and in one with mixed infection, the control of the infection might have been a result of reaming debridement and pulsatile lavage. In our opinion, reducing the possibility of additional surgeries to maintain better limb function is the goal of treating osteomyelitis.

MRSA is the leading pathogen in musculoskeletal infections and, therefore, orthopedic surgeons are justified in their use of vancomycin to combat it.[17–20] The mechanical and pharmacokinetic characteristics of vancomycin-loaded cement have been well evaluated. After being mixed into the cement, high local concentrations and low serum levels of vancomycin were identified eluted from the cement. Its safety was proposed because no evidence of allergic reaction and toxicity were noted.[30] No adverse reaction related to vancomycin was noted in our series. Based on the results of our study, we believe that vancomycin-loaded PMMA cement rod insertion combined with systemic antibiotic treatment is an effective method for eliminating intramedullary osteomyelitis. The benefits of a single surgery and rapid infection control cannot be overemphasized.

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