**Treatment of Infected Tibial Nonunion with Tobramycin-Impregnated Calcium Sulfate: Report of Two Cases**

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The treatment of infected tibial nonunion usually includes a staged reconstruction protocol. We present 2 patients with tibial nonunion and plate loosening with oxacillin-resistant *Staphylococcus aureus* infection. The patients were treated using the removal of the plate, radical debridement, and implantation of gentamycin-impregnated cement beads during the first stage. During the second stage, plate fixation was performed and tobramycin-impregnated calcium sulfate (Osteoset T®) was used as a bone graft substitute. Neither an autogenous bone graft nor an allograft was used. At 3 years of follow-up, each tibia showed good union, and there was no recurrence of infection. We consider tobramycin-impregnated calcium sulfate to be an alternative method of bone grafting to treat infected tibial nonunion.

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**Key words:** osteomyelitis, osteoset, tibia.

Tibial osteomyelitis is a challenging problem for orthopedic surgeons. The successful treatment of osteomyelitis associated with nonunion often requires debridement and parenteral antibiotics initially. The pre-existing fixation device needs to be removed, and external fixation applied to the lower leg is sometimes indicated. Local deposition of antibiotics with polymethylmethacrylate cement (PMMA) therapy is effective and significantly increases local tissue levels of antibiotics around the infected tissues. However, with the use of PMMA, additional surgery to remove the beads is needed when there is a bone defect. Autogenous cancellous bone graft and vascularized bone graft are the most common methods used to fill in the bone defect for the union process.

Recently, a bone graft substitute has been used as an alternative method for conventional bone grafting. Osteoset® (Wright Medical Technology, Inc, Arlington, Tenn), patented medical-grade calcium sulfate, has shown to be effective as a bone void filler in many studies. Another product, Osteoset T®, tobramycin-impregnated calcium sulfates, has been introduced to provide a high local level of antibiotics and is effective against gram-positive *Staphylococcus aureus*.

The purpose of this paper was to present our experiences in treating two patients of tibial infected nonunion with Osteoset T®.

**CASE REPORTS**

Two patients with infected tibial nonunion were treated with plate fixation and Osteoset T® in our hospital in 1999. They were male adults with minimum follow-up of 3 years. Neither of these patients had been harvested autogenous bone graft from the iliac crest or elsewhere.

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Case 1

An 80-year-old man who experienced a traffic accident and had right tibial lower third fracture was sent to a local hospital in September 1998. Plate fixation was performed immediately. He had a history of hypertension and diabetes mellitus that were being treated. In May 1999, there was a persistent discharge from the wound, and the skin showed progressive erosion with bone exposure. He was referred to our orthopedic department. With the expectation of localized swelling and poor wound healing, lower leg deformity was noted. The erythrocyte sedimentation rate was elevated to 52 mm per hour, and the C-reactive protein level was elevated to 12 mg per liter. The leukocyte count was 7800 per microliter. Radiography revealed plate loosening and tibial nonunion (Fig. 1A). Culture of the discharge showed the growth of *Staphylococcus aureus*.

Under the impression of chronic osteomyelitis, we performed removal of plate, surgical sequestrectomy, and implantation of gentamycin-impregnated PMMA beads (Fig. 1B). During the operation, we found a few infected tissues and a 2-cm gap over the fracture site. A short leg splint was applied and two combined intravenous antibiotics (oxacillin and gentamycin) were given. Four days later, *Enterococcus facecalis* and oxacillin-resistant *Staphylococcus aureus* grew on culture of a tissue specimen. Thus, intravenous vancomycin (2 g per day) was given for more than 10 days.

Two weeks after the first operation, the C-reactive protein level had decreased to 3 mg per liter. We performed surgical debridement with removal of gentamycin-impregnated PMMA beads. The nonunion site seemed to have no signs of active infection, and the soft-tissue coverage was sufficient. Then dynamic compression plate fixation using Osteoset T® as a bone void filler was performed (Fig. 2A). No brace or short leg splint was applied after this operation, and ambulatory crutch walking was encouraged for him. Vancomycin was continued for 1 week. The condition of the wound seemed to heal well, and the patient discharged with the oral antibiotic agent, sulfamethoxazole-trimethoprim (0.96 gram per day), for 2 weeks. One month after discharge, the erythrocyte sedimentation rate had decreased to 28 mm per hour, and the C-reactive protein was down to 2 mg per liter. The patient showed no evidence of infection, and the skin had healed well. Four months after the operation, the radiograph showed Osteoset T® absorption and callus formation (Fig. 2B).

![Fig. 1 Case 1. (A) Radiograph of the right tibia shows plate loosening and angulation. (B) After removal of the plate, surgical debridement and implantation of septopal; there was a 2-cm gap at the fracture site.](image1)

![Fig. 2 Case 1. (A) Plate fixation with Osteoset T. (B) Four months after surgery, a radiograph shows osteoset absorption and callus formation (arrow).](image2)
At a follow-up examination 3 years after the operation, there was no evidence of clinical recurrence of the infection and the bone revealed good union on radiograph. The patient had full activity without pain.

Case 2
A 28-year-old man who had a motorcycle accident had upper-third tibial fracture in October 1998. He was treated with open reduction and plate fixation at a local hospital. Two months after surgery, a discharge sinus from the wound was found and he felt discomfort while walking. He was seen at our hospital in July 1999 due to the persistent discharge. Radiography revealed plate loosening and nonunion of the fracture site (Fig. 3A). The erythrocyte sedimentation rate was 4 mm per hour and the C-reactive protein was 3.28 mg per liter. The leukocyte count was 7200 per microliter. Removal of the plate, surgical debridement, and implantation of gentamycin-impregnated PMMA beads were performed. There were infected tissues and a 3-cm bone gap at the fracture site (Fig. 3B). A short leg splint was applied, and cefamerzine and clindamycin were given after surgery. Four days after surgery, bacterial culture revealed oxacillin-resistant Staphylococcus aureus growth. Intravenous vancomycin was given for 10 days. Because the erythrocyte sedimentation rate and the C-reactive protein were not elevated, we decided to perform plate fixation with Osteoset T filling in the gap after surgical debridement during the second operation (Fig. 4A). The soft-tissue coverage of the wound was achieved by primary closure. He used crutches to walk without a short leg splint. Vancomycin was administered for 1 week. No infective signs were noted around the wound. The patient was discharged with oral sulfamethoxazole-trimethoprim for 12 days. Three months after his discharge, the patient showed the well-healed skin, and radiography confirmed new bone formation.

At a 3 years follow-up examination, no recurrence of the condition was found. The patient had full range of motion of the lower leg, without pain or instability (Fig. 4B).

DISCUSSION

Infected tibial nonunion is usually treated in two stages. Radical debridement, external skeletal fixation, and local antibiotic bead chain therapy are performed during the first stage. Bone grafting and soft tissue reconstruction should be performed during the second stage.\textsuperscript{12,19-15} The time between the two stages of treatment is about 2 to 6 weeks. Culture-specific antibiotics are recommended for 4 to 6 weeks.\textsuperscript{2,12}
Autogenous bone graft obtained from the iliac crest is the gold standard among graft materials because it contains osteoinductive factors, osteoconductive factors, and osteogenic stem cells. However, an autogenous bone graft has major disadvantages that include insufficient amount for use, particularly in children and for treating large osseous defects, significant postoperative morbidity at the donor site and increased operative time, costs, and blood loss. Major complications have been reported at a rate of 8.6% and minor complications at 20.6%. Donor site complications include infection, prolonged wound drainage, large hematomas, need for reoperation, prolonged pain, sensory loss, fractures, pelvic instability, meralgia paresthetica, and unsightly scars.

Recently, bone graft substitutes have been developed to fill and repair osseous lesions. Osteoset, a calcium sulfate (plaster of Paris) product with osteoconductive factors, has been proved effective in healing bone defects. An advantage of Osteoset is the ability to incorporate antibiotics into the calcium sulfate. Aminoglycosides are ideal antibiotics because of their prolonged elution characteristics. Mousset et al. presented an in vitro study of antibiotic-loaded calcium sulfate in which aminoglycosides had the best thermal stability and antibacterial activity for 21 days. Thus, Osteoset T pellets are commercially made of medical-grade calcium sulfate containing 4% tobramycin sulfate that is effective against Staphylococcus aureus.

Local antibiotic therapy with PMMA beads is often used for the treatment of open fractures and osteomyelitis. Some authors have also shown that in vivo studies can be used to achieve the effects of antibiotics on bone graft healing, and concluded that antibiotic-impregnated bone grafts did not alter the healing process. However, Miclau et al. reported that plaster of Paris and PMMA with 25 mg of tobramycin were better for long-term coverage of established osteomyelitis than were a bone graft and demineralized bone matrix in antibiotic released from locally implantable materials. Bowyer and Cumberland reported that the release of antibiotics from plaster of Paris was at least four-fold greater than that from corresponding PMMA pellets.

In our patients, the infections were well controlled by effective radical debridement during the first stage and by a high local level of antibiotics during the second stage of reconstruction. Although the use of internal fixation is recommended, we used plate fixation and Osteoset T during the second stage without the application of an external fixator and shortened the course of intravenous antibiotics. These two patients achieved good bone union, and they had no recurrence of infection at 3 years of follow up.

In conclusion, the main concern of the 2-stage treatment protocol of osteomyelitis is to eliminate infection. Although the use of tobramycin-impregnated calcium sulfate pellets in the infected nonunion can increase local resistance to infection, correspond to the rate of new bone growth, and avoid postoperative morbidity at the donor site of the iliac crest, Osteoset T should be carefully used in cases of severe osteomyelitis. We consider that tobramycin-impregnated calcium sulfate is an alternative method of bone grafting to treat infected nonunions.

REFERENCES
以含抗生素人工骨治療膝骨感染性癒合不良：二例報告

蔡耀鴻 黃聰仁 施信農 許文蔚

治療膝骨骨髓炎癒合不良通常用階段性重建。我們報告2位因抗藥性金黃色葡萄球菌感染導致膝骨骨髓炎及癒合不良病人，經第一階段拔骨釘、擴創術及置入抗生素骨水泥珠和第二階段之骨釘板固定和含Tobramycin之人工骨後，在術後3年追蹤中，病人的骨頭癒合良好，且無復發感染。因此含抗生素之人工骨移植是治療骨髓炎併癒合不良的另一種選擇。(長庚醫誌 2004;27:542-7)

關鍵字：骨髓炎，人工骨，膝骨。