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Application of personalized spacers made with 3D-printed mold in the two-stage procedure for periarticular infection

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Abstract. – BACKGROUND: Cement spacers treat periarticular infection after bone tumor resection in patients with bone defects. Complications such as poor joint function, poor soft tissue reconstruction, and poor postoperative daily living ability are present. We present a case of periarticular infection treated successfully after distal femoral osteosarcoma surgery with a personalized spacer made with a 3D-printed mold.

CASE REPORT: A two-stage procedure was performed on an 18-year-old patient with high-grade conventional osteosarcoma of the left distal femur. After two biopsies, the boy developed a periarticular infection of the affected limb during neoadjuvant chemotherapy. We had a microbiologically confirmed methicillin-resistant *Staphylococcus aureus* (MRSA) infection. Because of the infection risk associated with primary joint replacement, a two-stage procedure was planned. In the first stage of surgery, we prepared a personalized spacer using a 3D-printed mold, antibiotic-loaded polymethylmethacrylate (PMMA), and an intramedullary needle. This spacer restored the function of the knee joint and the daily activities of the affected limb, and the infection was effectively eradicated. This spacer was firmly fixed two years after the surgery, and there were no surgical or spacer-related complications. The patient underwent a second stage of surgery to replace a permanent metal mega-prosthesis, and the knee joint functions returned to near normal.

CONCLUSIONS: This case report describes limb-salvage surgery following distal femoral resection for periarticular infection. The personalized spacers prepared by a 3D-printed mold can be used in periarticular infection after long bone resection, mega-prosthetic infection, or limb-salvage surgery for temporary joints in small children.

Key Words:
Osteosarcoma, 3D-printed, Periarticular infection, Spacer, Mega-prosthesis.

Abbreviations

3D: 3-dimensional, MRSA: methicillin-resistant Staphylococcus aureus, MDT: multidisciplinary team meeting, CT: Computed Tomography, MRI: Magnetic Resonance Imaging, PMMA: polymethylmethacrylate, ROM: Range of motion, MSTS: Musculoskeletal Tumor Society, NCCN: National Comprehensive Cancer Network, ESMO: European Society of Medical Oncology.

Introduction

Osteosarcoma is the most common bone cancer in adolescents, and most commonly occurs in the distal femur[1]. Both European (ESMO)[2] and North American National Comprehensive Cancer Network (NCCN) guidelines[3] recommend neoadjuvant chemotherapy, followed by surgery, and continue adjuvant chemotherapy after surgery for adolescents with osteosarcoma. The rate of tumor necrosis after neoadjuvant chemotherapy is related to the prognosis[4].

After chemotherapy, most osteosarcoma patients usually have low immunity. Periarticular biopsy wound infection may occur during chemotherapy. If a prosthesis is placed in the first stage, there is a risk of periprosthetic infection, and the patient may incur high costs and functional impairment[5]. A cement spacer has become the standard procedure for the two-stage treatment of periprosthetic joint infection[6]. Patients can benefit from temporary joint stability provided by a cement spacer; antibiotics can be added to cement to improve anti-infection ability. Cement is simple to shape, can be used in various joints, and is inexpensive[7]. The operator often manually shaped the cement spacer, but the articular surface of the cement spacer is rough, poorly shaped, and poorly matched with the surrounding tissue[24]. Therefore, it cannot effectively reconstruct the patient's soft tissue structure.

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3D (3-dimensional) printed molds are used in clinical practice as 3D printing auxiliary technology advances[8]. An 18-year-old patient with distal femur osteosarcoma developed a periarticular infection of the affected limb during neoadjuvant chemotherapy. We present the patient's case who was treated with a temporary personalized cement spacer developed with 3D-printing technology, followed by mega-prosthesis reconstruction, focusing on our unique surgical suggestions for a personalized cement spacer developed with 3D-printing technology.

Case Presentation

An 18-year-old boy presented to our clinic with worsening pain in the left distal thigh. Osteosarcoma was suspected radiographically. A coarse needle biopsy was nondiagnostic in this case. Finally, open biopsy revealed high-grade conventional osteosarcoma. The tumor was initially staged as IIB T2N0M0, AJCC (American Joint Committee on Cancer)[3], and the patient was subjected to MAP (high-dose methotrexate, doxorubicin, cisplatin) neoadjuvant chemotherapy[2]. After two cycles of neoadjuvant chemotherapy, the pain was alleviated. Imaging assessment confirmed tumor shrinkage after neoadjuvant chemotherapy completion (Figure 1), and limb-salvage surgery was planned. After two biopsies, the boy developed a periarticular infection of the affected limb during neoadjuvant chemotherapy. We had a microbiologically confirmed infection of methicillin-resistant *Staphylococcus aureus* (MRSA). Inflammatory indicators returned to normal after one week of intravenous sensitive antibiotics, which continued for one more week, and oral antibiotics for two weeks. Because the tumor had already infiltrated the epiphyseal plate of the left distal femur at the time of diagnosis, osteoarticular resection was deemed necessary to obtain a negative surgical margin. Primary joint replacement was not recommended after a multidisciplinary team meeting (MDT) because of the risk of infection. We performed a two-stage procedure on the patient.

First Surgery

We designed a 3D-printed mold to make a personalized cement spacer because the hand-made spacer was rough and had poor shape matching. We used 3D reconstruction technology to reconstruct the normal shape image of the patient's affected distal femur based on the patient's computed tomography (CT) and magnetic resonance imaging (MRI) data and the shape of the contralateral distal femur as a reference. We made a 3D-printed mold based on the reconstructed image that accommodated the morphology of the distal femur of the affected limb (Figure 2A).

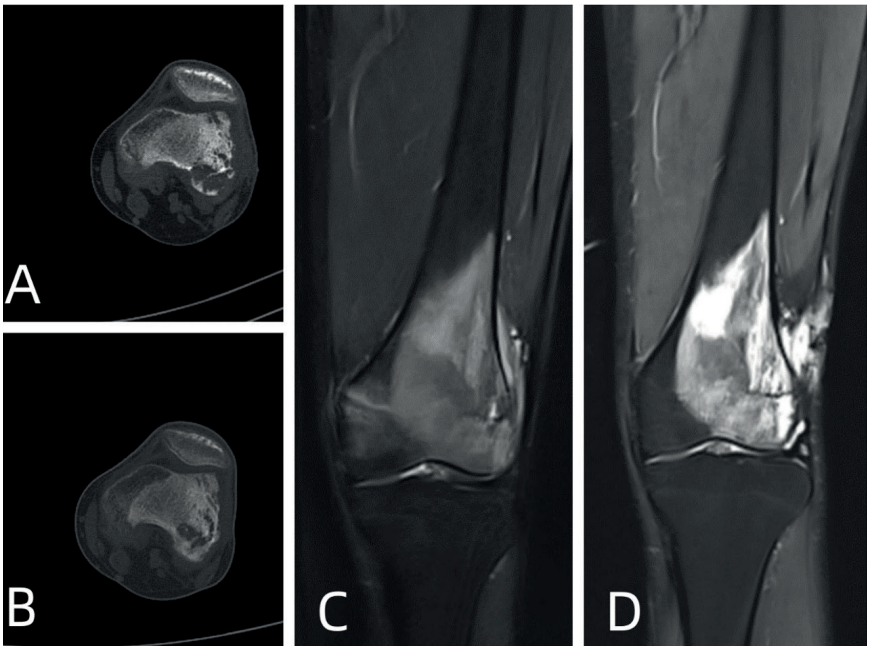

Figure 1. The patient local tumor image. **A**, CT images before neoadjuvant chemotherapy. **B**, CT images after neoadjuvant chemotherapy. **C**, MRI images before neoadjuvant chemotherapy. **D**, MRI images after neoadjuvant chemotherapy, the lateral condyle was considered as an infection channel.

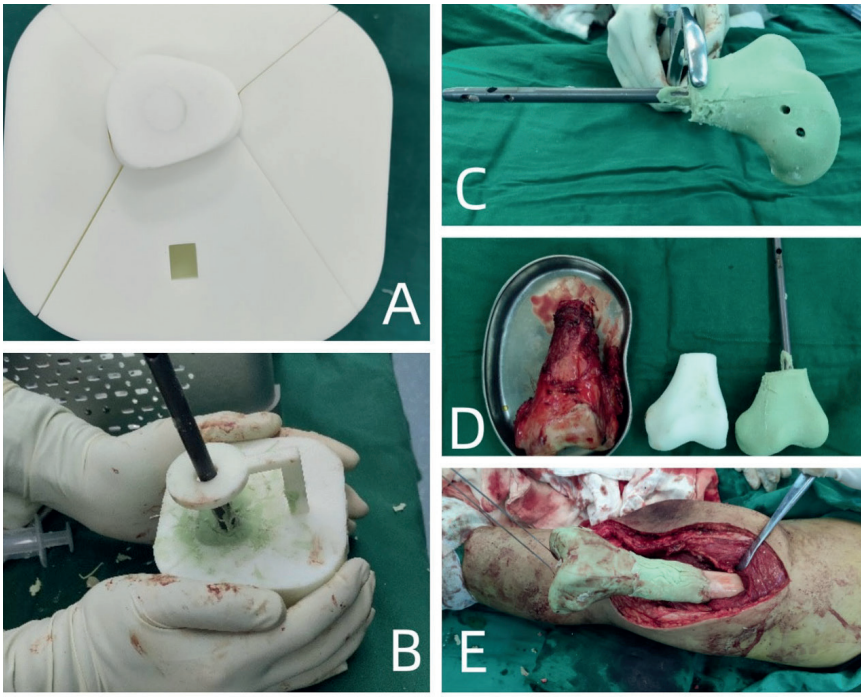

Figure 2. The cement spacer production and installation process in intraoperative. **A**, 3D-printed mold. **B**, Production of the personalized cement spacer. **C**, Appearance of the cement spacer. The hole was used to secure the cruciate ligament. **D**, Comparison of bone tumor, mold, and cement spacer. **E**, Installation of the cement spacer.

The patient was positioned in the supine position under general anesthesia. The anterolateral approach was used to incise the skin and resect the original biopsy channel. We designed the osteotomy length to be 2 cm away from the tumor edema area based on the MRI of the patient before neoadjuvant chemotherapy. According to the preoperative measurement, the osteotomy was performed 13 cm from the lateral femoral condyle. During the surgery, the anterior and posterior cruciate ligaments were cut 0.5 cm from the femoral attachment point. The tumor was completely resected (R0). The residual proximal femur was reamed slightly, and a suitable intramedullary nail was selected. The selected intramedullary nail was shorter than the standard and only entered the intramedullary by about 10 cm. The spacer was prepared using a 3D-printed mold and antibiotic-loaded PMMA with an intramedullary nail in the center (Figure 2B). The portion of the residual bone segment not covered by the mold was reconstructed with hand-made PMMA, and the spacer length was restored to 13 cm. Three anti-rotation screws were used to secure the proximal intramedullary nail to the femur. The anterior and posterior cruciate ligaments were fixed to the above-prepared cement spacer, and no osteotomy was performed on the proximal tibia. The range of motion (ROM) of the left knee was 0-120° after the wound was sutured during the operation.

After the surgery, the patient received intravenous injections of sensitive antibiotics for one week. The knee joint was immobilized straight for one week after the surgery. The patient then stretched exercise by passive bending knee and ambulated early. Three weeks after the operation, active knee flexion was performed. Adjuvant chemotherapy was continued for four cycles initiating two weeks after surgery. The infection was completely controlled after surgery, and there was no sign of infection recurrence. An imaging evaluation was performed every three months, and the position of the spacer was excellent and stable. After two years of follow-up, the patient could perform normal activities with a single crutch. The musculoskeletal tumor society (MSTS) score was 22 out of 30 points[9]. The muscle strength of the quadriceps recovered to manual muscle test (MMT) level 5. The ROM of the left knee was 0-90° (Figure 3).

Second Surgery

Two years later, secondary surgery was performed to replace the permanent metal prosthesis. The residual femoral bone quality was found to be good during the operation, the metal prosthesis was routinely replaced, and the scar tissue around the knee joint was loosened simultaneously. The patient could walk without assistance three weeks after the second surgery. The MSTS

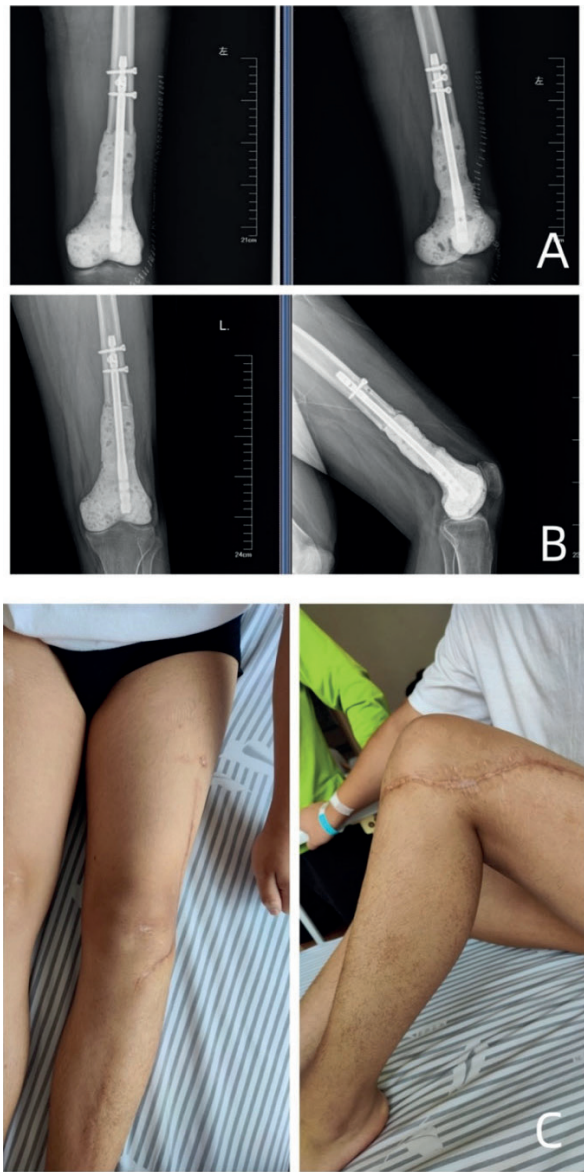

Figure 3. Postoperative review after the first surgery. **A**, X-ray images one week after surgery. **B**, X-ray images two years after surgery. **C**, Knee joint range of motion 2 years after surgery.

score was 28 out of 30 points three months after the procedure. The ROM of the left knee was 0-135° (Figure 4).

Discussion

Surgical therapy and (neo-)adjuvant chemotherapy represent the two main pillars of osteosarcoma treatment. With modern treatment strategies, limb salvage surgery is the most common surgical procedure[10]. Following wide resection of extremity osteosarcomas, the most common reconstruction method for non-pediatric patients is a mega-prosthetic replacement[11]. However, neo-adjuvant or adjuvant chemotherapy is initiated immediately after the biopsy or mega-prosthetic replacement procedure. Both chemotherapy and malignant tumors will cause low immunity of patients. At the same time, the implantation of prostheses can result in bacterial infections to the prosthesis itself[12]. These elements may result in a periarticular incision or prosthetic infection[13]. Patients with periarticular infection face a dilemma in the choice of surgical protocol. Primary metal replacement is commonly associated with a high risk of infection. Therefore, cement spacers can be selected after tumor resection. The metal prosthesis will be implanted after chemotherapy and without infection. A two-stage procedure with a cement spacer is a common treatment protocol for periarticular and prosthetic infections[5].

The majority of cement spacers are hand-made. However, hand-made cement spacers molded in the operating theatre do not have reproducible mechanical properties, and there is a risk of component fracture[14]. Industrially prefabricated knee spacers can achieve high, prolonged, and standardized antibiotic release while maintaining the excellent mechanical performance guaranteed by the industrial manufacturing process[15,16]. Several industrial preformed PMMA spacers are available, such as the Spacer-K® (Teres S.P.A, Verona, Italy) or the Inter Space Knee® (Exactech Inc, Gainesville, FL, USA). These commercially manufactured antibiotic-containing spacers are designed as surface knee prostheses. A hand-made spacer made from prefabricated molds is another option for the cement spacer. For instance, making a cement spacer using commercial molds is easy, such as Stage One® (Biomet, Warsaw, IN, USA)[17]. Although performed spacers or molds can reduce the operating time, they have some limitations, such as limited size variations and the inability to fit all patients' knees[18]. There are no prefabricated spacers or mold for bone defects after tumor resection.

The length of osteotomy varies by limb tumor patients, and current commercial spacers and molds cannot accurately match the bone defect. Hoshino et al[18] indicated that antibiotic-loaded cement spacers produced with a hand-made silicone mold performed well in knee function and infection control. However, only cement spacers may cause spacer fragmentation in our patient with a large femoral defect. Simultaneously, the cement spacer cannot be attached to the femur. Noia et al[19] reported that a hand-made cement spacer

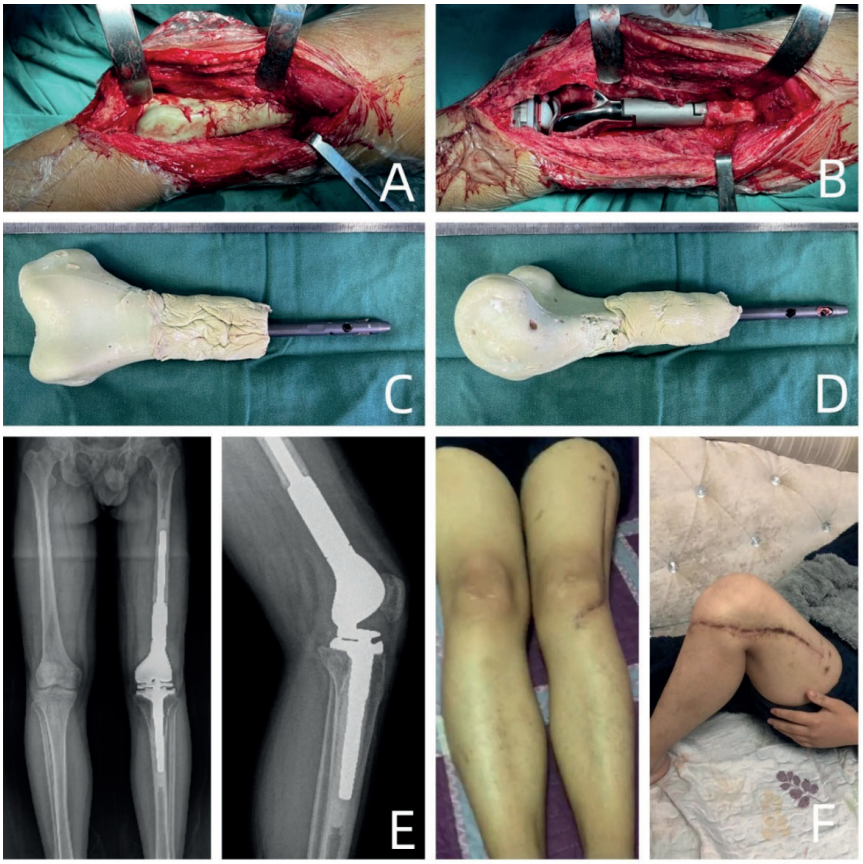

Figure 4. Intraoperative and post-operative process of the second surgery. **A**, Intraoperative cement spacer status. **B**, The replacement of metal mega-prosthesis. **C**, Front view of the removed cement spacer. **D**, Side view of the removed cement spacer. **E**, X-ray images six months after surgery. **F**, Knee joint range of motion six months after surgery.

was used to treat mega-prosthetic infection. The cement spacer was attached to the bone with cement strips, but this method lost the function of the knee joint. Imanishi et al[20] demonstrated that a custom-made ceramic spacer with an 8 mm smooth straight stem reconstructed the distal femoral resection of osteosarcoma. The ceramic spacer was distinguished by its anatomical fit to the anatomical distal femur, and its smooth surface is suitable for articulation. There were no anti-rotation screws between the intramedullary nail and the residual bone. They used PMMA to fix the spacer and prevented rotation of the bone-spacer junction. However, the stem and varus deformity loosening was observed 18 months after surgery.

Based on the above studies[18-20], there are significant flaws in the spacers for bone defects after distal femoral resection. Custom prostheses are now widely produced using 3D-printing technology[21]. We used 3D-printing technology to design a custom mold to produce cement spacers for patients during surgery. Simultaneously, an intramedullary nail was used to reinforce the mechanical strength of the cement spacer, and three anti-rotation screws were used to secure the cement spacer to the residual bone *via* the intramedullary nail. This personalized cement spacer precisely reconstructed the distal femoral resection of osteosarcoma. It also conformed to the anatomical shape of the distal femur and had a smooth surface suitable for articulation. It also overcame defects in rotation and spacer fragmentation. This spacer was firmly attached two years after surgery, and no complications such as infection, displacement, and fragmentation occurred. After the hemiarthroplasty with cemented spacer, the patient could walk with a single crutch to bear weight on the affected leg without support.

The infection rate in long-bone tumor resection with prosthetic reconstruction is higher when compared with rates of conventional replacements. The infection rate for lower-extremity limb salvage surgery with mega-prosthetic reconstruction was approximately 10%[22]. Two-stage revision remains a viable treatment option for patients with a prosthetic infection and resistant organism[23]. A periarticular infection with MRSA developed in our case, and a two-stage surgery was performed to prevent catastrophic complications from a periprosthetic infection. The

3D-printed spacer achieved good knee function and activities of daily living in the first stage of surgery, and the infection was effectively eradicated. However, to avoid wearing and breaking the spacer due to excessive weight-bearing activities, the patient used a single crutch for activities following the first stage of surgery, which still caused some inconvenience. A second-stage surgery was performed on the patient to replace the metal mega-prosthesis. The soft tissue was loosened during the operation, and the knee joint function and daily life activities returned to near normal afterward. The patient was able to walk normally without any assistance.

Conclusions

This case report describes limb-salvage surgery following distal femoral resection for periarticular infection. After the first stage of surgery, the personalized cement spacer prepared by a 3D-printed mold can effectively reconstruct soft tissue and bone defects and preserve joint function. This two-stage surgical procedure can be used in periarticular infection after long bone resection, mega-prosthetic infection, or limb-salvage surgery for temporary joints in small children.

Ethics Approval

This study was approved by the Affiliated Cancer Hospital of Zhengzhou University (research protocol identification number: 2022-200-001).

Informed Consent

Written consent was obtained from the patient's mother for the publication of this case report and accompanying photos and images.

Availability of Data and Materials

The data of the manuscript was presented in the paper.

Conflict of Interest

The authors declare that they have no competing interests.

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None.

Authors' Contributions

YWT and DXH made a decision to perform the series of surgeries. QGX collected the patient's clinical data, performed a literature review, and drafted the whole manuscript. ZCL assisted in data collection and literature review. QGX, DXH, and YWT were in charge of the treatment of this case. YWT and ZCL helped QGX with the revision of the manuscript. All authors read and approved the final manuscript.

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