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Novel reconstruction method by mega-prosthesis wrapped with vancomycin-containing cement after resection of malignancies

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Abstract

To introduce wrapping vancomycin-containing cement around a mega-prosthesis (MP) as a novel method to prevent prosthetic joint infection after reconstruction surgery for malignant bone and soft tissue tumors. Five patients with malignant bone and soft tissue tumors treated at our hospital from April 2009 to December 2019 were included. The average age was 71.4 years. Four males and one female were included. Three patients had a bone tumor, and two had a soft tissue tumor. Three right thighs and two left femurs were affected. These tumors were identified histologically as undifferentiated pleomorphic sarcoma, spindle cell sarcoma, diffuse large cell B-cell lymphoma, metastasis of renal cancer, and metastasis of lung cancer. All patients underwent tumor resection and reconstruction with a MP. In all cases, vancomycin-containing cement (2 g/40 g) was wrapped around the implant at the extension. The average follow-up period was 30.4 months. We surveyed whether infection occurred after surgical treatment. We also investigated the Musculoskeletal Tumor Society score and clinical outcome. We observed no postoperative infection. One case of local recurrence was observed, and a hip dissection was performed. The Musculoskeletal Tumor Society score was 79.26 ± 1.26 (mean ± standard deviation) (range: 76-80.3). Three patients remained disease-free, one survived but with disease, and one died of disease. Wrapping vancomycin-containing cement around the MP may be a useful method of preventing postoperative joint infections.

Abbreviations: KLMS ® = Kyocera Modular Limb Salvage, MP = mega-prosthesis, OSS ® = Orthopedic Salvage System, PJIs = periprosthetic joint infections.

Keywords: extension part, mega-prosthesis, prosthetic joint infection, sarcoma, vancomycin-containing cement

1. Introduction

The use of a mega-prosthesis (MP) is increasing as limb-sparing procedures become the norm in malignant bone and soft tissue tumor surgery.[1] MP is a widely accepted technique for joint reconstruction after the resection of bone and soft tissue tumors, but it has a relatively high complication rate.[2] Among the various complications, postoperative infection is the most frequent and difficult problem.[3] In fact, the incidence of periprosthetic joint infections (PJIs) has been reported as 0.25% to 2.0% for hip and knee joint revisions[4] and as 4% to 20% after tumor resection.[5–7]

PJI is also reported as a major cause of premature MP failure and revision.[8] The management of PJI after reconstruction by MP is very costly and difficult, requiring repeat surgery, prolonged antibiotic treatment, and hospitalization, with a high risk of limb amputation and increased mortality.[9,10] Although, over the years, several options have been proposed in an attempt to reduce the risk of PJI, including long-term prophylaxis with pre- and postoperative antibiotics and implant coating with silver or iodine, we have not yet completely eliminated the risk of PJI.[11,12]

The purpose of the current study was to introduce a new vancomycin-containing cementation technique in MP reconstruction alongside a literature review.

2. Methods

Five patients with malignant bone and soft tissue tumors treated at our hospital between April 2009 and December 2019 were included in the current study (Table 1). The average age was 71.4 (range: 66-75) years. Four males and one female were included. Three of the patients had bone tumors, and two had soft tissue tumors. Three right thighs and two left femurs were the affected tumor sites. Histological diagnoses included an

The authors declare that they have no conflict of interest.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

This study was conducted in accordance with the Declaration of Helsinki. Written consent is also obtained from the patients.

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undifferentiated pleomorphic sarcoma, a spindle cell sarcoma, a diffuse large cell B-cell lymphoma, a renal cancer metastasis, and a lung cancer metastasis. Regarding comorbidities, one patient had diabetes mellitus, one had adrenal insufficiency, one had a myocardial function, one had a uterine myoma, one had a past history of renal cancer, and one had a past history of lung cancer. All patients underwent tumor resection and reconstruction with an MP. The average operating time was 181 (range: 157-445) minutes. One operation used a Kyocera Modular Limb Salvage (KLMS ®) for reconstruction, while the other four used the Orthopedic Salvage System (OSS ®). Each MP was fixed by screws within bones. In all cases, vancomycin-containing cement (2 g/40 g) was wrapped around the implant at the extension after the MP was fixed (Fig. 1a and b). Endurance® cement was used in four cases, and Palacos® cement was used in one case. Postoperative x-ray images are shown in Figure 1c and d. The average follow-up period was 30.4 (range: 13-84) months. We surveyed whether infection

Table 1

The patient characteristics of the current study.

Age	Sex	Site	Histology	Ope-time (min.)	Bleeding (cc)	Follow-up period (months)	Implant	Cement	MSTS score
72	M	Right thigh	UPS	360	1779	84	KLMS	Endurance	80.3
72	M	Right femur	Renal Cancer	159	129	15	OSS	Endurance	80
72	M	Left femur	Lung Cancer	445	443	26	OSS	Endurance	80
66	M	Right thigh	Dedifferentiated liposarcoma	181	878	14	OSS	Endurance	76
75	F	Left femur	DLBCL	157	223	13	OSS	PARACOS	80

DLBCL = diffuse large B-cell lymphoma, F = female, KLMS = Kyocera Modular Limb Salvage, M = male, min = minutes, MSTS = Musculoskeletal Tumor Society, Ope = operation, OSS = Orthopedic Salvage System, UPS = undifferentiated pleomorphic sarcoma.

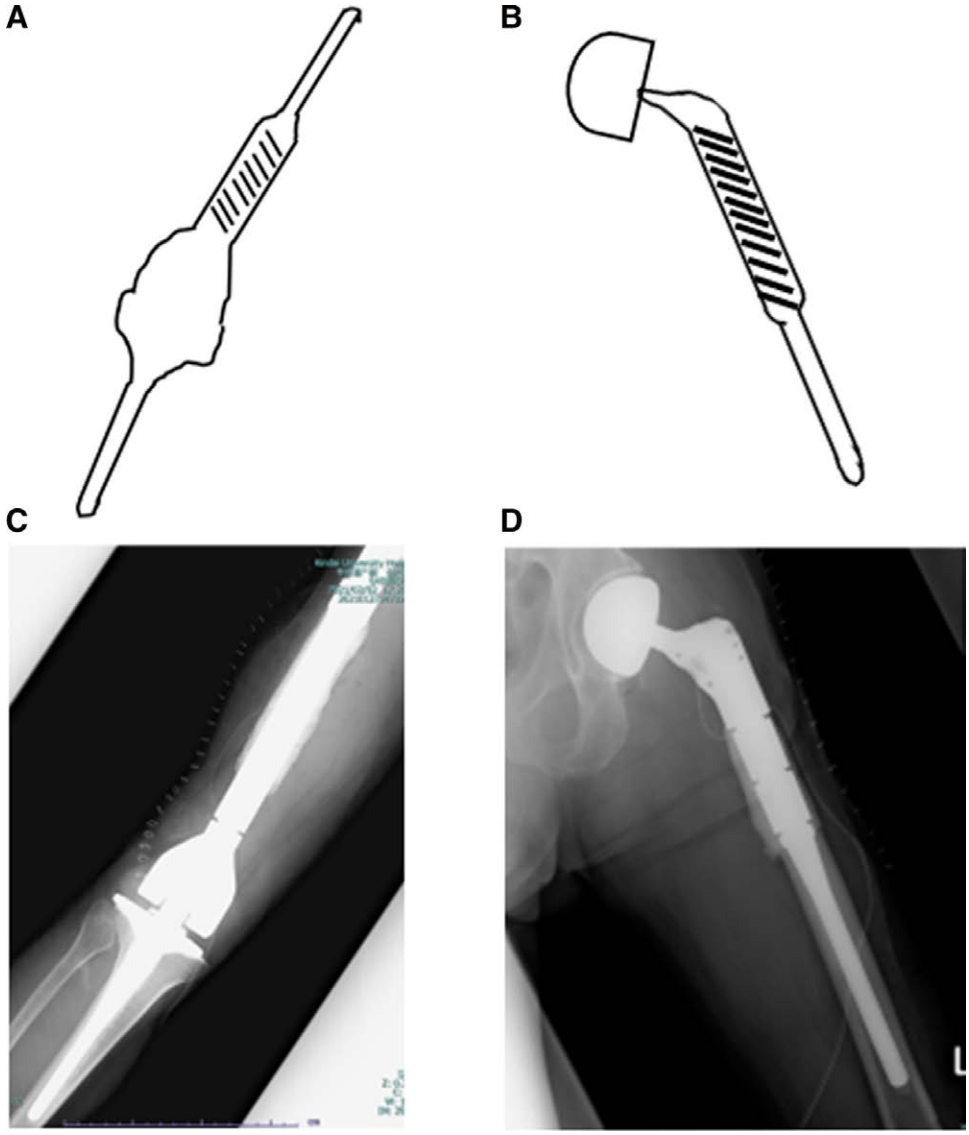

Figure 1. (a) Schematic diagram of the distal femoral type implant. (b) Schematic diagram of the proximal femoral implant. The oblique shaded area indicates the extensional area; vancomycin-containing cement was wrapped around the extensional area. (c) Postoperative X-ray image showing a distal femoral type implant. **d** Postoperative X-ray image showing a proximal femoral implant.

occurred after surgical treatment. We also investigated the Musculoskeletal Tumor Society score[13] and final clinical outcome.

3. Results

There were no cases of postoperative infection. One case of local recurrence was observed, and a hip dissection was performed as a result. The Musculoskeletal Tumor Society score was 79.26 ± 1.26 (mean ± standard deviation) (range: 76-80.3). Three patients remained disease-free, one survived but with disease, and one died of disease.

We present the case of one patient as follows. The patient was a 75-year-old woman who became aware of full left thigh pain 1 year ago. She was suspected of having a lumbar spine disorder and was treated with medication, but her condition did not improve. MRI showed a mass in the left proximal femur (Fig. 2a). Bone biopsy of the femoral lesion was performed from the lateral femur, and a diagnosis of diffuse large B-cell lymphoma was confirmed with pathological findings. Extensive resection and reconstruction with an MP were performed. The vancomycin-containing cement (2 g/40 g: vancomycin/cement) was wrapped around the extension of the stem (Fig. 2b). Two months after surgical treatment, the patient could walk with a cane, and there was no evidence of tumor recurrence or metastasis.

4. Discussion

One of the most serious and concerning complications of reconstruction with an MP after extensive resection of bone and soft tissue malignancies is PJI.[14] In the current study, we described the novel method of wrapping an implant with vancomycin cement to avoid PJI.

The outcome of MP reconstruction after resection of malignancy remains unsatisfactory.[15] Overall survival rates for knee prostheses were reported to be 91% at 2 years, 83% at 5 years, and 68% at 10 years.[15] PJI is the most common failure of MP reconstruction, with an incidence of 5% to 40%.[14,16,17] Relatively high infection rates have also been reported in sites such as the tibia, ranging from 14% to 36%.[17–20] Furthermore, the risk of secondary amputation due to PJI is high, ranging from 23.5% to 87%.[17] Thus, prevention and control of PJI are important in MP reconstruction, with the method described herein as a potential solution to prevent infection.

Risk factors for PJI after reconstructive surgery by MP include soft tissue tumor with bone invasion, using radiation therapy, a surgery time exceeding 8 hours, and a tumor site of the tibia.[17,21,22] In the current study, we did not observe the risk factors as previously described.[17,21,22] In the future, it will be necessary to confirm the presence or absence of infection using this method in cases with these risk factors.

Staphylococcus species were reported to be the most common organisms responsible for PJI, with *taphyloccous epidermidis* being the most common, followed by methycillin-resistant *Staphyloccous aureus*.[22] Moreover, it has been reported that multiple pathogens are isolated in about one-fourth of all cases.[16,23] The most common combination is reported to be coagulase-negative Staphylococcus and group D Streptococcus.[16,23] These findings suggest that a response focusing on Staphylococcus and its resistant strains is necessary.

Infection in prostheses is classified as either early (4 weeks to 2 years postoperatively) or late (2 years and up), with an average reported time to PJI of 1451 days (30-5825 days) for surgery with MP.[22] Furthermore, the incidence of late infection (6.3%) has been reported to be significantly higher than that of early infection (0.9%-1.4%).[23] Therefore, when reconstructive surgery with MP is performed, it is considered necessary to pay attention mainly to late infection.

Bone cement is widely used in implant fixation in arthroplasty and in vertebral body fixation surgery.[24] Generally, antimicrobial agents are mixed into the bone cement base in advance to prevent infection.[25] An in vitro study found that the vancomycin-containing cement showed a steady increase in elution until day 8, after which elution was observed until day 60.[26] The study also reported that more than vancomycin 0.25 g/40 g was effective in eliminating methicillin-resistant *S. aureus*.[26] Moreover, vancomycin 0.5 g/40 g or more is reportedly effective in eliminating *S. aureus* as a whole 26. Therefore, the current method involving of vancomycin 2 g/40 g will be effectively in preventing infections within 60 days, including infections caused by Staphylococcus species.

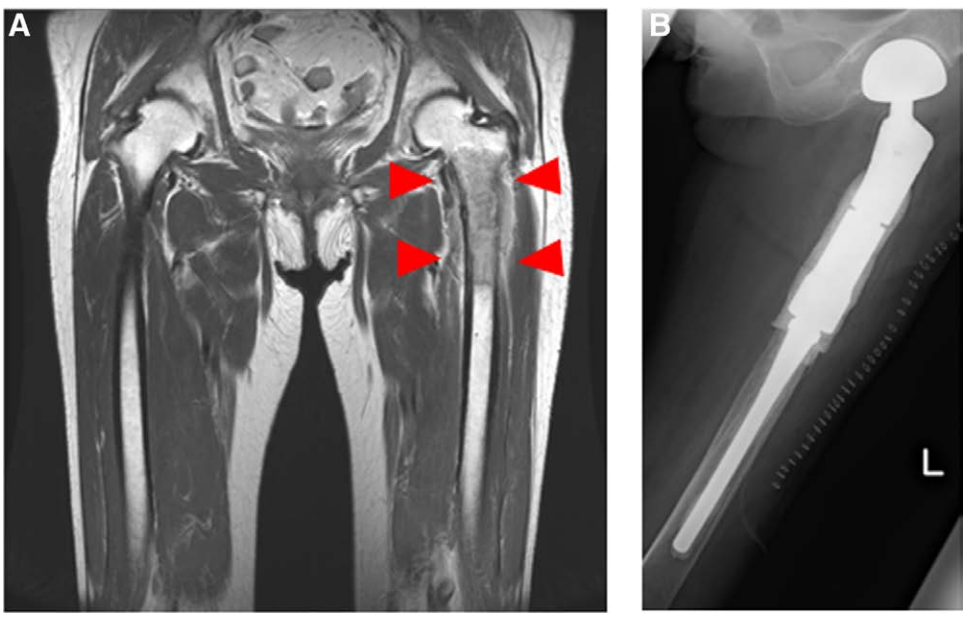

Figure 2. (a) MRI image of a patient's left-sided tumor. The red arrow heads show the tumor. (b) X-ray image after MP reconstruction. The cement line is observed around the implant.

In general, Palacos® bone cement is high viscosity bone cement that has high contrast with the surrounding tissue, making it highly visible. It is also easy to handle intraoperatively.[27] Palacos® bone cement with added antimicrobials has been reported to have the lowest rate of total hip arthroplasty revision due to infection.[28] The Palacos® spacer showed higher elution levels than the Simplex® spacer in total knee arthroplasty and exceeded the minimum inhibitory concentration of the bacteria when used for an extended period of time.[29] Furthermore, in vitro studies have reported that Palacos® bone cement eluted more antimicrobials than CMW1.[30] Therefore, Palacos® cement may be relatively effective in preventing infection.

One previous in vitro study showed that too much antimicrobial addition significantly reduces the mechanical properties of cement.[31] However, the compressive strength, flexural strength, and flexural modulus reportedly remained above the ISO minimum specifications even with the addition of 1 or 2 g of vancomycin per 40 g of cement.[25]

Because the rate of antimicrobial contamination in the current study was 2 g/40 g, strength was not a problem.

In general, management of the dead space is important to prevent infection.[32]

Additionally, the rectus abdominis skin valve was reportedly effective in the dead pelvic cavity because of blood flow.[33] Although there is no blood flow in this method, the dead space around the extension can be reduced by wrapping the implant with cement.

This study has some limitations. First, it included a small cohort, short follow-up, and retrospective study design and did not compare the results with those of infected cases. Second, the method in this study may only be effective for relatively early infections of 60 days rather than the entire duration of vancomycin leakage. However, the current methods may prevent long-term infection by reducing dead spaces. Third, recent studies are controversial on whether antimicrobial-containing cement is effective in preventing PJI.[34,35] However, this method may prevent PJI long-term by reducing dead space. Despite these limitations, this method could be useful as an infection control measure. Therefore, we believe that further studies with a larger sample size are needed.

In conclusion, we described five cases of vancomycin-containing cement implantation in MP reconstruction. The use of this method may lead to a reduction in the PJI rate with the MP reconstruction method.

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Author contributions

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