PERIPROSTHETIC JOINT INFECTION AFTER WIDE RESECTION BONE TUMOR AND ENDOPROSTHETIC RECONSTRUCTION IN A PATIENT WITH OSTEOSARCOMA: A CASE REPORT

Puwadon Veerapan, Sittichoke Watcharamasbonkkot

Department of Orthopedics, Phramongkutklao Hospital, Bangkok, Thailand.

Abstract

Bone and connective tissue cancer treatment has been improved to achieve a significant survival rate. Limb salvage surgery, an efficient surgical technique, has been established to preserve limbs. Endoprosthesis reconstruction constitutes an essential part of the treatment method, and the attending medical team requires knowledge to reduce the side effects of this operation. The consequential infection is a common complication, often leading to worse use of the limbs when finishing the treatment. This report describes a patient presenting an infection in a prosthesis after endoprosthesis reconstruction using a limb salvage surgery technique. Due to the comprehensive resection surgery, the typical structure has been significantly damaged, which could lead to a high risk of neurovascular structure damage during adequate debridement and lead to the need for amputation. Thus, the decision to treat an infection resulted in patients undergoing multiple surgeries and reducing their functional outcomes until crucial. These patients should be carefully monitored to prevent infection and obtain a good quality of life in the long term.

Keywords: Endoprosthesis reconstruction, Periprosthetic joint infection

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Correspondence to:
Watcharamasbonkkot S, Orthopedics Department, Phramongkutklao Hospital, 315 Rajvithi Road, Ratchathewi, Bangkok, Thailand 10400
Email: birdsw@hotmail.com

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Introduction

Bone sarcoma is a common cancer that can affect people at any age. Approximately 50% of bone cancer is diagnosed among people under the age of 35 years and is more often found on the limbs than in other regions, with about one half coming across the bones around the knee.[1, 2] The treatment among patients with bone sarcoma affects movement, walking, routine activity in daily life and quality of life in the long term. In the past, treating bone sarcoma has shown a progressive improvement achieving better survival rates. The decrease in amputation treatment can increase limb salvage surgery. However, the survival rate and postoperative disease-free status showed no difference.[3] As limb salvage surgery requires knowledge of reconstructive surgery, a method has to be provided to affect patients' quality of life positively.[4] One such method is endoprosthesis reconstruction allowing the patient to return to everyday life as quickly as possible. On the other hand, side effects can occur using this surgical method. Endoprosthesis reconstruction treatment, including infections, can occur at the rate of up to 8.5% in distal femoral replacement and 16.8% in proximal tibial replacement.[5] This study reports the infection problem in a patient with endoprosthesis reconstruction. It comprises an essential issue, though found infrequently, because it directly affects patients' treated outcomes and quality of life. The infection issue can be solved in many ways including increasing the duration of patient administration of antibiotics while in the hospital, needing repeated surgery, and may result in the patient undergoing an amputation.[6]

Case report

The patient was a 31-year-old single woman. Before visiting the hospital, she recognized a mass in the right knee, and a slow-moving lump was felt in the right knee two months earlier. She was slightly uncomfortable and did not fully move, especially in flexion. She denied havingother symptoms, including nocturnal discomfort, anorexia, weight loss and any history of underlying sickness, no history of drug use, alcohol consumption or smoking. A history of ibuprofen and diclofenac allergies were known occurrences.

The physical examination revealed a 7-cm diameter mass that was palpable at the small area of the left knee. The mass was hard in substance, fixed to the bone, did not hurt, presented a rough surface, was poorly circumscribed and showed no pulsatile activity. No wounds or unusual skin lesions were present. The left knee's range of motion was 0 degrees at full extension and 110 degrees at full flexion. The popliteal, posterior tibial, and dorsalis pedis were pulsatile at a regular rate and rhythm. At the left groin and left lower extremity, the lymph node was not palpable.

Plain X-ray AP and lateral views of the left knee showed the lesion at the metaphysics-diaphyseal junction region of the distal left femur; it involved a mixed osteoblastic and osteolytic lesion with an uneven moth-eaten kind of boundary, as shown in **Figure 1.** Soft tissue development and periosteal sunburst reaction were observed. The osteoid matrix type was identified, and no significant pathologic fracture was observed.

Using Magnetic Resonance Imaging (MRI), the plain X-ray revealed a bone lesion and parosteal osteosarcoma was suspected. The other investigation showed no sign of visceral organs or bonny metastases, and the core needle biopsy showed a low-grade spindle cell tumor detected by core needle biopsy. Murine double minute 2 (MDM2) strain was positive, supporting the diagnosis of parosteal osteosarcoma.

A wide excision was performed on the left femur by removing the suspected cancerous area and adjacent normal or healthy tissue margins to remove all cancer and repair using an endoprosthesis. According to the histopathology investigation, the largest dimension of the dedifferentiated posterior osteosarcoma with posterior boundary at the medial and posterior border was 9 cm. After surgery, the patient underwent four cycles of chemotherapy with cisplatin, doxorubicin and 70 grays of external radiation therapy. The patient responded well to treatment, with no recurrence or metastasis detected in other organs. Furthermore, the patient expressed satisfaction with the functioning of the right knee.

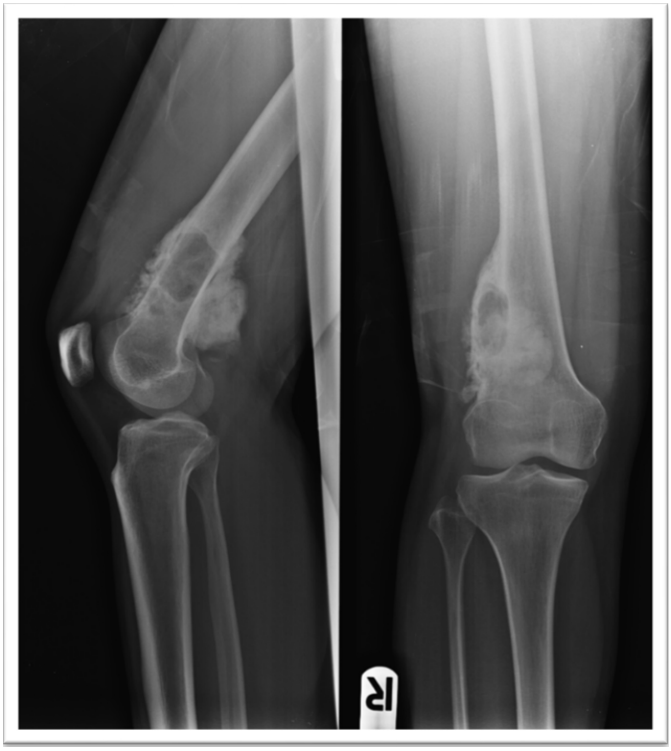

Figure 1. Mixed osteoblastic and osteolytic lesions with an irregular moth-eaten border at the metaphysic-diaphyseal junction area of the distal of the left femur are shown. Sunburst periosteal reaction and soft tissue production are observed. The matrix comprised osteoid type identified from plain X-ray.

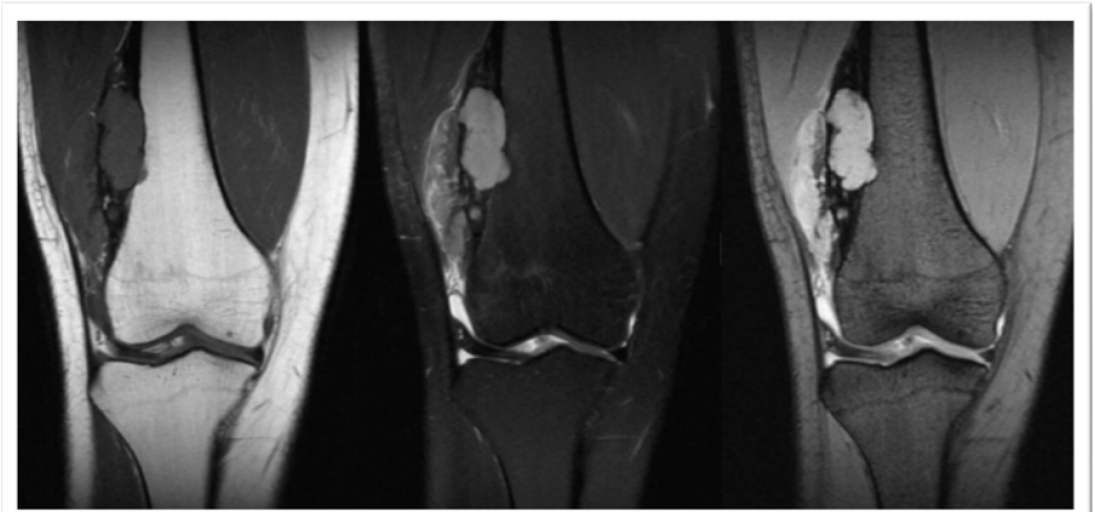

Figure 2. MRI shows suspected parosteal osteosarcoma, irregular mass on the postero-lateral cortex of the right distal femur and invasion of the medullary-trabecular component with hypointense on T1 and hyperintense signal on T2 intensity with peripheral soft tissue edema.

On 14-12-2019, the patient was involved in a car accident two years later. The left knee was crushed, resulting in an abrasion wound over the prosthesis area. The patient reported warm, red, swollen and painful symptoms. The knee examination showed a positive ballottement sign representing increased intra-articular fluid. During the arthrocentesis, 180 mL of pus was found. Subsequently, an arthrotomy was conducted to debride the left knee and perform polyethylene exchange.[6] Tissue samples were sent for laboratory examination. The hemoculture bottle used for tissue culture demonstrated a positive result for *Escherichia* coli but was negative

for *Staphylococcus coagulase.* The histologic investigation did not reveal any evidence of recurring malignancy.

In cases where the pathogen cannot be identified, antibiotics are prescribed based on suspected infecting organisms to ensure broad coverage against potential pathogens. Identification of the specific pathogen may be hindered by various reasons, such as the techniques used for specimen collection. Nonetheless, every effort was made to maximize the accuracy of pathogen identification.[6] This patient received the following antibiotics medications: 2 gm of ceftriaxone intravenous once daily: 14 to 23 December 2019, 500 mg of metronidazole intravenous every 8 hours: 14 to 23 December 2019, 2.2 gm of augmentin intravenous every 12 hours: 24 December 2019 to 4 January 2020, 400 mg of ciprofloxacin intravenous every 8 hours: 4 to 0 January 2020 and 500 mg of ciprofloxacin per oral twice daily: 30 days after that infection subsided. The evaluation of infection subsiding was determined by improvements in patient symptoms and laboratory test results indicating a decrease in inflammation including reduced white blood cell count, particularly neutrophils and decreased inflammatory markers such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP).

On 08-08-2020, eight months later, the patient complained that her knee had returned to warm, red, swollen and painful. The periprosthetic infection was identified by laboratory examination. The blood test revealed a white blood cell count of 18,000 cells/mL, with 82% polymorphonuclear leukocytes (PMN). The ESR was 114 mm/hr, and the CRP level was 98 mg/dL. Additionally, synovial fluid analysis showed a white blood cell count of 90,000 cells/mL, with 98% PMN. No organisms were detected in the joint fluid. The patient initially received conservative treatment with 400 mg of ciprofloxacin intravenously every 8 hours from 8 August 2020 to 5 December 2020. However, due to the clinical evaluation and laboratory test results indicating the persistence of infection, the patient required extended intravenous antibiotic therapy. Therefore, she was prescribed 200 mg of rifampicin twice daily for 90 days and 500 mg of ciprofloxacin orally twice daily for 140 days.

On 21-06-2021, ten months later, the first-stage revision of the endoprosthesis was carried out, involving the complete removal of the prosthesis device and its replacement with an antimicrobial cement spacer. A standard surgical intervention for the first-stage revision was recommended to treat periprosthetic infection, even without prosthetic loosening. This was accomplished

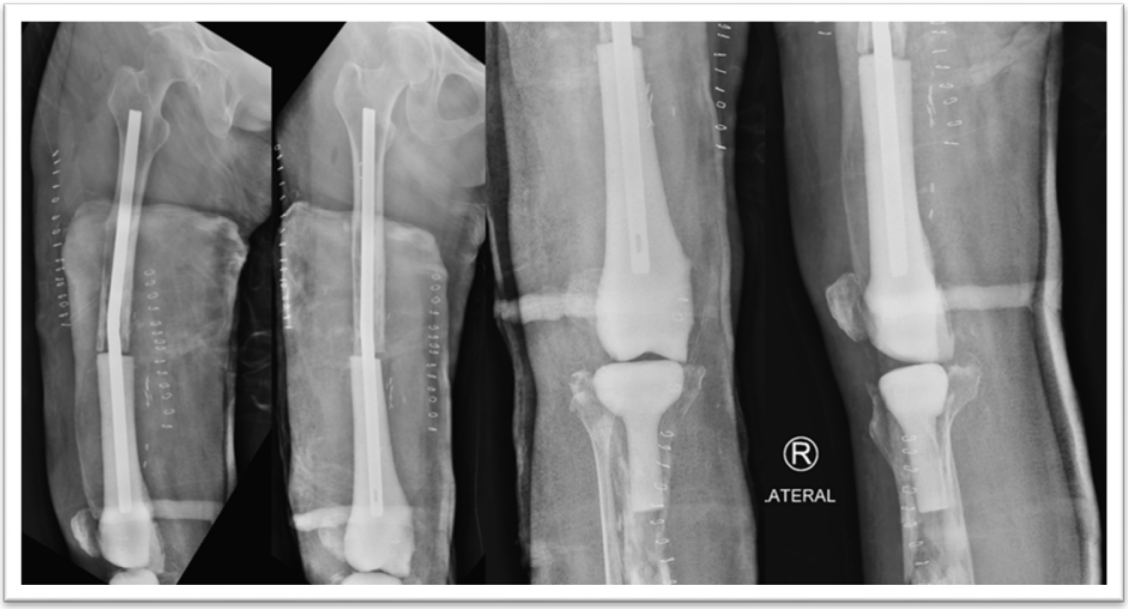

Figure 3. After 1ST stage revision endoprosthesis, radiography was performed by removing the prosthesis and replacing it with an antibiotic cement spacer.

to eliminate any potential source of infection originating from the prosthesis itself. [6] For this procedure, Palacos® cement, containing 0.8 gm of gentamicin and 0.5 gm of gentamycin sulfate, was mixed with 2 gm of vancomycin powder. The surgical technique employed an intramedullary Kuntscher nail to secure the cement spacer to the remaining femur. Due to limited space on the tibia side, additional fixation was not required because surrounding soft tissue solely supported the cement spacer. The patient received 400 mg of ciprofloxacin intravenously every 8 hours from 21 June 2021 to 28 July 2021.

On 25-06-2022, one year later, the infection subsided. The second stage revision endoprosthesis was performed with wound coverage from the medial gastrocnemius muscle flap and split-thickness skin graft. The tissue analysis revealed that the tissue removed from the tibial portion of the bone tested positive for high grade conventional osteosarcoma but negative for bacterial culture. Afterward, the patient received 500 mg of ciprofloxacin twice daily for one month. After the surgery, the patient was ready to receive adjuvant chemotherapy.

On 16-10-2022, four months later, the patient presented at the Emergency Department with signs of a right knee infection and a skin tract on the front of the right leg. The treatment was designed to remove the prosthesis and perform debridement. The intra-operative testing revealed 200 mL of pus around the prosthetic mechanical tube. Pus and tissue were sent to the laboratory for examination, and a cement spacer was applied as a temporary replacement.

After the patient underwent surgery, she received 400 mg of ciprofloxacin intravenously every 8 hours from 16 October to 16 November 2022. She also received 200 mg of rifampicin twice daily and 500 mg of ciprofloxacin orally twice daily for 140 days following that. According to the pus culture, Staphylococcus coagulase was identified that was sensitive to this antibiotic. Various symptoms and laboratory indicators showed an improvement in the infection. The surgical wound was closed tightly without pus, only occasional serum oozing discharge. The patient was evaluated to ensure that the infection was resolved entirely before proceeding with the second-stage surgery.

Discussion

The complications of endoprosthesis reconstruction can occur in several forms, but every study reported that infection was a devastating complication leading to repeat surgery among patients treated with this procedure. Berger et al. [7] found that the primary cause that resulted in repeated surgery among patients with

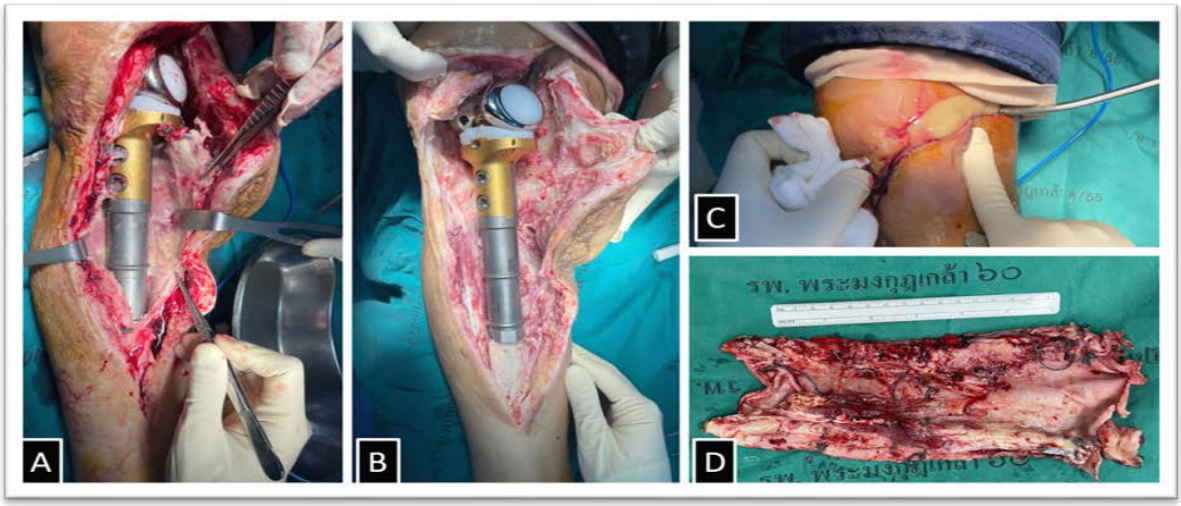

Figure 4. Signs of infection from intra-operative A&B: pus was observed around the prosthesis at the proximal tibia, and a sinus tract leading to the distal femur was also identified. C: pus drainage from the thigh wound. D: the surgical prosthetic tube was removed.

endoprosthesis reconstruction was infection (22%) and soft tissue failure (13%). In contrast, the causes of aseptic release, mechanical failure and tumor recurrence were fewer than the above reasons. The conclusion of this study reported that 17% of patients presenting the complication were no longer able to use the replacement endoprosthesis. Moreover, the study by Zan and colleagues showed that 30% of patients receiving endoprosthesis reconstruction for deep infection experienced recurrence infections that may have required re-surgery or led to amputation. Zajonz et al.[9] also found similar data that these events occurred in 37% of cases. This finding was consistent with Zajonz et al. reporting the data on 37% of such events.[9]

Several studies provided similar information about the pathogens. In 1984, Klenerman[10] determined that 75% of those patients were infected with gram-positive bacteria consisting of Staphylococci (40-45%) and gram-positive anaerobes or micro-aerophilic organisms (30-35%). Gram-negative anaerobes bacteria were rarely found. Only Escherichia coli or Pseudomonas sp. were found, similar to the study of Zajonz et al.[9] in 2016, even though the reports are 32 years apart.

The validity of the diagnostic criteria is crucial because the treated outcomes will directly affect the quality of life of such patients. Tsukayama et al.[11] classified the characteristics of pathogen infection after endoprosthesis reconstruction and applied them to patients experiencing joint replacement after surgically removing the bone sarcoma. The Tsukayama classification divided pathogen infection in four categories as follows, type I; positive culture of intra-operative samples with no previous indication of infection, type II; early infection: onset of symptoms within one month, type III; chronic infection: symptoms after one month and type IV; acute hematogenous infection.

This case was classified as a type 4 pathogen infection because the infection was detected two years after surgery. The initial symptoms when the patient met a doctor indicated an infection in a joint replacement after surgery. After aspirating from the knee joint, 180 mL of pus was found. Then this patient received antibiotic treatment, NS the required surgical pus drainage, joint lavage and excision of dead tissue (arthrotomy and debridement). From the Tsukayama and college recommended guidelines[13], the surgical treatment for joint lavage in acute hematogenous infection should remove the polyethylene inserts. However, polyethylene removal among patients with an endoprosthesis may be delayed because it requires special equipment. Therefore, the medical team consulted with the patient and agreed concurrently that all parts of the endoprosthesis must be retained in the first round of surgery, then treated with antibiotics to inactivate any infection. After the surgery, the medical team administered the treatment providing six weeks of intravenous and oral antibiotics for four weeks until the infection subsided. Although the patient exhibited symptoms suggesting a re-infection of the prosthesis ten months later, the synovial fluid test did not detect any infection. The patient received additional intravenous and oral antibiotics and cotreatment with rifampicin[12, 13], expecting to reduce Staphylococcal biofilm. In this case, the patient's symptoms indicated severe inflammation and purulence in the joint, but the exact pathogen could not be identified. Therefore, administering broad-spectrum antibiotics became necessary to cover all possible infectious agents and limit the spread of infection. In the absence of definitive pathogen identification, the physician relied on the assumption that Staphylococcus species were likely, despite the potential for errors in the identification process.

The medical team consulted about the patient's treatment plan and agreed concurrently to suggest the patient continue using that prosthesis joint with avoiding the revision arthroplasty because the repeated surgery and prolonged length of stay would seriously affect the quality of life of working-age patients. The period after infection and treatment in this patient was about one year. The physical examination and laboratory tests revealed a recurrent infection in the prosthesis; accordingly, the medical team and patient concurred that surgery should be performed to replace the

prosthesis. The surgery was divided in two stages (two-stage procedures). The first stage involved joint lavage surgery, dead tissue excision and implant removal. Once the debridement had been completed, the cement with antibiotic beads was inserted into the joint cavity to ensure the complete clearance of infection before going to the second stage. During the first stage, the patient was monitored closely for infection, such as symptoms, the culture from periprosthetic tissue, blood samples and other laboratory tests. The pus culture was performed using hemoculture bottles, which might have been unsuitable as the thickness of the pus could impede proper mixing with the culture medium, limiting the growth of infectious agents. However, pus obtained from knee aspiration is often more fluid due to its mixture with synovial fluid. This is similar to using hemoculture bottles for culturing bacteria from ascites fluid[14], pleural fluid[15] or joint fluid.[15] Hemoculture bottles for ascites fluid or joint fluid yielded a better identification rate of causative agents than the standard culture bottle. Similar results were obtained in a study to detect bacteria in pleural fluid in the UK, where the hemoculture bottle method increased the pathogen identification rate by 20.8% compared with sterile culture bottles. [15]

The medical record showed that the medical team followed the patient for one year until ensuring the first stage procedure results before proceeding to the second stage. However, one problem was found in the second stage, namely, soft tissue coverage. The medical team conducted the surgery using the medial gastrocnemius muscle and split-thickness skin grafts.

The treatment of patients with prosthetic infections remains a delicate and difficult decision. While various recommendations exist to shape a diagnosis and make treatment guidelines, many factors remain that the medical team must discuss with patients. The standard treatment guidelines may be inappropriate for the patient's living context at those times. Therefore, when the treatment method must be adjusted to accommodate the needs of patients, it may have to accept that the following side effects could occur. As the example from this patient, the subject developed recurrent infection four months after the second stage procedure. The results of the physical and laboratory examination confirmed the prosthesis infection. Consequently, the patient had repeated surgery to remove the prosthesis, lavage the joint, excise dead tissue and insert the cement with antibiotic beads into the joint cavity a second time.

This report aims to highlight the limitations of the treatment among patients with an infected prosthesis, especially ones undergoing arthroplasty after the bone sarcoma has been removed. In this case, the difference from the typical prosthetic patients involved more than cutting and destroying the surrounding tissues. Because of the oncological outcome, the remaining minimal natural tissue became easily infected, and once the infection had occurred, it could be more sensitive to re-infection. Zajonz and colleagues [9] reported that although treatment was performed according to the recommendations of the Tsukayama classification[11] applied to this group of patients, the limitation of salvage procedures induced the incidence of re-infection as high as 36 to 43%. In addition, the treatment may often significantly affect patients' functional outcomes, even though some patients may require amputation. This study also emphasized that when it became necessary to repeat surgery for prosthesis after an infection, carefully considering both the medical team and the patient was essential. Subjects in the group of multi-morbid patients with previous joint infections Especially need to be highly and carefully monitored.

Conclusion

The infection of the acquired prosthetic joint following bone sarcoma removal surgery remains a common complication and constitutes the primary cause of revision surgery in this patient group. Specific classifications and treatment recommendations for this infection have yet to be established; only guidelines were applied from the treatment recommendations for common knee joint infection. However, context differences and treatment limitations

between the common knee joint infection and acquired prosthetic joint contribute to the high probability of re-infection. In addition, the tissue damage from the surgical procedure of sarcoma removal also leads to repeated surgeries and eventually affects the efficacy of functional outcomes of patients. This present report would like to highlight the limitations of treatment decisions for this group of patients and the complications following that treatment. Thus, caregivers should be careful and decisive in treating this condition from the beginning of infection prevention, which may prove the best way to improve the patient's quality of life.

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