CASE REPORT

Contribution of Sonication to the Identification of Megaprosthesis Infection in Culture Negative Oncologic Patient

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Abstract

Conventional central osteosarcoma mainly affects the metaphysis of long bones in young people. The use of megaprostheses in oncological patients has increased in recent years. However, this type of surgery is not exempt from complications, with infections being the most common. In recent years, the presence of biofilm-forming bacteria has increased. Biofilm characteristics allow bacteria to resist hostile environmental conditions. The application of long wave ultrasound (process known as sonication) on the rescued inert material before culture interrupts the biofilm and generates a significantly higher recovery of bacterial growth compared to conventional tissue culture. We present the case of a 12-year-old patient with osteosarcoma of the femur, who, after surgery, developed a prosthetic infection detected by sonication, with negative soft tissue culture.

Level of evidence: IV

Keywords: Megaprostheses, Osteosarcoma, Prosthetic infection, Sonication

Introduction

Conventional central osteosarcoma is the most common primary malignant bone tumor in children, adolescents, and young adults,[1] arising mainly in the metaphysis of the long bones and gradually invading the epiphysis and diaphysis and eventually the entire joint space.[2] The most frequently affected sites are the distal femur and the proximal tibia. With increasing survival rates after chemotherapy, limb-sparing surgeries are now the standard of care for most of these osteosarcomas.[3,4] Due to the great bone loss after tumor resection, especially in those areas near a joint, prosthetic reconstruction is required in most patients. This concept is mainly applied in those skeletally immature patients, with the aim of preserving joint function as much as possible.[5] The use of modular megaprostheses in cancer patients has gradually increased.[6] Since its inception in the 80s, they have been used for the reconstruction of bone defects after tumor resection thanks to their immediate fixation and ability to allow weight bearing.[7] On the other hand, this type of implant is not without complications; one of the most frequent is infection, present in 3% to 30% of cases.[9,10]

To apply the right antimicrobial treatment, pathogen identification is essential. Most common techniques rely on the recovery of samples from periprosthetic tissue followed by inoculation in culture media.[10] However, this technique may be interfered with by certain factors that decrease its sensitivity, such as the negligent use of previous antibiotics, sampling errors, inadequate amounts of bacteria or inaccurate transport.[11] Another reason for the failure of microbial culture is the presence of bacteria organized in biofilms. This concept refers to certain complex communities of microorganisms that can be found attached to a surface. Biofilm characteristics allow bacteria to resist hostile environmental conditions. For these reasons, they are considered a major cause of persistent nosocomial infections in immunocompromised patients; and can prevent microbiological diagnosis and eradication of the microorganism due to poor response to antibiotic treatment.[12, 13] The presence of this biofilm on implant surfaces is responsible for the preservation of implant-related infections, since it has the ability to alter the activation of the phagocytic and complement immune system.[14, 15]

In this sense, the application of long wave ultrasound (process known as sonication) on the rescued inert material (implant, plastic, prosthesis) before culture interrupts the

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biofilm and generates a significantly higher recovery of bacterial growth compared to conventional tissue culture.[16] We present the case of an oncological patient with postoperative pain, with subsequent biopsy without microbiological recovery, and later positive culture after sonication of the extracted material, confirming periprosthetic infection.

Case Presentation

We present the case of a 12-year-old female patient with a clinical history of grade I obesity (BMI: 32). She consulted our service in July 2020 due to atraumatic right gonalgia of 10 days of evolution, which gradually increased in intensity, with gait intolerance at the time of consultation. He presented with an increase in the diameter of the right thigh at distal level with knee flexion up to 50° limited by pain. X-rays of the right knee were requested showing a heterogeneous radiopaque image involving the lateral cortex of the diaphysis, metaphysis, physis and epiphysis of the right femur, with soft tissue involvement in the medial, lateral, anterior and posterior region of the distal third and partially in the middle third of the right femur [Figure 1 A-B]. With a strong suspicion of a diagnosis of osteosarcoma, in the first instance, metastatic lesions were ruled out.

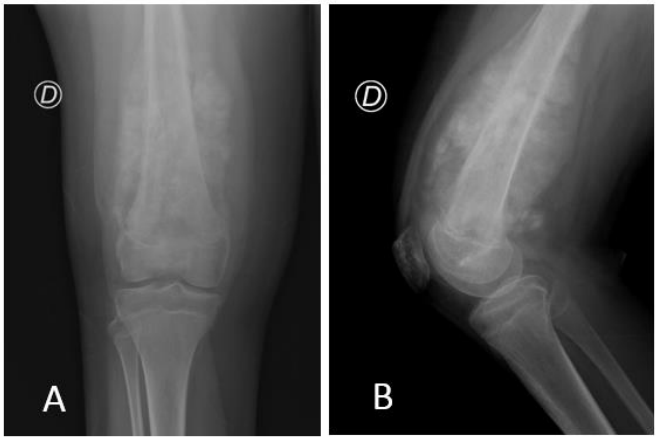

Figure 1. X-rays of the right knee showing a heterogeneous radiopaque image involving the lateral cortex of the diaphysis, metaphysis, physis and epiphysis of the right femur, with soft tissue involvement in the medial, lateral, anterior and posterior region of the distal third and partially in the middle third of the right femur

A nuclear magnetic resonance of the right thigh and knee was requested, which reported a bone lesion of pathological aspect. It presented a heterogeneous signal, with endomedullary involvement, significant periosteal reaction and associated soft tissue component [Figure 2].

A bone puncture was performed under CT and the histopathological substrate confirmed the diagnosis of conventional central osteosarcoma.

Fifteen days after the diagnosis of osteosarcoma, the patient receives the first infusion of doxorubicin - cisplatin as neoadjuvant therapy. Two days later, she intercurred with coronavirus infection in August 2020. The patient did not receive neoadjuvant therapy for 25 days because at that time, the interaction of the coronavirus with chemotherapy drugs was unknown. After that period, she received the second dose of chemotherapy infusion; however, 10 days later, she had another coronavirus infection. In view of this situation, after an interdisciplinary meeting, it was decided to perform oncologic resection surgery with free margins and reconstruction with megaprosthesis in October 2020 [Figure 3 A-B].

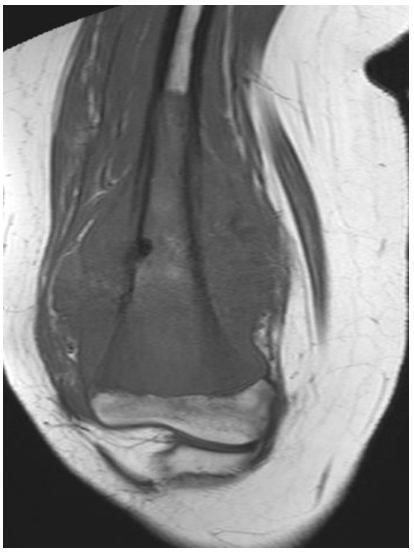

Figure 2. MNR (STIR) of the right thigh and knee which reported a bone lesion of pathological aspect. It presented a heterogeneous signal, with endomedullary involvement, significant periosteal reaction and associated soft tissue component

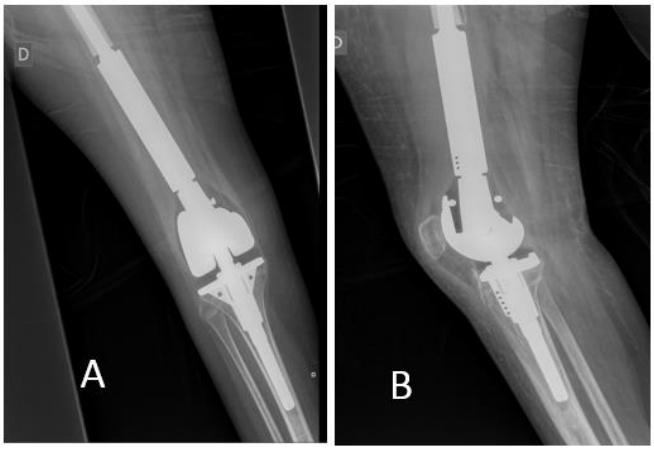

Figure 3. X-ray of right knee after oncologic resection surgery and reconstruction with megaprosthesis

After surgery, and during adjuvant therapy, the patient had numerous hospital admissions due to fever, mucositis and adverse effects of medication, in addition to two coronavirus infections.

Eight months after surgery, she referred us to right gonalgia secondary to physical exertion that gradually increased in intensity. On physical examination he presented with non-

deficient palpatory pain, with no clinical signs of infection. A laboratory was requested for infection parameters with white blood cell count of 3900 mm3, C-reactive protein of 0.6 mg/dL and erythrocyte sedimentation rate of 7 mm/h. Pain was continuously increasing, with no improvement with NSAIDs or opioids. Control X-rays were requested, showing alteration in the structure compatible with signs of acute periostitis around the femoral prosthetic component [Figure 4]. Due to persistent pain, a bone and soft tissue biopsy was performed, without microbiological recovery. In view of this picture of increased pain and radiological signs with the presence of periostitis, the prosthesis was converted to a right knee spacer due to suspicion of chronic prosthetic infection [Figure 5 A-B]. In this surgery, culture samples were sent to the microbiology service and the prosthetic plastic component was sent for culture by sonication. The patient underwent intravenous antibiotic treatment initially with clindamycin / ceftazidime for a week and then started oral antibiotic therapy. Twelve days after the intervention, the soft tissue cultures sent were still negative, but the material sent by sonication obtained positive culture results for Staphylococcus epidermidis and Corynebacterium aurimucosum. The patient underwent prophylactic antibiotic treatment for 4 months and after this period the spacer was converted to a right knee megaprosthesis [Figure 6 A-D]. Currently, the patient has been 18 months since the last intervention. She is walking without the use of assistance, with infectious laboratory parameters within normal values, without reporting any pain.

Figure 4. X-ray showing alteration in the structure compatible with signs of acute periostitis around the femoral prosthetic component (red circle)

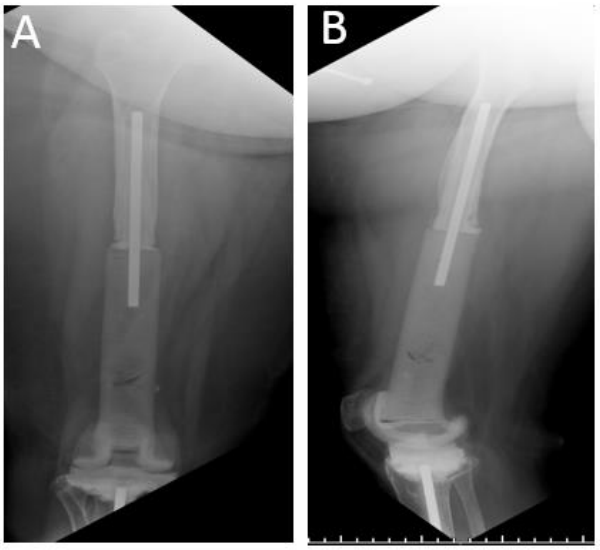

Figure 5. X-ray of right knee spacer

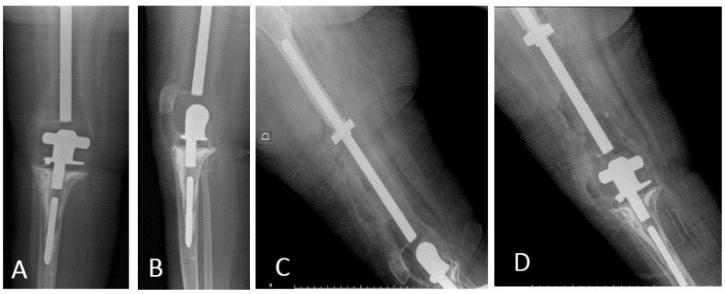

Figure 6. X-ray of right knee megaprosthesis

Discussion

Periprosthetic infections are one of the most frequent complications after joint replacement, especially in modular megaprostheses; with rates from 3% to more than 30%.[17] considering this, the detection of the infectious microorganism is absolutely necessary to choose the appropriate antibiotics and improve the pathogen elimination route.

Currently, the usual conventional method of diagnosis is the culture of tissue and periprosthetic fluid.[18] However, the presence of biofilms, prior antibiotic exposure and the effect of previous surgery may render standard cultures falsely negative.[18] The use of gentle ultra-sonication to disrupt adherent microbes thanks to biofilms formed was first used on peritoneal catheters[19] and ureteral stents.[20] Tunney et al.[21] were the first to use this method in prosthetic implants as a complementary method in the diagnosis of infection. In the study carried out by Trampuz et al.[22] on a total of 79 patients diagnosed with periprosthetic infection, 62 cases (78.48%) had positive cultures by the traditional method and by sonication; while the remaining 17 cases (21.52%) only had positive cultures by sonication method. In another

article published by Ribeiro et al., [23] out of a total number of 148 prostheses analyzed from patients with suspected prosthetic infection, 67% had positive culture results by sonication method, while only 39% did so by traditional culture methods. In our case, cultures by traditional method were negative, while the prosthetic component analyzed by sonication was positive for Staphylococcus epidermidis and Corynebacterium aurimucosum. Purchner et al.[24] evaluated whether sonication culture improved the microbiological diagnosis of periprosthetic megaprosthetic infections compared to conventional tissue culture. Out of a total of 31 megaprostheses analyzed by both methods, in 25 (80.64%) pathogens were detected by sonication and 12 (38.70%) were detected by tissue culture. Staphylococcus epidermidis was the most frequently detected microorganism in both groups (n: 11 in the sonication group and n: 5 in the tissue group). On the other hand, there are few published studies on Corynebacterium and periprosthetic infections, most of which were performed before the identification of recently described Corynebacterium species. In 2004, Roux published a study of Corynebacterium species isolated from bone and joint infections.[25] Of the 31 patients reported, 8 had joint prosthesis infection (2 each with C. amycolatum and C. striatum, 3 with C. aurimucosum, and 1 with C. jeikeium).

Conclusion

In conclusion, bacterial culture by sonication method is nowadays one of the most sensitive methods in the diagnosis of joint prosthesis infections.

The negative culture of preoperative joint aspiration and periprosthetic soft tissues obtained intraoperatively does not exclude the presence of bacteria in the implants. Where possible, orthopedic surgeons should use this method to confirm or refute the diagnosis of periprosthetic infection, especially in cases of suspected chronic low-grade infection.

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