Case Report

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Sonication of Extracted Prosthetic Implants Improves Diagnosis of Early Prosthetic Joint Infection – Bacteriological Diagnosis Depends on Duration of Infection and Route of Dissemination

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Abbreviations: CLI: Clindamycin; CXM: Cefuroxime; MEM: Meropenem; MNZ: Metronidazole; RIF: Rifampicin; VAN: Vancomycin

ABSTRACT

Introduction: Joint replacement is one of the most important innovations of the 20th century, and it has improved the quality of life of millions of people worldwide by providing restored joint function, pain relief, and independence. Prosthetic joint infection (PJI) is a feared complication, and both diagnosis and treatment are challenging. Diagnosis of PJI is based on clinical signs, laboratory tests, and microbiological examinations. Staphylococcus epidermidis and Staphylococcus aureus cause the majority of PJIs. Among microbiological examinations has sonication of extracted implant proved to be a useful tool to release bacteria associated to biofilm on implants prior to culture.

Case: we report a case of suspected PJI in which 23 periprosthetic and sonication of three implants specimens were examined. Only the sonicated tibia implant yielded substantial growth of S. epidermidis. All other 23 specimens including 18 tissue specimens were culture negative.

Discussion: when evaluating patients with suspected PJI and using sonication of implants it is essential to recognize that outcome of microbiological culture from implants- and tissue specimens depend on the route of transmission and stage of infection.

Conclusion: In the present case, only implants were infected without dissemination to the periprosthetic tissue. However, the current definition of PJI was not fulfilled, because sonication of implants is not included in the current guidelines. Also, the present report illustrates the usefulness of sonication of extracted implants for diagnosis of PJI also in a case without prior antimicrobial treatment. In the present case, despite comprehensive prosthetic and periprosthetic sampling, only one implant was infected without dissemination to the nearby periprosthetic tissue illustrating the usefulness of sonication for diagnosis of PJI also in a case without prior antimicrobial treatment. The current definition of PJI was not fulfilled because sonication of implants is not included in the current guidelines. The discrepancy in diagnosis between outcome sonication and periprosthetic specimens depend on the duration of infection and route of transmission/dissemination.

Introduction

Prosthetic joint infection (PJI) is a feared complication that involves a joint implant and nearby tissue. The increased knowledge regarding diagnosis, management, and prevention of biofilm-associated infections has led to more successful treatment of patients with these challenging conditions. Sonication of implants in diagnosis of PJI is now an established technique but is still not included in current guidelines [1-3].

Case Report

We describe a patient with a history of hospitalization due to leg ulcers. The patient had pain and walking problems with x-ray findings of arthrosis in the right knee. Subsequently, the patient was accepted for arthroplasty. On the day of prosthetic surgery (index day 0) a body mass index (BMI) of 34.7 and ASA score 2 were recorded. At start of the surgery, the patient received antimicrobial prophylaxis according to national recommendations: cloxacillin 2 g i.v. followed by 1 g at 2.5, 8.5, and 14.5 h after the initial dose (Figure 1). The prosthetic surgery lasted 113 minutes. On the following day (day 1), the patient fell, which caused minor bleeding in the surgical wound that delayed flexion exercise for 3 days. After 7 days, the patient was discharged from the hospital with no further issues. The scheduled follow-up control (via telephone) approximately 4 weeks after surgery identified no further problems. However, on day 43, the patient experienced local oedema and pain, and the right knee felt hot. A general practitioner was consulted, and the patient was scheduled for a visit to the Orthopaedic department. No antibiotics were given. On day 54 after surgery, an Orthopaedic examination of the knee showed a wound without signs of infection, moderate hydrops, and a normal skin temperature. A knee puncture yielded a turbid fluid with no presence of bacteria on microscopic examination and culture. A CRP of 132 mg/L and a blood leukocyte count of 8.3 109/L were noted, and the surgeon concluded that a PJI should be excluded. However, no antibiotics were introduced pending the results of tissue culture. The patient was scheduled for re-examination within a few weeks.

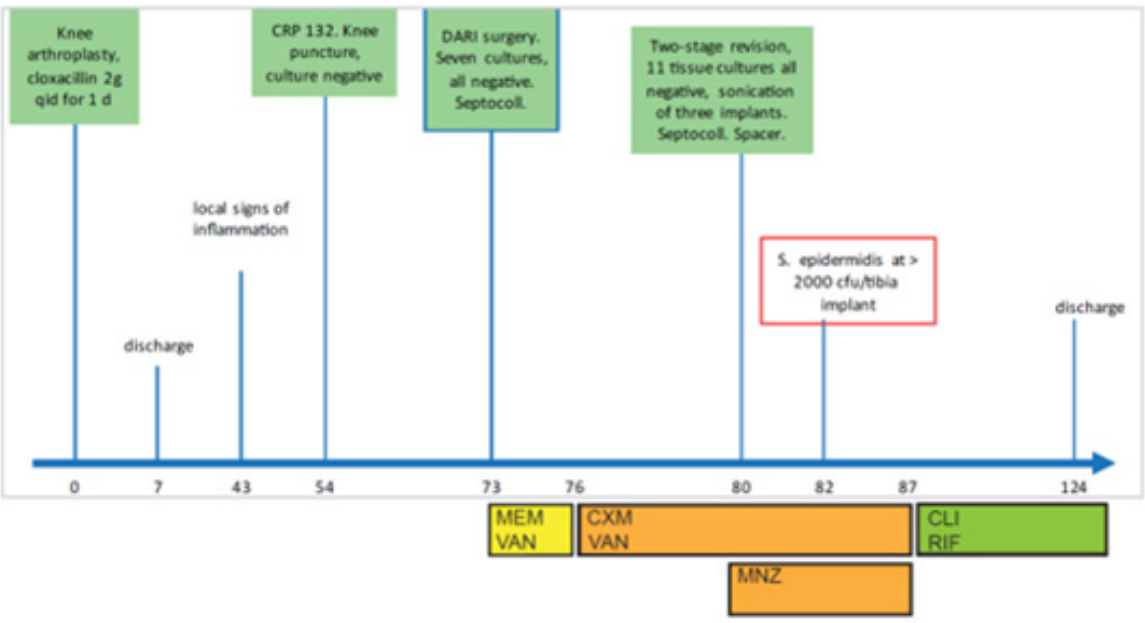

Figure 1: Timeline of patient with prosthetic knee infection (days).

On day 73, the patient contacted the Orthopaedic department due to worsening symptoms, and a CRP of 154 mg/L was found. Upon examination, it was decided to perform a debridement, implant retention, and antibiotic treatment (DAIR regimen). During the surgery, 250 mL of synovial fluid was removed, which was described as turbid and viscous, with colour and texture similar to "vanilla custard". The plastic liner was removed, and a clean-up procedure was performed in which the joint was flushed with 12 L of saline and a new liner was inserted. The joint prosthesis with all metallic parts remained cemented. Seven specimens were collected: two from synovial fluid, both for microscopy and culture, and five periprosthetic tissue biopsies for culture. Specimens were cultured on blood, haematin, and anaerobic blood agar plates for 7 days in air, 5% C02, and anaerobic conditions, respectively. Microscopic

examination was conducted after Gram and methylene blue staining and showed that all specimens were negative. At the end of surgery, Septocoll® E sheets (Biomet Biomaterials, Darmstadt, Germany) 140 mg x 4 gentamicin were inserted in the joint space prior to wound closure. The patient was then referred to the department of infectious diseases, and meropenem 1 g t.i.d. and vancomycin 1 g b.i.d. were administered i.v. After 2 days, meropenem was replaced with cefuroxime 1.5 g t.i.d., and the combined treatment was continued for 2 weeks (until day 87).

On day 80, due to lack of improvement with the DAIR regimen, a two-stage revision was performed: the implants (tibia, femur and liner) were extracted and replaced with a cement spacer. During the opening of the joint, a suspected infectious haematoma was evacuated. Suboptimal fixation of the tibia implant was found and, according to the surgical records, a suspected site of infection on the medial side of the bone surface with a possible septic loosening was identified (Figure 2). In all, 11 specimens were collected for culture: synovia/joint capsule (two), joint fluid (two), cement (one), periprosthetic tissue biopsies (six), implants for sonication (three). A spacer was implanted, and the surgery ended with insertion of four Septocoll® E sheets (gentamicin 140 mg x 4) in the joint prior to skin closure. After surgery, metronidazole 500 mg b.i.d. i.v was added to the ongoing vancomycin/cefuroxime treatment until day 87 (Figure 1). In the laboratory, the femur, tibia, and plastic implants were sonicated separately at 37 KHz for 7 minutes as previously described [2]. The specimens were cultured at 35oC on blood, haematin, and anaerobic blood agar and incubated in air, 5% CO2, and anaerobic conditions for 2, 2, and 7 days, respectively. All specimens were culture negative except the sonicated tibia prosthesis, which was positive for S. epidermidis at > 2,000 colony forming units (cfu)/implant. The isolate was susceptible to clindamycin, rifampicin, vancomycin, linezolid, and ciprofloxacin but showed reduced susceptibility to cefadroxil, penicillin, isoxacillin, cefuroxime, and gentamicin. On day 87, the treatment was switched to clindamycin 300 mg t.i.d. and rifampicin 600 mg q.d. for 6 months (day 240). The patient was released from the hospital on day 124.

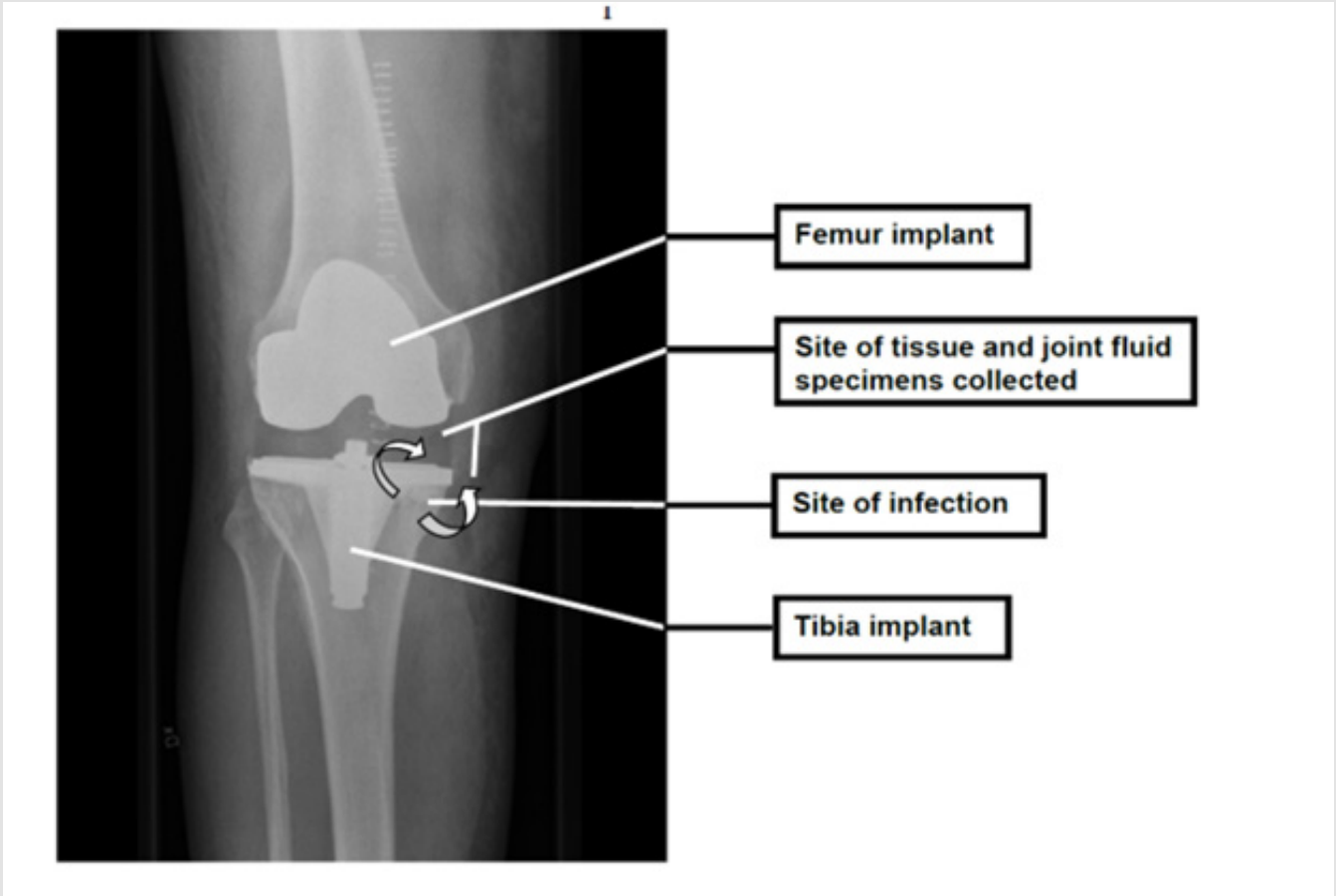

Figure 2: Knee implant (right) with a suspected infection from which 23 specimens were collected at different occasions. The figure illustrates the site of infection (beneath tibia plateau) and the collection site of pre- and per-operative tissue specimens. The arrows indicate the possible routes of transmission/dissemination without sinus to nearby tissue or joint fluid and not confirmed in the present case.

On day 305 after the primary surgery, CRP had declined to 12 mg/L, and the spacers were replaced with a new implant. During surgery, five periprosthetic tissue cultures were collected from the tibia, the femur, and underneath the spacer. All five of those specimens and the sonicated spacer specimens were culture negative. At the end of surgery, two Septocoll® E sheets were inserted, and ekvacillin 2 g q.i.d. and vancomycin 1g t.i.d. were given i.v. for 24 h. Ten years later, the patient returned with a suspected infection of the implant in the right knee. Due to weak health and a liver disease, a femur amputation was performed. Both preoperative blood cultures showed growth of S. epidermidis susceptible to all tested antibiotics.

Discussion

Infection and aseptic loosening are common causes of prosthetic failure after joint replacement. Accurate diagnosis including culture and antimicrobial susceptibility profiling of the infecting microorganism is essential to guide the clinician towards successful treatment. In the current case of suspected PJI, all 23 specimens (synovia/joint capsule, joint fluid, tissue biopsies) collected pre-and perioperatively during the DAIR procedure and during the two-stage revision surgery were culture negative. Importantly, the patient was not given any antimicrobial treatment prior to DARI surgery. After the surgery, during the two-stage exchange arthroplasty and with the patient on cefuroxime and vancomycin treatment, each extracted implant (femur, tibia, and plastic component) was sonicated separately, and only the tibia implant yielded substantial growth of S. epidermidis. However, the cut off (cfu/implant or similar) has been discussed in many studies. From our experience using he sonication technique in more than a decade, is that it is difficult to set a "cut-off" (cfu/implant or cfu/mL) for PJI due to lack of standardized implant extraction and sonication procedures. A "rough" handling of implants during extraction procedure may lead to extensive loss of implant-associated biofilm and/or biofilm that remains within the bone cavity which affects bacterial outcome of culture from the extracted implant.

In the present case, a biofilm-associated infection of the tibia implant concurred with the suspected infection site noticed by the surgeon and found at X-ray examination showing osteolysis beneath the tibia implant. We sonicated each implant component separately which might be too labour intensive to be recommended in clinical practice, despite the benefits as illustrated in the current case where the infection was located only in the tibia implant confirming the osteolysis found at X-ray examination. Nonetheless, the low contamination risk of implant components during surgery is indicated by the observation that sonication and culture of the other two extracted implant parts were culture negative. Overall, sonication of implants has proven to be superior to other methods [1,4-6] since sonication permits "examination" of the total implant surface. However, we propose that sonicated specimens should be a complement to the five periprosthetic tissue specimens, often recommended, and for this reason perceived as the sixth "tissue" [7]. The present case also demonstrates that the stage and duration of infection, site and route of transmission/dissemination which must be considered when evaluating a case of suspected PJI [8]. We consider each implant infection as an outcome of three events: first, contamination of implant at insertion surgery (as in present case); second, due to dissemination of bacteria from wound, peri prosthetic tissue or joint fluid; third, from a hematogenous seeding. With this in mind, an implant infected at insertion we expect that periprosthetic tissues to be culture-negative since lack of dissemination of the infected implant has not occurred to the nearby tissue, as illustrated by the present case. Similarly, infected periprosthetic tissue are expected culture positive before dissemination and infection of the implant. In a fulminant infection both tissue and implant are expected culture positive. The discrepancy in outcome of culture from periprosthetic tissue and implants are often found and not blamed on methodological, culture or other failures but due to the stage and route of transmission/dissemination of infection and to some extend also due to surgeon's skill at extraction of implant. Of these reasons it is difficult to compare which of the examinations should be considered gold standard.

The present PJI does not fulfil the criteria set by the Musculoskeletal Infection Society, the Infectious Diseases Society of America or the newly revised score-based definition by the International Consensus Group [1,9] due to lack of sinus tract, identical microorganisms in two or more cultures, or purulence surrounding the prosthesis. Also, there is a lack of supporting evidence, such as acute inflammation upon histological examination of the periprosthetic tissue, single culture of any microorganism, single culture of a virulent microorganism, or elevated synovial fluid leukocyte counts or neutrophil percentage in joint fluid. The only finding in the present case was an elevated CRP. In Scandinavia, diagnosis of PJI relies on bacterial culture, microscopy of synovial fluid, and laboratory tests, whereas histological examination is not performed due to a shortage of specialists in pathology. Irrespective of stage of infection, some locations (e.g., the interface between femur and implant) are more prone to be culture positive [10]. Single culture-positive specimens can be considered clinically significant when supported by clinical signs, symptoms, and other tests, as defined by the above-mentioned current guidelines [1]. However, sonication of implants is not included in those guidelines. Improvements in the diagnostic sensitivity of PJI is warranted, especially as culture-negative PJI is expected in 5–35% of the cases [11].

Conclusion

The present case illustrates the usefulness of sonication of extracted implants for diagnosis of PJI. Even though the patient with suspected PJI was not on antimicrobial treatment prior to DARI surgery, all 7 synovial and periprosthetic tissue specimens were culture negative. Later during the two-stage exchange procedure, only the sonicated tibia implant was culture positive. This case did not fulfil the definitions of PJI, because the sonication technique, cut-off or interpretation of outcome are not included in the current guidelines, despite the usefulness of the method. We suggest that sonication of implants be included in the present expert guidelines for diagnosis of PJI. Discrepancy in bacteriological outcome of culture between sonicated implants and periprosthetic tissue biopsies is due to the stage of infection and route of transmission.

Author Statements

Authors and Contributors

LW, NW and TM investigated the case and performed formal analysis of medical charts and cultures results. All authors participated in interpretation of data and drafting of the original manuscript. MW provided clinical relevance and manuscript editing, and critically reviewed the manuscript. All authors read and approved the final manuscript.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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