Case Report
https://doi.org/10.21823/2311-2905-2021-27-1-175-182

Copper-Coated Spacer for Total Femoral Replacement in Recurrent Periprosthetic Joint Infection: A Case Report

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Abstract

Background. There are few cases of entire femur modular replacement with hip and knee joints in patients with periprosthetic joint infection (PJI) in literature. They report encouraging results in patients of elderly and senile age. We present case of a copper-coated femoral spacer implantation to 50-year-old patient with multiple PJI episodes and osteomyelitis of the entire femur. ***Clinical presentation.*** A 40-year-old male patient after resection of the proximal part of the right femur for fibrotic osteodysplasia underwent total hip arthroplasty with replacement of 15 cm of the femur. In December 2010 (20 months after implantation), instability of the femoral component developed, revision arthroplasty was performed with stem recementation. After 4 months, sinus tract formed in the area of the postoperative scar. After another 4 months, the head of the prosthesis was dislocated. In September 2011, the endoprosthesis components were removed and a unipolar cement spacer was implanted. The limb immobilized in a hip spica cast. Methicillin-sensitive *S. epidermidis* (MSSE) was detected in the preoperative joint aspiration puncture and periprosthetic tissues. After 3 months (December 2011), patient underwent revision total hip arthroplasty (25 cm defect was replaced). 5 years of PJI remission followed. In November 2016 after PJI recurrence the endoprosthesis was removed, and an articulating spacer was implanted. *P. aeruginosa* was detected in periprosthetic tissues. For the past 2.5 years there were periodically sinus tracts formations. In August of 2019 spacer's migration resulted in an intercondylar fracture of the right femur. In September 2019, spacer was removed, and MSSE was detected in the surrounding tissues. An articulating cement spacer based on an oncological modular total femur copper-coated endoprosthesis was implanted. At each control examination during the year copper concentration in blood serum was determined, it did not exceed 900–1200 mcg/l. No local or systemic side effects were detected. The patient started working 3 months after surgery. After 6 months poor functioning sinus tract formed in the postoperative scar area in the lower third of the thigh. Eighteen months after the operation, the functional condition is satisfactory. ***Conclusion.*** The use of the copper-coated spacer based on modular total femur endoprosthesis with hip and knee joints in a patient with multiple PJI allowed to improve the function of the limb and reduce the severity of the infectious process. No local or systemic toxic effects of copper were detected.

Keywords: total hip replacement, periprosthetic joint infection, periprosthetic fracture, articulating spacer, copper coating.

Funding: state budgetary funding.

Cite as: Belokobylov A.A., Batpenov N.D., Balgazarov S.S., Serikbayev V.D., Krikliviy A.A., Plotnikov S.V., Turlybekuly A., Rimashevskiy D.V. [Copper-Coated Spacer for Total Femoral Replacement in Recurrent Periprosthetic Joint Infection: A Case Report]. *Travmatologiya i ortopediya Rossii* [Traumatology and Orthopedics of Russia]. 2021;27(1):175-182. (In Russian). https://doi.org/10.21823/2311-2905-2021-27-1-175-182.

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Received: 04.09.2020. Accepted for publication: 21.01.2021.

Introduction

Compared with the traditional primary total hip arthroplasty (THA), the results of the proximal end of the femur replacement with oncological endoprostheses are less favorable. With the exception of the underlying disease progression, infectious complications, dislocations, aseptic loosening of the endoprosthesis stem most often lead to revision surgery [1]. It is known that with periprosthetic infection (PPI), at least three reservoirs of microbes are formed in the patient's body: abscesses in soft tissues and bone marrow, microbial biofilm on the implants surface, colonized bone canales.

It is possible that intracellular colonization of bone cells and leukocytes by bacteria also plays a role in the development of chronic PPI [2]. The current understanding of the PPI etiopathogenesis explains the high frequency of revisions with spacers implantation, the local antibacterial effect of which is based only on antibiotics of bone cement [3, 4, 5, 6]. The question remains open: what to do with patients with a total lesion of the femur after repeated unsuccessful attempts to treat PPI using spacers with antibiotics? The literature describes the use of oncological endoprostheses with a silver coating for the prevention of infection and prolonging the endoprostheses service life [7], but there is no extensive experience in the use of such structures for therapeutic purposes in the world.

It is known that copper nanoparticles are able to inhibit the growth of clinical isolates of *S. Aureus*, including MRSA [8, 9]. In animal experiment, intravenous administration of copper nanoparticles in generalized infection caused by *Pseudomonas aeruginosa*, *Staphylococcus aureus*, showed greater effectiveness in comparison with ceftriaxone, without having a side effect [10]. *In vitro*, *in vivo* studies and isolated clinical observations using copper-coated implants have shown encouraging results [11, 12, 13, 14]. There have been no reports of the copper coated spacer use that replaces the femur with the hip and knee joints in recurrent PPI.

Clinical case

A 40-year-old patient underwent surgery on in March 2009 for the right proximal femur neoplasm. Resection of the proximal femur, THA with an oncological endoprosthesis were performed. According to the results of histological examination of the intraoperative biomaterial, fibrous osteodysplasia was diagnosed (Fig. 1). In December 2010 (20 months after the initial surgery) due to the implant loosening development, the revision with the stem recementation was performed. In August 2011 (9 months after the first revision), the patient was hospitalized for the first time in NIITO (Nur-Sultan, Republic of Kazakhstan) with the presence of fistula wounds on the background of the endoprosthesis head dislocation and X-ray signs of implant instability (Fig. 2).

A methicillin-sensitive *S. epidermidis* (MSSE) was detected in the preoperative punctate and periprosthetic tissues. The endoprosthesis was removed, radical debridement was performed. A monopolar cement spacer (vancomycin+ceftazidime) and gentamicin buds were installed (Fig. 3). Pathogen-specific antibiotic therapy was prescribed for 8 weeks. During 3 months, immobilization was performed in a hip spica cast.

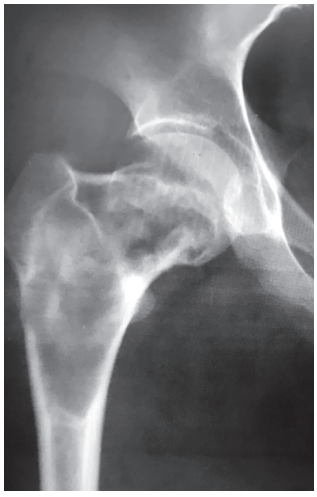

Figure 1. X-ray of the right hip joint before arthroplasty

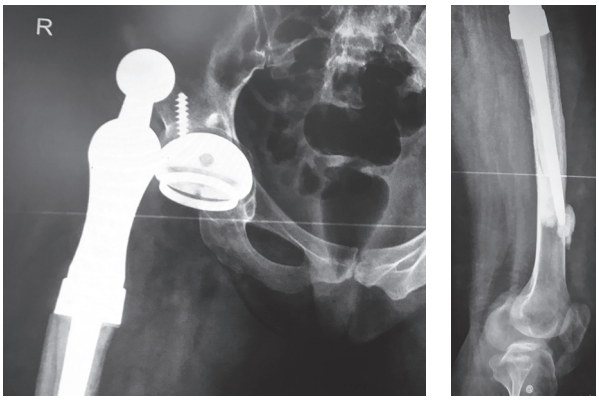

Figure 2. X-ray of the right hip joint.
The line of enlightenment is determined at the border of bone-cement (stem) and bone-implant (cup).
The distal end of the stem perforates the femur, where the bone cement is visible

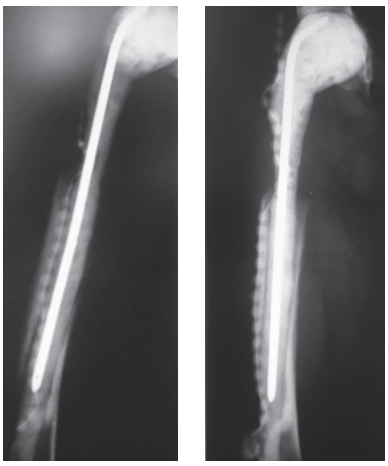

Figure 3. X-ray of the right thigh. Extensive defect of the cortical bone at the border of the middle and distal thirds of the femur

In November 2011, 4 months after the first spacer implantation, clinical and laboratory confirmation of PPI remission was received. The endoprosthesis of the right hip joint was reimplanted by MATI-CITO (Implant MT, Russia) with a Biolox delta ceramic head, (CeramTec AG; Phlochingen, Germany) 40 mm and a Trident cup (Stryker, Mahwah, USA) (Fig. 4). Pathogen-specific antibiotic therapy was prescribed for 6 weeks.

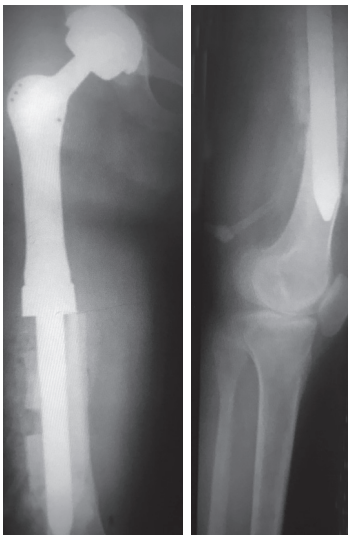

Figure 4. X-ray of the right hip after prosthesis implantation.
The length of the replaced femoral fragment was 25 cm

During the next 5 years, there was a stable remission of PPI with satisfactory functioning of the endoprosthesis: assessment on the Harris Hip Score — 74 points. At the beginning of 2016, pain appeared in the right hip with irradiation to the right knee joint, which worsened when walking, and mobility restriction in the right hip and knee joints progressed. A fistula opened. In November 2016, 5 years after the revision, the endoprosthesis was removed, radical debridement was performed, and an individual articulating spacer of the right hip joint was implanted. P. aeruginosa was detected in periprosthetic tissues. During the following 2.5 years fistulas were periodically functioning. Due to the patient's refusal of surgical treatment, conservative therapy was carried out. The support of the limb was preserved during this period, the patient walked with a cane. Since August 2019, the condition has worsened, against the background of open fistula wounds, the ability to limb weight-bearing has been significantly reduced. The X-ray revealed an intercondylar pathological periprosthetic fracture of the femur with displacement, spacer migration, shortening of the right lower limb by 10 cm (Fig. 5). At admission, the patient walked on crutches. There was a fistula wound

in the postoperative scar area. Movements in the right hip are limited: flexion up to 90°, extension up to 10°, abduction up to 20°, adduction up to 5°, internal rotation 15°, external rotation 10°. There was no movement in the right knee joint. In the preoperative punctate and during the subsequent analysis of intraoperative tissue samples, a methicillin-sensitive *S.epidermidis* (MSSE) was detected. Radical debridement was performed, the remaining fragments of the femur were removed, was implanted spacer, made on the basis of oncological total endoprostheses of the knee and hip joints of the MATI-CITO, connected to each other by a titanium sleeve. The spacer had a combined coating (copper anodizing + bone cement with antibiotics (ceftazidime and vancomycin). Copper was applied to the spacer with an antibacterial purpose by electroplating in a cylindrical galvanic bath with solution of copper sulfate electrolyte in the Vostokmashzavod laboratory (Ust-Kamenogorsk, Republic of Kazakhstan). Before anodizing, the implant surface was cleaned and washed in a solution of sulfuric acid. The thickness of the copper coating layer was up to 50 microns (Fig. 6, 7).

The length of the limb was compensated. The wound was healed by primary tension. The patient was discharged from the hospital on the 14th day after the operation in a satisfactory condition. The copper content in the blood ranged from 900 to 1200 mcg/l in different follow-up periods, which does not exceed the values observed in healthy people [15, 16].

After 18 months, there are no radiological data indicating instability or migration of the endoprosthesis components. A fistula wound functioning along in the postoperative scar area in the lower third of the thigh with an extremely poor discharge. The range of motions in the right hip joint at the time of article writing: flexion up to 90°, extension up to 10°, abduction up to 20°, adduction up to 15°, internal rotation 20°, external rotation 20°. Movements in the right knee joint: flexion 40°, extension 180°. Weight-bearing on the right lower limb in full. The patient started working.

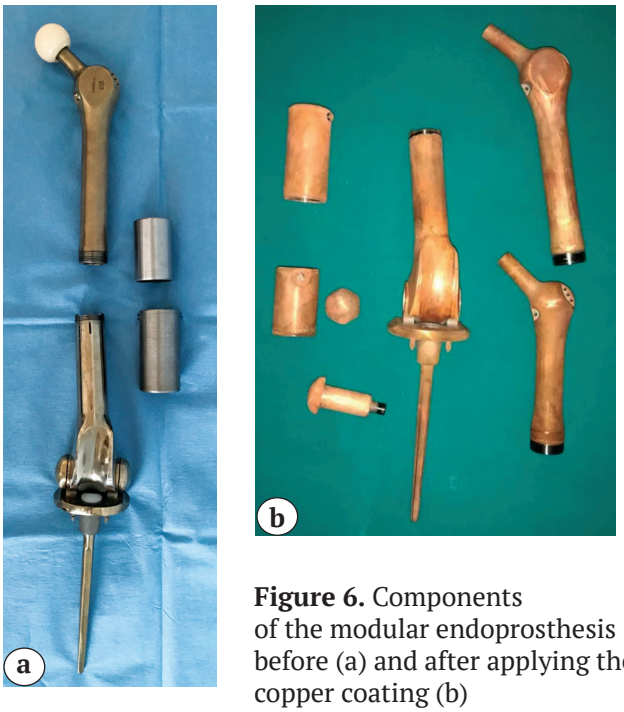

Figure 6. Components of the modular endoprosthesis before (a) and after applying the copper coating (b)

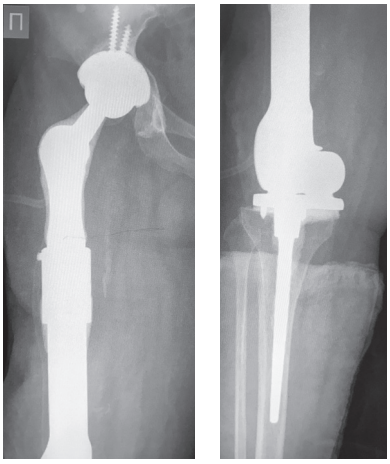

Figure 7. X-rays of the right lower limb. Spacer based on the "total femur" implant with cementation of the tibial stem and press-fit cup

Discussion

Antimicrobial activity of copper against gram-positive and gram-negative flora, including methicillin-resistant *S. Aureus* (MRSA), *Clostridium difficile*, vancomycin-resistant enterococci (VRE), strains with an extended spectrum of betalactamases, as well as adenoviruses and fungi, has been known for a long time [17, 18]. Spacers coated with copper nitrite showed encouraging results [12]. The widespread clinical use of copper in implants is interfered by its toxicity against not only microorganisms, but also human tissues. In particular, it has recently been proved that copper (Cu II) promotes the formation of oxygen and nitrogen active forms in the body, which have cytotoxic and genotoxic effects on human blood cells [19]. Heavy metals cause multiple organ injuries and are considered as systemic toxic agents [20]. Copper is one of these metals, necessary for many vital biological functions, since it is an integral part of many enzymes and proteins.

The body of an adult weighing 70 kg contains approximately 110 mg of copper [21]. We get about 1 mg of copper per day with food [22]. The implant we installed had a very thin layer of copper (50 micrograms) on the surface, but despite this, we tried to cover the surface of the implant with bone cement with antibiotics to reduce the likelihood of toxic effects of copper to the maximum extent that the tension of soft tissues allowed. Copper acts as a catalytic cofactor of more than 20 enzymes, mainly those involved in energy metabolism and cellular respiration, iron metabolism, neurotransmitter biosynthesis, gene transcription, connective tissue biosynthesis and antioxidant protection [23]. Although copper is a biologically important microelement, it can exhibit toxicity depending on the concentration and duration of exposure [24].

An increased concentration of copper in the blood may be a risk factor for cardiovascular diseases and myocardial infarction [25, 26, 27]. All this was taken into account when conducting a regular examination of the patient. No signs of systemic toxicity of copper were detected. There is evidence that use of implants with a galvanically applied copper coating has an antibacterial effect and does not lead to a significant increase in the concentration of copper in the blood serum. C. Prinz et al. experimentally performed osteosynthesis of rabbits femurs with Kirschner wires made of Ti6Al4V, the surface of which was first subjected to plasma electrolytic oxidation, and then galvanically coated with copper in load of 1 microgram/mm^2. At the same time, bacteria (*S. Aureus* strain ATCC 25923) at concentration of 105 CFU/ml were inoculated into the fracture zone. After the nails were implanted, the concentration of copper ions in the blood did not increase, which indicates that the copper released from the implant surface did not leave the fracture zone. After 4 weeks the analysis of the extracted implants revealed a distinct antimicrobial effect of copper, which prevented the adhesion of film-forming bacteria to the implant and stimulated bone fusion [28]. In our study, we also did not observe an increase in the concentration of copper in the blood serum above the permissible values and any manifestations of the systemic toxic effect of copper. We managed to radically reduce the inflammatory process activity, which fits with the results of the experimental study of A. Mauerer et al. [14]. Unfortunately, we did not eliminate the infection, but the patient walks with a full load on the treated leg, started working, has no pain. The literature describes isolated cases of antibiotic spacers use that replace the entire femur with the hip and knee joints in PPI. The authors report very encouraging results, but the patients are usually elderly and senile [29, 30].

In our case, taking into account the multiple recurrences of PPI in the anamnesis and the young age of the patient, the use of a copper-coated femoral spacer was clinically justified, and the result was satisfactory.

Conclusion

The use of the implant-based spacer for total femoral replacement with hip and knee joints with a galvanically applied copper coating in a patient with multiple recurrences of PPI allowed to improve the function of the limb and reduce the severity of the infectious process. There is no local or systemic toxic effect of copper.

Ethical expertise

Permission was obtained from the local ethics committee (protocol No. 2 of the meeting of the ethical commission of the NIITO (14.09.2019) for the use of copper-coated spacers in patients with repeated relapses of PPI as part of a clinical study.

Informed consent

The patient gave informed written consent to the use of a copper-coated spacer and the publication of a clinical observation.

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Serikbayev V.D. — patient treatment, preparation of the text

Krikliviy A.A. — patient treatment, preparation of the text

Plotnikov S.V. — review of the literature

Turlybekuly A. — review of the literature

Rimashevskiy D.V. — review of the literature. author's coordination, text preparation and editing for important intellectual content

All authors made a significant contribution to the research and preparation of the article and read and approved the final version before its publication. They agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Competing interests: the authors declare that there are no competing interests.