https://doi.org/10.35401/2541-9897-2022-25-2-59-66

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The use of an antibacterial implant in the treatment of periprosthetic infection in an HIV-positive patient

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Received: February 1, 2022. Received in revised form: February 22, 2022. Accepted: March 15, 2022.

Abstract
Background: The frequency of occurrence of infectious complications after hip arthroplasty in HIV-infected patients is extremely high. Revision arthroplasty for periprosthetic infection is the leader (64%) among the causes of early revision interventions. The search for ways to increase the efficiency of the sanitizing stage of treatment due to antibacterial coatings of the endoprosthesis components continues.
Objective: Demonstration of a clinical case of treatment of periprosthetic infection in an HIV-positive patient using a spacer and a femoral component of a hip joint endoprosthesis coated with linear Sp1 carbon chains and silver. 123 months after hip arthroplasty for stage 3 dysplastic coxarthrosis in HIV-positive patient of 42 years old developed an instability of the acetabular component with the growth of Staphylococcus aureus in punctates. A revision was performed with the removal of the endoprosthesis and the installation of an articulating spacer with the addition of antibiotics. 12 weeks later, a recurrence of periprosthetic infection occurred, and Enterococcus faecalis was detected in punctates. During re-endoprosthetics, there was an installation of an articulating spacer covered with a two-dimensionally ordered linear-chain carbon doped with silver, based on the Zimmer CPT femoral component and bone cement with antibiotics addition. After 3 months, the second stage of revision arthroplasty was performed with implantation of an individual acetabular component and a femoral component coated with two-dimensionally ordered linear-chain carbon doped with silver.
Conclusion: 4 months after the operation the patient returned to work, 12 months later the functional results were satisfactory. The use of components coated with two-dimensionally ordered linear-chain carbon doped with silver in an HIV-positive patient with recurrent periprosthetic infection made it possible to stop the infectious process, improve limb function and the quality of life.
***Keywords*:** periprosthetic infection, revision arthroplasty, antibacterial coating, articulating spacer, antibiotic resistance, HIV infection
Cite this article as: Nikolaev N.S., Malyuchenko L.I., Karpukhin A.S., Yakovlev V.V., Maksimov A.L., Grigor'eva E.V., Rozhkov N.I. The use of an antibacterial implant in the treatment of periprosthetic infection in an HIV-positive patient. *Innovative Medicine of Kuban*. 2022;(2):59–66. https://doi.org/10.35401/2541-9897-2022-25-2-59-66

Использование имплантата с антибактериальным покрытием в лечении перипротезной инфекции у ВИЧ-позитивного пациента

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Поступила в редакцию 1 февраля 2022 г. Исправлена 22 февраля 2022 г. Принята к печати 15 марта 2022 г.

Резюме
Актуальность: Частота инфекционных осложнений после эндопротезирования тазобедренного сустава у ВИЧ-инфицированных больных в два раза выше, чем у ВИЧ-негативных пациентов. Ревизионное эндопротезирование по поводу перипротезной инфекции лидирует (64%) среди причин ранних ревизионных вмешательств. Продолжается поиск путей повышения эффективности санирующего этапа лечения, в том числе за счет антибактериальных покрытий компонентов эндопротеза.
Цель работы: Продемонстрировать случай лечения перипротезной инфекции у ВИЧ-положительного пациента с использованием спейсера и бедренного компонента эндопротеза тазобедренного сустава, покрытого линейными Sp1-углеродными цепями

и серебром. Через 123 мес. после эндопротезирования тазобедренного сустава по поводу диспластического коксартроза 3 ст. у ВИЧ-инфицированной пациентки, 42 лет, развилась нестабильность вертлужного компонента с ростом Staphylococcus aureus в пунктатах. Выполнена ревизия с удалением эндопротеза и установкой артикулирующего спейсера с добавлением антибиотиков. Через 12 нед. произошел рецидив перипротезной инфекции, в пунктатах выявлен Enterococcus faecalis. В ходе реэндопротезирования установлен артикулирующий спейсер, покрытый двумерно-упорядоченным линейно-цепочечным углеродом, легированный серебром, на основе бедренного компонента Zimmer CPT и костного цемента с добавлением антибиотиков. Спустя 3 мес. выполнен второй этап ревизионного эндопротезирования с имплантацией индивидуального вертлужного и бедренного компонентов, покрытых двумерно-упорядоченным линейно-цепочечным углеродом, легированным серебром.

Заключение: Через 4 мес. после операции больная вернулась к труду, через 12 мес. отмечены удовлетворительные функциональные результаты. Использование компонентов с покрытием на основе двумерно-упорядоченного линейно-цепочечного углерода, легированного серебром, у ВИЧ-позитивной пациентки с рецидивами перипротезной инфекции позволило купировать инфекционный процесс, улучшить функцию конечности и повысить качество жизни.

Ключевые слова: перипротезная инфекция, ревизионное эндопротезирование, антибактериальное покрытие, артикулирующий спейсер, антибиотикорезистентность, ВИЧ-инфекция

Цитировать: Николаев Н.С., Малюченко Л.И., Карпухин А.С., Яковлев В.В., Максимов А.Л., Григорьева Е.В., Рожков Н.И. Использование имплантата с антибактериальным покрытием в лечении перипротезной инфекции у ВИЧ-позитивного пациента. *Инновационная медицина Кубани.* 2022;(2):59–66. https://doi.org/10.35401/2541-9897-2022-25-2-59-66

Introduction

Surgical treatment of the hip joint pathology in the scope of its arthroplasty is becoming an ordinary method due to the demand for this type of medical care in the conditions of the incidence of coxarthrosis increase, the good results of the operation and the rich accumulated experience of such interventions. At the same time an increase in the number of hip arthroplasties inevitably entails an increase in repeated revision surgeries caused by various complications: their share ranges from 13 to 18% of the number of primary arthroplasties [1–3]. In patients, who have undergone revision surgeries, infectious and mechanical complications (dislocations, periprosthetic fractures) occur up to 15 times more often [4–5].

According to the endoprosthesis registry of the Federal State Budgetary Institution "Russian Scientific Research Institute of Traumatology and Orthopedics named after R.R. Vreden" of the Ministry of Health of Russia, deep infection is the main reason for revision interventions in the first 5 years after primary endoprosthesis (64%) [6, 7].

In recent years, the use of spacers coated with linear Sp1-carbon chains and silver, which have a pronounced ability to prevent the formation of microbial biofilm, in the treatment of the hip joint periprosthetic infection has increased [8]. The antibacterial properties of silver make it the most used metal in biomedicine due to its wide spectrum of antimicrobial activity and lower bacterial resistance than traditional antibacterial medications [9].

Repeated surgical intervention in the conditions of periprosthetic infection is complicated by the bone defects and muscle deficiency that occurred due to the limited range of motion in the joint due to pain. Various methods of revision hip joint arthroplasty effectively eliminate pain, restore motion range of the joint to a certain extent, generally improving life quality of patients and their satisfaction with the treatment. However, a favorable prognosis is complicated by previous surgical interventions. Following surgeries contribute to the occurrence and progression of the focus of infection, as well as various types of dislocation in the joint. The results of repeated operations in such cases are less predictable in terms of a full recovery of motor functions.

An even more difficult task for a traumatologist-orthopedist is primary and repeated hip arthroplasty in patients with chronic infections, especially in conditions of secondary immunodeficiency, which happens, in particular, in patients with HIV infection.

As of December 31, 2020, almost 1.5 million cases of immunologically verified diagnosis "HIV infection" were registered in Russian Federation, as well as 1.1 million of people living with HIV. Modern diagnostics and antiretroviral therapy, prescribed in the early stages of the disease, lead to an increase in the number of patients with HIV in the age group of 50 years and older. This category of patients often needs a large joint replacement and has the highest risk of developing postoperative infectious complications.

Data on the incidence of periprosthetic infection (and its relapses) after arthroplasty in HIV-positive patients vary greatly: from 15.3% according to some authors [10] to 21% according to others [11].

The insufficient number of clinical observations, the lack of a clear picture and an unambiguous opinion about the results and complications after the large joints arthroplasty in HIV-infected patients should be noted.

Objective

Demonstration of a case of a periprosthetic infection treatment in an HIV-positive patient using a spacer and a femoral component of a hip endoprosthesis coated with linear Sp1-carbon chains and silver.

Clinical case

A clinical case of periprosthetic infection treatment in an HIV-positive patient is described. The study was carried out in accordance with the ethical standards stated in the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects" (2013), Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly

Work in Medical Journals prepared by the International Committee of Medical Journal Editors (section II E "Protection of Research Participants"). The patient gave written informed consent to the use of an implant coated with silver-doped two-dimensionally ordered linear chain carbon and publication of a clinical observation.

Patient T., 42 years old, since 1994 complained about the pain and limited movement of the left hip joint, use of a cane when walking, and difficulties in self-care. In June 2009, the patient was admitted to the Federal Center of Traumatology, Orthopedics and Arthroplasty where she was diagnosed with left-sided dysplastic coxarthrosis of stage 3 with severe pain syndrome (figure 1), which was surgically treated with cementless left hip arthroplasty with a Zimmer endoprosthesis (acetabular component Trilogy 48 with additional fixation with a 20 mm screw, Cross linked Standard liner, Alloclassic SLO 1 femoral component, Versys 28/+7 head). The postoperative period and rehabilitation were uneventful, the patient returned to work. The control radiograph is shown in figure 2.

123 months after the primary operation (September 2019), the patient's condition deteriorated, her support ability decreased, she had to use crutches when walking, persistent functional limitations appeared in the left hip joint. The radiograph revealed instability of the acetabular component with upward and medial migration (figure 3), confirmed by multislice computed tomography (MSCT) (figure 4).

Punctures of the left hip joint were performed three times with ultrasound navigation. All samples showed high levels of cytosis (22500–25450 cells per 1 μl), neutrophilia (97%), lymphocytosis (1%), and monocytosis (2%). According to the 2018 International Consensus Meeting on Musculoskeletal Infection, the rate of cytosis with the presence of a hip joint endoprosthesis is up to 3,000 cells per 1 μl. Microscopy revealed cocci; microbiological examination revealed the growth of Staphylococcus aureus in all punctates. A nasal swab analyses revealed growth of Staphylococcus epidermidis Methicillin-Resistant Staphylococcus Epidermidis (MRSE). The complete blood count showed an increase in erythrocyte sedimentation rate (ESR) (40 mm/h), an increase in presepsin (448 pg/ml). Functional impairments according to the Harris Hip Score equaled 26 points; to the EQ-5D-5L scale – 0.155; to the questionnaire EQ VAS – 30%; visual analog scale of pain (VAS) – 9 points. Septic instability of the acetabular component of the left hip joint endoprosthesis was diagnosed against the background of chronic viral hepatitis C; HIV infection stage 4B, in remission, against the background of antiretroviral therapy. The indications for two-stage revision arthroplasty of the left hip joint were determined.

At the first stage of the revision, the instability of acetabular component was intraoperatively confirmed, as well as the presence of the central defect of the acetabulum of irregular shape measuring 6×2 cm, and a defect of the posterior-superior wall of the acetabulum type II B–C (according to Paprosky). The femoral component was found to be stable. A cement articulating spacer with an outer diameter of 46 mm and an inner diameter of 32 mm was installed with addition of 4 g of vancomycin per 60 g of cement. The installation of the resterilized Zimmer CPT 1 femoral component, a Zimtron 32/S head (figure 5) was also performed.

The removed endoprosthesis components were processed in a BRANSON 8510 ultrasound machine (USA) for 5 minutes at a frequency of 40 ± 2 kHz and a power of 0.22 ± 0.04 W/cm^2 with the following microbiological examination of the obtained swabs, which showed the increase of Staphylococcus aureus. The postoperative

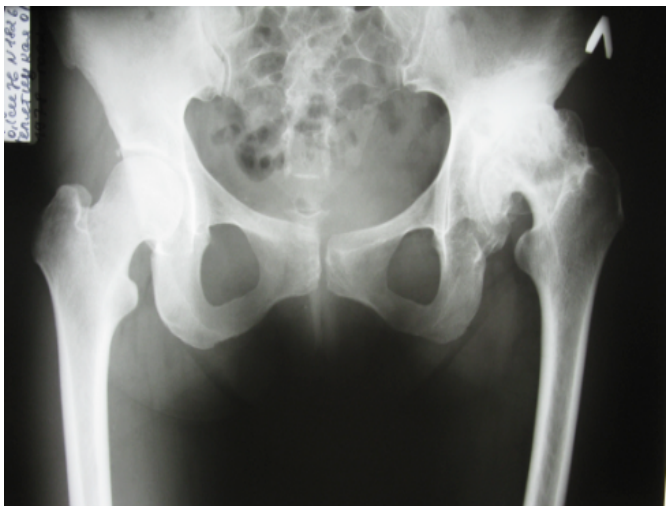


Figure 1. Preoperative plain radiograph of the left hip joint of patient T.
Рисунок 1. Обзорная рентгенограмма левого тазобедренного сустава пациентки Т. до операции

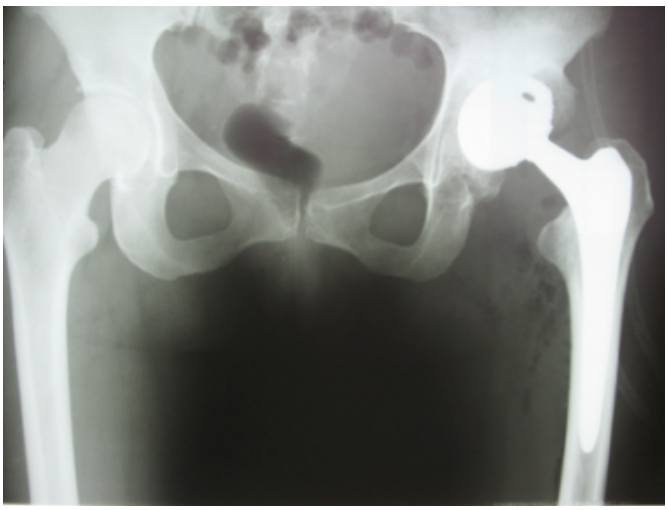


Figure 2. Postoperative plain radiograph of the left hip joint of patient T.
Рисунок 2. Обзорная рентгенограмма левого тазобедренного сустава пациентки Т. после операции

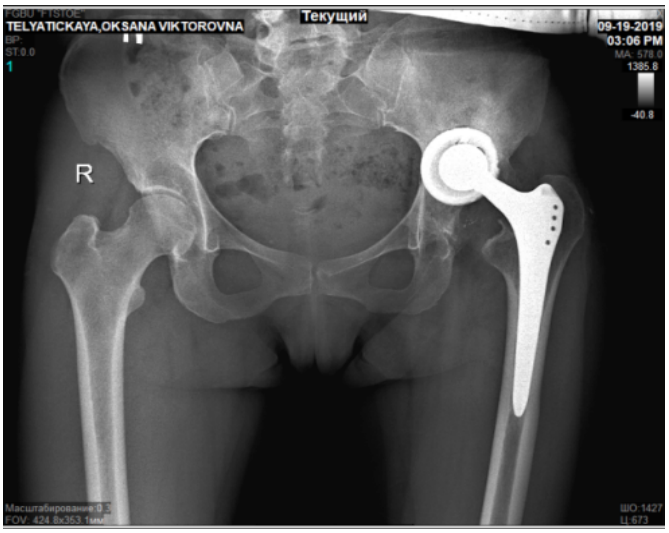


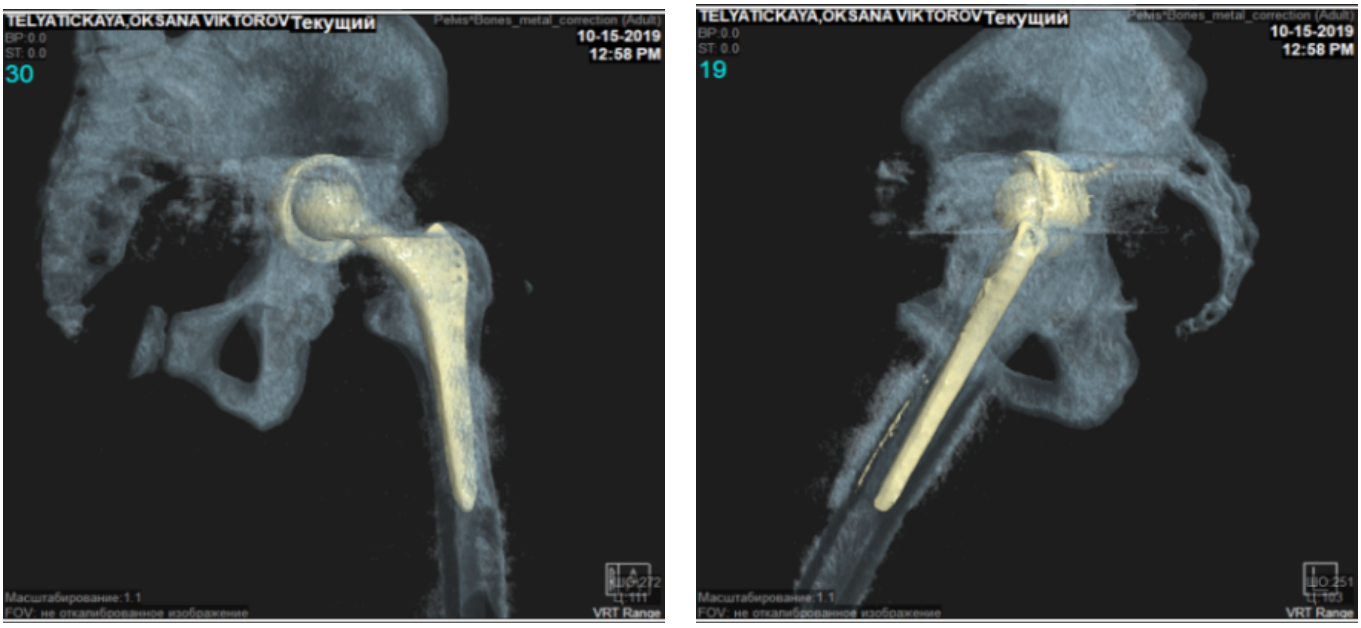
Figure 3. Plain radiograph of the pelvic bones of patient T. 123 months after primary arthroplasty
Рисунок 3. Обзорная рентгенограмма костей таза пациентки Т. через 123 мес. после первичного эндопротезирования

period was uneventful, the patient was discharged with the prescription of pathogen-specific antibacterial therapy.

12 weeks after discharge, the patient complained again about the body temperature increase to febrile values, as well as about the pronounced pain syndrome in the left hip joint. Laboratory and instrumental studies showed an increase in ESR (69 mm/h), an increase in D-dimer (650 ng/ml) and C-reactive protein (CRP) (6.5 mg/l). According to the Harris Hip Score the condition equaled 64 points; to the EQ-5D-5L scale – 0.661; EQ VAS – 60%; VAS – 5 points. In the left hip joint punctate – cytosis (3.5 thousand cells per 1 μl), neutrophilia (95%), lymphocytosis (5%), microscopy revealed cocci. Microbiological examination of the punctate revealed the increase of Enterococcus faecalis. It was decided to repeat the revision surgery (performed in April 2020). The spacer removal and debridement were performed, an articulating respacer (similar to the one installed at the first stage of the revision) and a resterilized Zimmer CPT 1 femoral component coated with silver-doped two-dimensionally ordered linear chain carbon, a Zimtron 32/L head (figure 6) were installed.

The postoperative period was uneventful, the patient was discharged with the prescription of pathogen-specific antibacterial therapy.

With this type of acetabular defect (II B–C according to Paprosky), the use of mass-produced endoprosthesis components would not allow restoring the biomechanics and anatomy of the hip joint, and therefore the decision was made to manufacture an individual acetabular component. Considering the patient's history and the number of previous surgical interventions, in order to prevent dislocation of the endoprosthesis head, a combination of an acetabular component with dual mobility and an individual acetabular component was used. To prevent periprosthetic infection, a femoral component coated with silver-doped two-dimensionally ordered linear chain carbon (TDOLCC+Ag) was used. The choice is justified by the proven bacterial activity against antibiotic-resistant strains of microorganisms,



a *b*

Figure 4. MSCT of the left hip joint with the 3D reconstruction in patient T. 123 months after surgical treatment: a – frontal projection, b – sagittal projection
Рисунок 4. МСКТ левого тазобедренного сустава с построением 3D реконструкции у пациентки Т. через 123 мес. после оперативного лечения:
а –фронтальная проекция, b – сагиттальная проекция

Figure 5. Plain radiograph of the pelvic bones of patient T. after the installation of an articulating spacer at the first stage of revision arthroplasty
Рисунок 5. Обзорная рентгенограмма костей таза пациентки Т. после установки артикулирующего спейсера на первом этапе ревизионного эндопротезирования

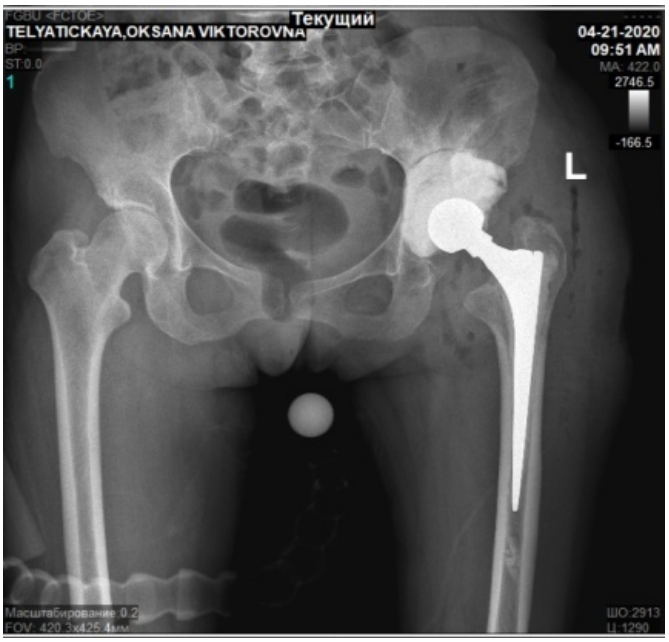


Figure 6. Control radiographs of the left hip joint of the patient T. after the installation of the respacer (direct projection)
Рисунок 6. Контрольные рентгенограммы левого тазобедренного сустава пациентки Т. после установки респейсера (прямая проекция)

the ability to prevent the microbial biofilms formation, high mechanical resistance, and the absence of a cytotoxic effect [12].

Before the second stage of the revision, inflammation markers were not detected in blood tests, in the left hip joint punctate, cytosis was 320 cells per 1 μl, the punctures were sterile. In August 2020, revision arthroplasty of the left hip joint was performed, the acetabular defect was replaced with an individual 3D component with cementation of a dual mobility system (Smith & Nephew POLARCUP Shell Cemented 47 mm) with bone cement (DePuy CMW 3–20 g with gentamicin) with the addition of vancomycin 1.0 g. Using bone cement (DePuy CMW 3–40 g with gentamicin) and the cement-in-cement technique, a femoral component (Zimmer CPT Cemented stem) was implanted with a TDOLCC+Ag coating, a head (Zimmer Zimtron Femoral Head Medium 28 mm) was installed (figure 7).

After 12 months radiographic features of instability or endoprosthesis components migration were not revealed. Postoperative scar was with no signs of inflammation. Range of motion in the left hip joint at the time of conducting this research: flexion up to 100 º, extension up to 10 º, abduction up to 30 º, adduction up to 15 º, internal rotation 20 º, external rotation 30 º. According to the Harris Hip Score the condition equaled 93 points; to the EQ-5D-5L scale – 1,000; to EQ VAS – 95%; to VAS – 1. Local or systematic toxic effects of silver were not detected. The pressure on the left lower limb is full, the lower limbs are of the same length. The patient returned to work.

Discussion

According to a study by the University of California, USA (2002–2008), the incidence of infectious complications after arthroplasty of large joints in HIV-infected patients is 0.6%, which is twice as high as in HIV-negative

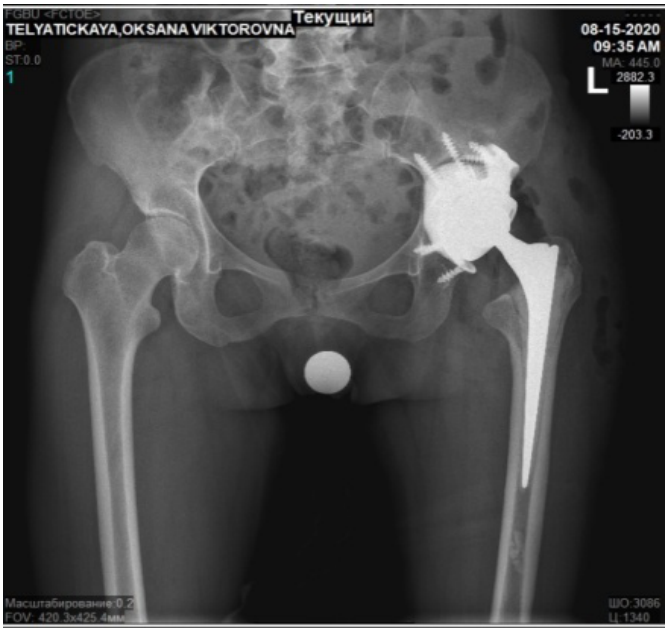


Figure 7. Control radiographs of the left hip joint of patient T. after implantation of a permanent endoprosthesis (direct projection)
Рисунок 7. Контрольные рентгенограммы левого тазобедренного сустава пациентки Т. после имплантации постоянного эндопротеза (прямая проекция)

patients [13]. Short-term observations of N. Lubega, et al. did not reveal any specific features in the postoperative period in 14 HIV-positive patients who underwent 18 total arthroplasties [14]. According to other researchers, in the period 2011–2015 the development of complications after hip arthroplasty occurred with approximately similar frequency in both HIV-positive and HIV-negative patients [15].

N.S. Fedorova, et al. proved that during dental prosthetics with clasp prosthesis made of cobalt-chromium alloy coated with TDOLCC+AgSp1, their biocompatibility improves, the hardness of the surface layers of the metal frame is 1.48 times higher and pronounced corrosion resistance is noted [16]. D.A. Mallin, when studying long-term present (4–7 years) ultrathin polymer plates coated with TDOLCC Sp1 and used in otolaryngological practice, showed the bactericidal role of the polymer implants carbon coating used in tympanoplasty [17]. V.V. Trubin in his works studied the reaction of soft tissues of rats to the installation of implants made of various metals without coating and coated with linear chain carbon. It has been noted that a carbine-containing coating improves the biocompatibility of implants made of various materials [18]. V.G. Babaev et al. report that, due to their structural and biological properties, TDOLCCs have high adhesion to the substrate, strength, elasticity, and good biocompatibility. TDOLCC is easily subjected to doping with various chemical elements, allowing one to impart additional physical and chemical properties to different surfaces [19].

In a clinical study by D.V. Tapalsky et al. *in vitro*, a pronounced surface bactericidal effect of TDOLCC+Ag coatings on microorganisms of several taxonomic groups, independent of their resistance to antibacterial drugs, was revealed. The ability of the coating to completely prevent the microbial biofilms formation by antibiotic-resistant clinical isolates of S. aureus and P. aeruginosa has been established. Mechanical stability of the silver-containing coating while maintaining the level of surface bactericidal activity even after prolonged abrasive treatment has also been revealed. Coatings based on TDOLCC did not cause any cytotoxic effects [20].

However, the experience of using an individual femoral component with an "anti-biofilm" coating as a permanent construction, especially in an HIV-positive patient with a high risk of perioperative infectious complications, was not found in the scientific literature.

N.S. Nikolaev et al. in an *in vivo* study showed statistically significantly better results in the treatment of periprosthetic infection when using spacers with implants coated with TDOLCC+Ag in comparison with the traditional method of treatment [14], which allowed us to successfully apply this method with the installation of a permanent component in relation to a patient from the increased infectious risk group.

Conclusion

The use of an individual 3D acetabular component in combination with dual mobility and the use of a femoral component coated with two-dimensionally ordered linear chain carbon with bone cement fixation with the addition of an antibiotic made it possible to stop the infectious process, improve limb function and improve the quality of life in an HIV-positive patient.

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Conflict of interest: *none declared.*

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Конфликт интересов

Авторы заявляют об отсутствии конфликта интересов.