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PERIPROSTHETIC JOINT INFECTION AFTER TOTAL KNEE ARTHROPLASTY. LESSONS LEARNED: A CASE REPORT AND LITERATURE REVIEW

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Introduction. The increasing proportion of the aging population and overweight people with various joint problems leads to an increased demand for joint replacements. As the number of joint arthroplasty surgeries continues to rise, the persistent incidence of periprosthetic joint infections highlights the need for a comprehensive and evolving approach. In addition to the preoperative period, it is also necessary to consider the course of the intraoperative, and to a greater extent the postoperative period, when the development of periprosthetic infection occurs. This case is indicative of the fact that underestimation of the importance of the postoperative period and control of risk factors can lead to the recurrence of infection. This negatively affects the economy due to an increase in the number of disabilities.

Case presentation. A 60-year-old female patient was diagnosed with a periprosthetic joint infection following total knee arthroplasty. The patient's premorbid background was aggravated by the presence of type 2 diabetes mellitus, arterial hypertension, secondary cardiomyopathy, and chronic iron-deficiency anemia. Single stage revision of knee arthroplasty, removal of prosthetic components, excision of degenerative tissue, prolonged antibiotic therapy as well as rehabilitation were ineffective, and the pain increased. Therefore, the patient is admitted for the two-stage revision surgery, removal of the endoprosthesis, and installation of a non-articulating cement spacer of the left knee joint.

Conclusion. Through a relevant literature search, we believe that uncorrected chronic iron-deficiency anemia in combination with uncontrolled diabetes mellitus, both in the preoperative and postoperative period for joint replacement, may increase the risk of the development of periprosthetic infection. Moreover, focusing patients' attention on the importance of the postoperative period and strict monitoring of health indicators will help reduce the likelihood of re-prosthetics.

Key words: periprosthetic joint infection; total knee arthroplasty; perioperative anemia; risk factors; a case report

INTRODUCTION

The progression of purulent-septic complications in orthopedic practice is a hot topic since it can lead to increased incidence of patients' disability, prolongation of hospital stay, and increased economic costs of patient treatment.

The demand for joint replacement surgeries in the United States is escalating, with about a million hip and knee replacements performed annually. Projections indicate a doubling of this number by 2030 [27]. While these procedures provide significant benefits, the incidence of periprosthetic joint infection (PJI) remains a challenging complication, affecting approximately 1% of patients undergoing total knee or hip arthroplasty [7]. Moreover, the one-year mortality rate for PJI after hip replacement is reported to be 4.22%. Over five years, the mortality rate increases to 21.12%. In particular, the mortality rate during total hip revision for infection is still high [20, 32].

In Kazakhstan, according to statistics from the National Scientific Center of Traumatology and Orthopedics named after Academician N. D.

Batpenov, orthopedic and traumatological activity over the past 20 years increased significantly. If in 2001 only 48 orthopedic surgeries for total joint replacement were performed, in 2020 the number of operations increased to 20 157. Of these: knee arthroplasty – 6 910 (34.3%), hip arthroplasty – 4 952 (24.6%), arthroscopic operations – 2 750 (13.6%), and spinal fusion – 1 175 (5.8%) [4]. Along with the growth in trauma and orthopedic care provided to the population of Kazakhstan, we have also encountered cases of postoperative complications, such as periprosthetic infections.

Treatment of periprosthetic infections often requires repeated revisions and prolonged antibiotic therapy. But despite these measures, treatment failure and reinfection are common [15, 31]. Considering the problems associated with the treatment of these infections, an in-depth study of risk factors and prevention of infection is needed.

In this article, we highlight all the problems associated with treating periprosthetic infection in Kazakhstan. This case is interesting due to the ineffectiveness of a one-stage revision and the development of persistent culture-negative periprosthetic joint infection. Moreover, the patient had a high chance of developing a periprosthetic infection due to the presence of all modifiable and non-modifiable risk factors such as age, overweight, knee replacement, diabetes mellitus, hypertension, and chronic heart insufficiency, as well as chronic iron-deficiency anemia. The presence of all these factors without correction probably led to the development of periprosthetic infection and the inefficiency of single-stage revision.

CASE PRESENTATION

Patient Information. A 60-year-old female patient was hospitalized in the purulent traumatology department with complaints of pain and limited movement in the left knee joint and with the presence of a wound.

It is known from the patient's history that pain in the left knee joint first appeared 8 years ago. Therefore, in June 2022, she underwent total left knee arthroplasty using the Stryker Triathlon® PS (non-antibiotic laded cement) system (USA). Then, in the early postoperative period, pain and dysfunction of the left knee joint appeared and started to intensify. The patient asked for medical help, and revision knee arthroplasty with the CHUNLI (gentamicin bone cement 40g) system (China) was performed in October 2022. The postoperative period was uneventful. But at the 2nd stage of rehabilitation, the patient noticed the appearance of a swelling on the left knee joint at the site of the postoperative scar. The suppuration was subsequently drained at a local clinic. With the symptoms mentioned above she was admitted to the hospital for two-stage revision knee arthroplasty.

The patient is registered with an endocrinologist with a diagnosis of diabetes mellitus type 2 with multiple complications, and takes metformin 850 mg twice a day. Glycemia varies between 8-15 mmol/l. She is also registered with a cardiologist for severe arterial hypertension with the highest risk of cardiovascular events and secondary cardiomyopathy with subsequent chronic heart failure. Do not take basic therapy.

Family, epidemiological and psycho-sociological, and gynecological history without any features.

Clinical Findings. At the initial examination, the patient weighed 73 kg (BMI = 30,1 kg/m2). The visible areas of the skin had a physiological color. The patient's initial body temperature was recorded as 36.4°C. The patient exhibited spontaneous breathing with a respiratory rate of 17-18 breaths per minute. Vesicular breathing sounds were heard in the lungs across all fields with SpO2 -98%. The patient's heart sounds were muffled and rhythmic. Blood pressure reached 130/80 mm Hg. with a heart rate of 73 beats per minute.

Local status: an aseptic bandage moistened with moderate serous-purulent discharge was applied to the left knee joint. Under the bandage, in the lower third of the postoperative scar, a fistula wound measuring up to 3.0 cm in diameter formed. Movements in the left knee joint are severely limited with no signs of peripheral circulatory impairment in the affected limb.

Timeline. The patient’s medical history is highlighted in Figure 1.

Diagnostic Assessment. The patient's primary laboratory test results showed the following changes in the general blood test in the form of moderate hypochromic anemia and an increase in the erythrocyte sedimentation rate. This pattern persisted throughout the entire period of hospitalization (Fig. 2). Coagulation values were relatively normal with a mild trend to hypocoagulation. Biochemistry showed only hyperglycemia within the range of 8-12 mmol/l with no other abnormalities.

There were no changes observed in the urine test.

Furthermore, cultures were taken several times from the patient's wound area during the hospitalization and before. Only one culture revealed the growth of opportunistic pathogenic flora – *Staphylococcus epidermidis*. It was sensitive to ceftriaxone, levofloxacin, gentamicin, vancomycin, doxycycline, meropenem, and oxacillin, but resistant to azithromycin, ampicillin, and amoxiclav. A sampling defect involving the skin cannot be ruled out.

Upon admission to the hospital, the patient underwent a full examination, including instrumental data from different systems. ESG showed mild

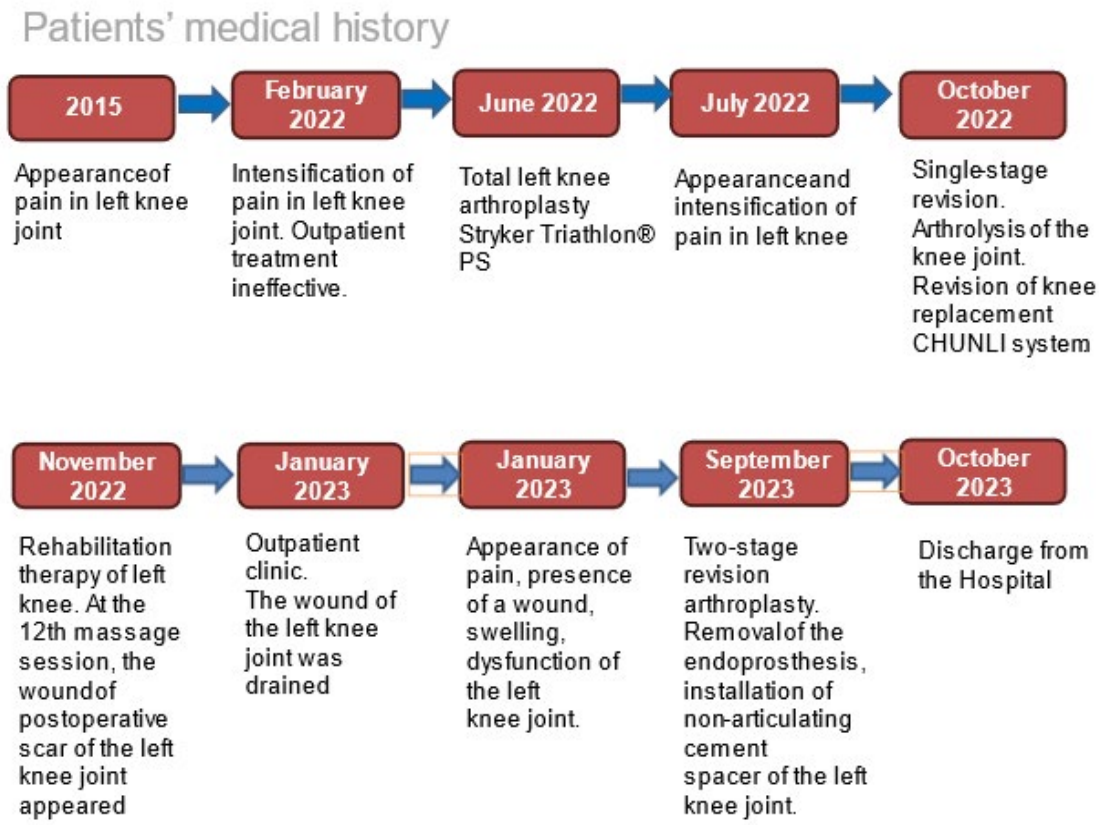

Figure 1 – The patient's medical history

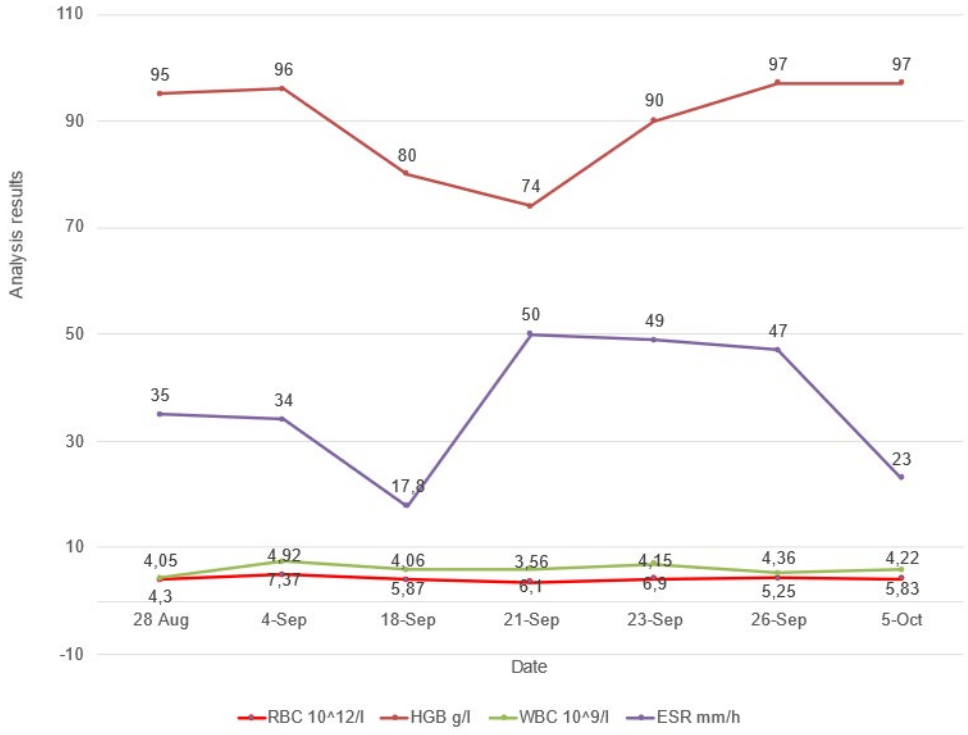

Figure 2 – Blood parameters during hospitalization

sinus tachycardia with a heart rate of 90 beats per minute. Ultrasound of the heart confirmed the diagnosis of chronic heart failure and showed ECHO signs of diastolic LV dysfunction with an ejection fraction of 53%. That was a superficial gastritis on fibrogastroduodenoscopy and a normal picture of the lungs on chest X-ray.

Ultrasound of the joint showed the presence of fluid in the left knee joint. X-ray showed condition after cemented revision knee arthroplasty, R-signs of endoprosthesis instability.

Before surgery, the patient also underwent fistulography. A contrast agent was injected into the fistulous tract located in the soft tissues along the anterior surface of the left leg. The contrast reached the contour of the proximal leg of the tibial component of the endoprosthesis, and extended proximally along the contour of the silicone liner and the femoral component of the endoprosthesis (Fig. 3A).

Based on the above, the preliminary diagnosis of periprosthetic joint infection after the total left knee arthroplasty in June 2022, condition after revision arthroplasty of the left knee joint from October 2022 with left peroneal nerve neuropathy was made. In addition, the patient was diagnosed with the following concomitant diseases such as chronic hypochromic

Figure 3 – Visual examination. A – fistulography at the time of admission before surgery; B – After revision, removal of the endoprosthesis, installation of non-articulating cement spacer of the left knee joint

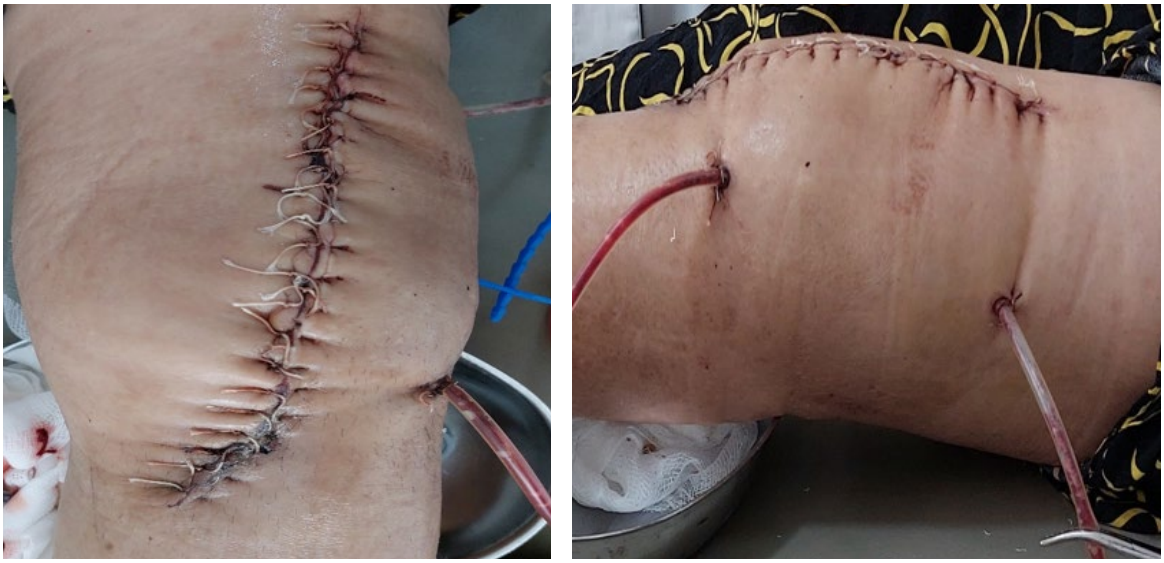

Figure 4 – Condition of the suture on the knee joint after 7 days of surgical intervention

anemia, diabetes mellitus, and arterial hypertension with a high risk of cardiovascular events, and secondary cardiomyopathy with an ejection fraction of 58%.

According to the results and diagnosis mentioned above, it was decided to perform a two-stage revision arthroplasty. After surgery, the patient underwent a control radiography of the left knee joint (Fig. 3B).

Surgical treatment. The patient underwent one of the two stages of revision arthroplasty of the left knee joint under spinal anesthesia. During surgery, the endoprosthesis was removed. Curettage was performed, pathological granulations and immobilized areas of muscles were removed, and corroded areas of the femur and tibia were removed. A non-articulating cement spacer was modeled and installed using 3 packs of cement with the antibiotic Vancomycin 2 g, and 2 packs of nanosilver. The wound was drained according to Redon and sutured tightly in layers. The operation was performed without the use of a tourniquet. The total intraoperational blood loss was 500 ml. The total duration of the intervention was 170 minutes.

Antimicrobial therapy. Initiation of empirical antibiotic therapy on the 5th day of hospital stay with ceftriaxone 1 g intramuscularly 2 times a day, reflecting a broad-spectrum choice to cover potential pathogens. The subsequent adjustment and switching to levofloxacin at a dosage of 500 mg intravenously 2 times a day was performed on the results of the sensitivity of isolated microorganisms.

Antianaemic therapy. RBC transfusion was performed in the patient to correct acute postoperative anemia and for correction of moderate iron-deficiency anemia patient received ferric sulfate in combination with ascorbic acid in the dosage 320mg/60 mg orally 2 times per day. Ferric (III) hydroxide destrane in the dosage of 200 mg intravenously 1 time a day also was used as antianaemic therapy for 5 days.

Nutritional Support. Nutrition was a vital component of managing diabetes and included adequate protein provision with a restriction on highly digestible carbohydrates.

Anticoagulant Therapy. The patient was administered nadroparin calcium 2850 IU/0.3 ml subcutaneously once a day.

Pain Management. Pain relief was carried out with Metamizole sodium 1000 mg and ketoprofen 100 mg intramuscularly, and lornoxicam 8 mg intravenously was also used.

Other. The patient also received basic therapy for the treatment of diabetes mellitus, antihypertensive drugs, and gastroprotective medications. Moreover, the patient received magnetic therapy and kinesiotherapy of the left lower limb. Condition of postoperative scar of the left knee joint showed no signs of inflammation (Fig. 4).

Follow-Up and Outcomes. On the 10th day after surgery, the patient was transferred to the outpatient stage of treatment. The patient followed all recommendations and was committed to treatment. Over the next months, the patient noted an improvement in her condition in the form of relief of pain in the left knee joint. No adverse or unanticipated events were observed in a patient after surgery.

DISCUSSION

Over the past few years, there has been an increased interest of researchers in the treatment of infections after large joint replacement, largely due to the treatment difficulties.

Two-stage revision of infected prosthesis is believed to be a gold-standard procedure and preferred method of treating deep periprosthetic infection, providing the highest eradication rate and disease-free course. However according to a systematic review published in 2014 by authors H. A. Leonard et al., single-stage revision is associated with similar reinfection rates but superior functional outcomes when compared with two-stage revision [14]. Moreover, Annemarie L. Goud et al. in their meta-analysis published in 2023 confirm that the incidence of reinfection in patients after one- and two-stage hip and knee arthroplasty was the same. The meta-analysis concludes that an individualized approach is necessary for selecting treatment tactics, taking into account the unique characteristics of each patient [8]. But it is also necessary to consider that most of the literature on two-stage arthroplasty follows patients for two years, so there is a huge risk of reinfection in the long term [21].

In this clinical case, the patient underwent one-stage revision arthroplasty, but we observed a recurrence of periprosthetic infection and, therefore, the treatment tactics were changed to two-stage revision arthroplasty. It is known that repeated surgeries are associated with higher morbidity and mortality and are poorly tolerated by patients. Increased length of stay in the intensive care unit and repeated orthopedic operations, particularly 2-stage reimplantation raises economic costs and reduces the quality of life of patients [25].

So, the patient's case presents a complex scenario where various modifiable and non-modifiable risk factors converged, significantly increasing the likelihood of developing a periprosthetic joint infection following knee replacement surgery. These factors collectively contributed to the inefficiency of a single-stage revision approach. Therefore, we are considering this clinical case to identify the causes of reinfection and study all risk factors.

According to systematic review and meta-analysis, such risk factors as diabetes mellitus and congestive heart failure as well as prior joint infection in this patient are considered significant risk factors for the development of PJI. [22, 24]

E. C. Rodriguez-Merchan et al. published a study where all risk factors are considered. For instance, authors confirm routine administration of tranexamic acid during orthopaedic surgery may reduce the risk of developing PJI. Perioperative administration of vancomycin or clindamycin was associated with a higher risk of PJI after total knee replacement compared with cefazolin. [23]

Two cohort studies concluded that men are at higher risk of developing PJI than women. In addition to gender, Korean authors found that length of stay (≥35 days) and the use of blood transfusions were also risk factors for the development of PJI. [13]. Whereas English scientists believe that patients older than 70 years are in a lower risk of developing PJI compared with patients younger than 60 years [16]. But in other studies frailty was associated with long-term risk of developing PJIs. And this is interesting because older patients usually have a high score of frailty [17].

The presence of diabetes mellitus in a patient is also considered a significant risk factor. M. A. Ahmad et al in their systematic review suggest that PJIs in patients with diabetes mellitus (1.9%) were significantly higher than in patients without diabetes mellitus (1.2%). Infection was more common in patients with diabetes (1.9%) [1] Other authors also support the statement that the presence of diabetes mellitus in patients undergoing primary TKA increases the risk of deep infection. [34] Moreover, poor glycemic monitoring was associated with a higher risk for SSI after TJA [26].

Also, the literature review showed an interesting formula for the development of PJI. The HbA1c/albumin ratio may have a higher prognostic capacity among other risk factors. It suggests that patients with an HbA1c/albumin ratio above 2.37 mg/dl should be closely monitored for the risk of periprosthetic infection [36]. These indicators were not considered in this case.

Since all synovial fluid cultures in our patient were negative, we can argue that two-stage revision arthroplasty was preferable in tactics. This theory confirmed by the study that the proportion of culture-negative periprosthetic joint infections can range from 5 to 42% of all PJIs. Additionally, the research suggests that a two-stage revision arthroplasty approach is preferable in these cases, with a reported success rate ranging from 70 to 100% [11]

It's worth noting that malnutrition can have various impacts on overall health and immune function, potentially increasing the susceptibility to infections. For instance, patients with albumin lower than 35 g/l are associated with a higher risk of PJI [29, 30]

Perioperative anemia may play a significant role in suppressing cellular mechanisms and autoimmune functions, potentially contributing to the increased risk of infection [9, 10, 33]. But some studies argue that in revision arthroplasty, low hemoglobin levels are not a negative factor for infection, and therefore blood transfusions should be avoided [35]. It should be noted that the use of tranexamic acid during revision arthroplasty reduces the risk of PJI [12]. In Kazakhstan, we are using TXA only in the presence of severe blood loss during the surgery.

Our patient had preoperative anemia, so we believe that it is a significant risk-factor. Some studies suggest that iron deficiency anemia is associated with a higher risk of SSI and PJI compared with other risk factors [3, 19, 28].

Furthermore, patients with coronary heart disease or anemia are associated with lower rates of successfully treated infections [6].

The duration of surgery (over 90 minutes) and prolonged tourniquet time (over 60 minutes) were found to be the most important risk factors in a case-control research by Blanco et al. Furthermore, among the important factors mentioned by the scientists include high ASA levels (III-IV), diabetes, obesity, and the use of cement without antibiotics [5]. Most of the criteria were present in our clinical case, which included a surgical time of more than 90 minutes for both the primary prosthesis placement and revision (120 minutes and 170 minutes). The patient was overweight, had diabetes mellitus, and had an ASAIII level. The primary prosthesis was placed without the use of antibacterial cement.

A perioperative care approach with modifiable risk factor correction is required, given the patient's high risk of developing a PPI due to the confluence of all known factors. For instance, using antimicrobial cement and managing surgical time during the initial prosthesis implantation may help avoid the development of a PPI.

Despite the fact that periprosthetic infection risk factors have been extensively researched, this case emphasizes the issue of patients' ignorance of these factors' significance. Periprosthetic infection can be prevented in large part by adopting a personalized, patient-centered strategy for each patient and perhaps by implementing awareness-raising campaigns like «PPI schools».

In summary, appropriate management of post-operative glycemia, obesity, malnutrition, metabolic syndrome, preoperative anemia, and smoking cessation, management of surgical time can help minimize the risk of PJI. To improve the functional

recovery of patients without infectious complications we need to manage a patient's rehabilitation course [2, 18].

Therefore, optimization of modifiable risk factors for PJI should be attempted in clinical practice and requires high-quality RCTs.

Patient Perspective. After the surgery and installation of a non-articulating spacer with an antibiotic, the patient had no active complaints. She moved independently on crutches, with a measured load on the left lower limb, and was relatively satisfied with the treatment received. However, the patient is afraid that pain in the joint may reappear. To avoid the recurrence of periprosthetic infection, the patient was given recommendations, in addition to standard rehabilitation therapy, to monitor and promptly adjust the level of glycemia and hemoglobin.

Author Contributions:

A. Konkayev, M. Konkayeva – conceptualization, supervision.

A. Konkayev, M. Konkayeva, B. Azimova – methodology.

M. Konkayeva – validation, project administration, funding acquisition.

A. Konkayev, M. Konkayeva, A. Yeltayeva – formal analysis.

A. Konkayev – investigation.

A. Konkayev, M. Konkayeva, A. Kadralinova, B. Azimova, A. Yeltayeva – resources.

B. Azimova, A. Kadralinova – data curation.

A. Kadralinova, B. Azimova, A. Yeltayeva, N. Zhanarystan – writing: original draft preparation.

A. Konkayev, M. Konkayeva – writing: review and editing.

A. Kadralinova, B. Azimova, A. Yeltayeva – visualization.

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Institutional Review Board Statement. The study was conducted in accordance with the Declaration of Helsinki, and approved by the Local Ethics Committee of the National Scientific Center of Traumatology and Orthopedics named after Academician N. D. Batpenov (Protocol №4 from 09 November 2022).

Informed Consent Statement. Written informed consent was obtained from the individual (-s) and their for the publication of any potentially identifiable images or data included in this article.

Data Availability Statement. The data presented in this study are available on request from the corresponding author. The data are not publicly available to ensure the confidentiality of the patients' personal information.

Conflicts of Interest. The authors declare no conflicts of interest.

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ПЕРИПРОТЕЗНАЯ ИНФЕКЦИЯ СУСТАВА ПОСЛЕ ТОТАЛЬНОГО ЭНДОПРОТЕЗИРОВАНИЯ КОЛЕННОГО СУСТАВА. ИЗВЛЕЧЕННЫЕ УРОКИ: КЛИНИЧЕСКИЙ СЛУЧАЙ И ОБЗОР ЛИТЕРАТУРЫ

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Введение. Увеличение доли стареющего населения, людей с избыточным весом и различными проблемами суставов приводит к увеличению спроса на замену суставов. Поскольку число операций по артропластике суставов продолжает расти, постоянная заболеваемость перипротезными инфекциями суставов подчеркивает необходимость комплексного и развивающегося подхода. Помимо предоперационного периода необходимо учитывать также течение интраоперационного периода, и в большей степени послеоперационного периода, когда происходит развитие перипротезной инфекции. Данный случай свидетельствует о том, что недооценка значения послеоперационного периода и контроля факторов риска может привести к инфекции. Это негативно влияет на экономику из-за роста случаев инвалидазации.

Клинический случай. У пациентки 60 лет после тотального эндопротезирования коленного сустава диагностирована перипротезная инфекция сустава. Преморбидный фон больной отягощался наличием сахарного диабета 2 типа, артериальной гипертензии, вторичной кардиомиопатии, хронической железодефицитной анемии. Одномоментная ревизия эндопротезирования коленного сустава, удаление компонентов протеза, иссечение дегенеративных тканей, длительная антибиотикотерапия, а также реабилитация оказались неэффективными, болевой синдром усилился. В связи с этим пациент госпитализирован на двухэтапную ревизионную операцию, удаление эндопротеза и установку неартикулирующего цементного спейсера с антибиотиком левого коленного сустава.

Заключение. На основании соответствующего поиска литературы мы полагаем, что некорригированная хроническая железодефицитная анемия в сочетании с неконтролируемым сахарным диабетом как в предоперационном, так и в послеоперационном периоде эндопротезирования суставов может повышать риск развития перипротезной инфекции. Более того, акцентирование внимания пациентов

на важности послеоперационного периода и строгий контроль показателей здоровья помогут снизить вероятность повторного протезирования.

Ключевые слова: перипротезная инфекция сустава; тотальное эндопротезирование коленного сустава; периоперационная анемия; факторы риска; клинический случай

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ЖАЛПЫ ТІЗЕ ЭНДОПРОТЕЗІНЕН КЕЙІН БУЫННЫҢ ПЕРИПРОТЕЗДІК ИНФЕКЦИЯСЫ. АЛЫНҒАН САБАҚТАР: КЛИНИКАЛЫҚ ЖАҒДАЙ ЖӘНЕ ӘДЕБИЕТКЕ ШОЛУ

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Кіріспе: қартайған халықтың, артық салмағы бар адамдардың және әртүрлі буын проблемаларының үлесінің артуы буындарды ауыстыруға сұраныстың артуына әкеледі. Бірлескен артропластика операцияларының саны артып келе жатқандықтан, буындардың перипротездік инфекцияларының тұрақты жиілігі кешенді және дамып келе жатқан тәсілдің қажеттілігін көрсетеді. Операция алдындағы кезеңнен басқа, операция ішілік кезеңнің барысын және перипротездік инфекцияның дамуы орын алған операциядан кейінгі кезеңді де ескеру қажет. Бұл жағдай операциядан кейінгі кезеңнің мәнін жете бағаламау және қауіп факторларын бақылау инфекцияға әкелуі мүмкін екенін көрсетеді. Бұл мүгедектік жағдайларының өсуіне байланысты экономикаға теріс әсер етеді.

Клиникалық жағдай: 60 жастағы пациентке тізе буынының жалпы эндопротезінен кейін буынның перипротездік инфекциясы диагнозы қойылды. Науқастың преморбидті фоны 2 типті қант диабеті, артериялық гипертензия, қайталама кардиомиопатия, созылмалы темір тапшылығы анемиясының болуымен ауырлады. Тізе буынының эндопротезін бір мезгілде қайта қарау, протез компоненттерін алып тастау, дегенеративті тіндерді кесу, ұзақ мерзімді антибиотикалық терапия, сондай-ақ оңалту тиімсіз болып шықты, ауырсыну синдромы күшейе түсті. Осыған байланысты пациент екі сатылы ревизиялық операцияға, эндопротезді алып тастауға және сол жақ тізе антибиотикімен артикуляцияланбайтын цемент аралығын орнатуға жатқызылды.

Қорытынды. Тиісті әдебиеттерді іздеу негізінде біз операция алдындағы және операциядан кейінгі бірлескен эндопротездеу кезеңінде бақыланбайтын қант диабетімен біріктірілген созылмалы темір тапшылығы анемиясы перипротездік инфекцияның даму қаупін арттыруы мүмкін деп санаймыз. Сонымен қатар, пациенттердің назарын операциядан кейінгі кезеңнің маңыздылығына аудару және денсаулық көрсеткіштерін қатаң бақылау қайта протездеу мүмкіндігін азайтуға көмектеседі.

Кілті сөздер: буынның перипротездік инфекциясы; тізе буынының толық эндопротезі; периоперациялық анемия; қауіп факторлары; клиникалық жағдай