

Acute kidney failure after total knee arthroplasty revision with antibiotic-impregnated cement spacer

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Abstract

Gentamicin-impregnated cement beads and spacers are frequently used in case of infective complications after Total Knee Arthroplasty (TKA). A great number of studies in the literature demonstrated that the local administration of gentamicin produces high local antibiotic levels but low serum and urine gentamicin concentrations. Gentamicin-impregnated cement spacer can induce nephrotoxicity in patients presenting major renal impairment susceptibility. We report a case of acute renal failure using a gentamicin-impregnated block spacer. An 83-year-old woman underwent a gentamicin-impregnated bone-cement spacer implant because of an infected TKA removal. Three days later patient clinical status got worse reporting a decreased urine output and increasing C-reactive protein (CRP), Serum Creatinine (SCr) and Blood Urea Nitrogen (BUN). Because the symptoms could be related to the knee spacer lead us to the decision of gentamicin-impregnated cement spacer removal. The day following the removal procedure showed progressive improvement of general condition with evidence of SCr and BUN normalization. Gentamicin-impregnated cement spacer can induce nephrotoxicity in patients presenting major renal impairment susceptibility.

Introduction

Deep infection after Total Knee Arthroplasty (TKA) is a serious complication with a reported incidence of 1% to 4.4%.^{1,2} Although different treatments have been described in the literature, 2-stage revision arthroplasty remains the most used and successful technique with a success rate averaging 92%.³⁻⁵

The major disadvantage of this method is the time between stages, which is often associated with pain, functional impairment

and knee instability.^{6,7} Furthermore, re-implantation is often challenging because of scar formation, shortening of the extensor apparatus of the knee and retraction of the joint capsule and ligaments.

Gentamicin-impregnated cement beads and spacers are routinely used in 2-stages revision procedures because considered effective and safe from gentamicin-induced complication showing high local antibiotic levels and low serum and urine drug concentrations.⁸ We report here a rare case of acute renal failure after the implantation of a gentamicin-impregnated block spacer for the treatment of an infected TKA.

Case Report

An 83-year-old woman with a medical history of chronic atrial fibrillation, hypertension, and dyslipidemia, referred to our department for left knee osteoarthritis and she underwent a TKA surgery. From the clinical record the surgery, the hospitalization and the early rehabilitation period were uneventful. Three months later she was re-admitted in our department because of a painful left knee, joint swelling, and wound dehiscence. The microbiological analysis of the wound showed a multi-resistant pseudomonas aeruginosa infection. Preoperative laboratory test showed serum creatinine (SCr) 1.2 mg/dL (reference range 0.5–1.5), blood urea nitrogen (BUN) 29 mg/dL (5–25), C-reactive protein (CRP) 10,70 mg/dL (normal <0.5), hemoglobin 12.1 g/dL (12–16) and WBC count 4,71 X 10³/mm³ with a normal differential. The first attempt of treatment was a deep wound revision and joint washing associated with postoperative intravenous cefepime and oral ceftazidime administration as required by the infectious disease specialist.

Because there was not local and laboratory test improvement with relapsed symptoms after 2 weeks of hospitalization, the patient underwent a TKA removal and a molded gentamicin-impregnated cement spacer implantation (0.5g gentamicin per 40 g batch), Refobacin® Bone Cement R, BIOMET-INC. (Figure 1).

Surgery progressed without complications. During the second postoperative day, hemoglobin dropped to 8.5 g/dL and 1 unit of packed red blood cells was administered. Knee and wound showed progressive improvement and stitches were removed fifteen days after surgery. C-reactive protein dropped to 3.8 mg/dL.

After the initial local and general improvement, three days later the patient's clinical status got progressively worse: the

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Statement of informed consent: Informed consent was obtained. The patient and the patients were informed that data concerning the case would be submitted for publication and they agreed.

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patient started presenting shortness of breath, fatigue, confusion, nausea, weakness, irregular heartbeat. Hemoglobin value dropped again to 8.1 g/dL (needing of 1 more unit of packed red blood cells), urine output decreased to 700 mL/day, CRP increased to 10,80 mg/dL, SCr increased to 2,00 mg/dL (Figure 2) and BUN to 40 mg/dL (Figure 3). Heart, abdominal and

vascular ultrasonography, thoracic CT-scan and brain MRI were performed and resulted negative for any other disease or medical condition that could explain the clinical worsening.

During the following 5 days, despite the administration of diuretics and modulation of an adequate fluid therapy as prescribed by the nephrologist, who performed daily consultation, serum creatinine continued to increase up to 6.4 mg/dL and BUN up to 67 mg/dL (Figure 2 and 3), then 3 cycles of hemodialysis were required. The serum level of gentamicin was investigated then resulted in a concentration of 0,5 mcg/mL. Despite the serum level of gentamicin was low, after a multispecialty audit, the clinical suspicion was nephrotoxicity caused by the gentamicin released from the knee spacer, and we decided to perform the removal of the spacer as a lifesaving procedure. The Gentamicin-impregnated spacer was removed the day after, and the knee was stabilized with an arthrodesis with an external fixator and the patient was admitted to the Intensive Care Unit for 7 days before her return in the orthopedic department, when the acute renal failure resolved.

SCr and BUN values showed a progressive decrease until normalizing in about 30 days after the spacer removal (Figures 2 and 3). After 1 year, at the X-rays evidence of knee bone fusion, the external fixator was removed. At the last follow-up, 3 years later, the patient continued to be asymptomatic for kidney failure and returned to her daily activity.

Discussion

The use of aminoglycoside-impregnated cement for the treatment of infected total hip and knee arthroplasties, in a two steps procedure, is a common practice. A cement spacer may be useful for tensioning the ligaments to facilitate the TKA revision after eradication of the infection. It allows high concentrations of antibiotics locally, avoiding systemic value increasing.⁹

It's well known that aminoglycoside antibiotics, such as gentamicin and tobramycin, show reliable effectiveness in osteomyelitis and prosthetic infections so they are frequently used despite potential side effects such as otovestibular and nephrotoxicity. Effectiveness of aminoglycosides is concentration-dependent,¹⁰ while their toxicity is time-related so once-daily administration of a high dose of aminoglycosides has been advocated as safe. To reach a high local concentration it's possible to use gentamicin-



Figure 1. Postoperative X-ray after the implantation of the gentamicin-impregnated knee spacer.

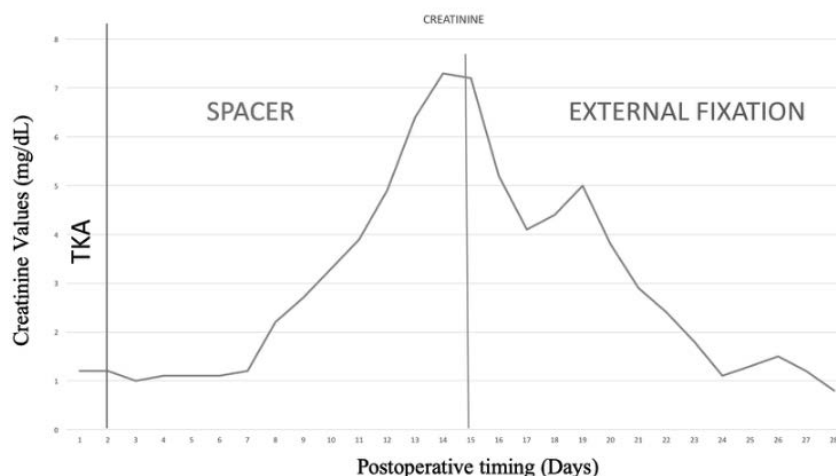


Figure 2. Time related variance of serum creatinine (SCr) level before and after spacer removal.

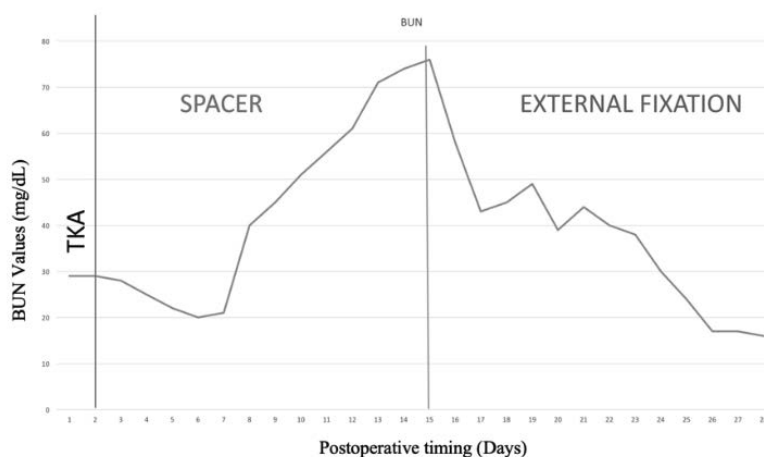


Figure 3. Time related variance of blood urea nitrogen (BUN) level before and after spacer removal.

impregnated cement as suggested by a lot of authors in literature with good and reproducible results.¹¹ Only a small quantity of gentamicin cement is released in the blood (5%–8%) as demonstrated by many studies⁸ depending on diffusion that is related to the surface area. To enhance the local concentration of gentamicin it's possible to use beads increasing diffusion area. This kind of local treatment produces high local antibiotic levels and low serum and urine gentamicin concentrations¹² resulting to be safe and effective in the majority of arthroplasty infections and showing a low rate of adverse events.¹³ However, few reports indicated patients developing acute renal failure after the placement of aminoglycoside-laden spacers.¹⁴

Menge *et al*¹⁵ showed a higher rate of acute renal dysfunction in a cohort of patients undergone antibiotic-impregnated cement spacer implantation presenting medical comorbidities. Especially in old age, the relevance of non-clinical apparent kidney insufficiency in patients who undergo total joint replacement is well known. Many authors have shown that a chronic kidney disease (CKD), defined as an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m², in patients undergoing TKA, can be a risk factor for greater hospitalization and post-operative morbidities, including a worsening of the renal function itself; a significant increase in these complications, is shown with eGFR values <45-50 mL/min/1.73 m².¹⁶⁻¹⁸

Our patient at admission presented mild renal impairment, atrial fibrillation, dyslipidemia, and hypertension, however from the first hospitalization until the gentamicin-impregnated cement spacer implantation, despite the appearance of PJI, no alteration of renal function was detected: the acute renal failure could reasonably be traced back to the procedure.

Conclusions

According to the literature review and others few case reports, our case report want

to suggest to be aware of the potential aminoglycoside-induced nephrotoxicity also in local treatment as the use of gentamicin-impregnated cement, block spacer and bread especially in patients presenting comorbidities and major risk factor of renal susceptibility, also without preoperative clinical signs of renal failure. In the patient with comorbidities and major risk factors, the serum gentamicin dosage cannot be used to discriminate patients that can benefit from implant removal.

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