



A Case of Hypercalcemia and Antibiotic-Related Acute Kidney Injury Following Implantation of Antibiotic Impregnated Calcium Sulfate Beads

Douglas Challener M.D. and Omar Abu Saleh , M.B.B.S.

Division of Infectious Diseases, Department of Internal Medicine, Mayo Clinic, Rochester, USA

Dear Editor,

Calcium sulfate beads are increasingly used during revision orthopedic surgery as a vehicle for local antibiotic delivery [1]. They offer several advantages over polymethylmethacrylate (PMMA) beads as they are absorbable, are more efficient at local delivery of antibiotics, and lack the exothermic reaction often associated with PMMA, which allows them to be used with less heat-stable antibiotics. However, given the high efficiency of drug elution and their absorbability, calcium sulfate beads carry the risk of both antibiotic toxicity and hypercalcemia. There is limited literature available regarding the risk of hypercalcemia associated with calcium sulfate beads. We present a case of hypercalcemia and antibiotic-related acute kidney injury following implantation of antibiotic impregnated calcium sulfate beads. This case study did not require Institutional Review Board approval.

A 90-year-old woman with a medical history of atrial fibrillation presented to the Mayo Clinic Hospital in Rochester, USA, in February 2017 following a fall during which she sustained a left trochanteric fracture. She underwent open reduction and internal fixation surgery that was complicated by atrophic nonunion requiring revision with exchange of hardware in June 2017. Her postoperative course was further complicated by a deep surgical site infection with methicillin-susceptible *Staphylococcus*

aureus and *Enterobacter cloacae*. On January 1, 2018, she underwent hardware removal, irrigation and debridement, and placement of PMMA beads loaded with 4.8 g of gentamicin and 4 g of vancomycin. Five days later, the PMMA beads were removed, and an intramedullary rod was implanted along with calcium sulfate beads loaded with 7.2 g of gentamicin and 6 g of vancomycin. She did well during the immediate postoperative period and was discharged to a rehabilitation facility.

On January 13, 2018, the patient was hospitalized with acute confusion, worsened renal function (WRF) with a creatinine level of 360 $\mu\text{mol/L}$ that had increased from a baseline of 80 $\mu\text{mol/L}$, and a serum calcium level of 3.44 mmol/L (corrected for hypoalbuminemia). Further evaluation revealed appropriately suppressed parathyroid hormone (PTH) of 7.2 ng/L, PTH related peptide of 3.7 pg/L, normal 25-hydroxy vitamin D and 1,25-hydroxy vitamin D levels, and normal serum protein electrophoresis. A renal ultrasound excluded post-renal obstruction, and the urinalysis was bland without casts.

A computed tomography scan of the lower extremity revealed accelerated resolution of the absorbable calcium sulfate beads. Her random gentamicin level one week after surgery was 6.1 $\mu\text{mol/L}$ (the toxic trough level is considered $>4.2 \mu\text{mol/L}$), and her random serum vancomycin level was 19.6 $\mu\text{mol/L}$. These

Received: January 11, 2019
Revision received: February 11, 2019
Accepted: April 10, 2019

Corresponding author: Omar Abu Saleh, M.B.B.S.
Division of Infectious Diseases, Department of Internal Medicine, Mayo Clinic, 200 First St S.W., Rochester, MN 55905, USA
Tel: +1-507-284-3309, Fax: +1-507-255-7767
E-mail: Abusaleh.Omar@mayo.edu

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findings raised suspicions of hypercalcemia related to absorption of the calcium sulfate beads and acute kidney injury secondary to hypercalcemia and antibiotic toxicity.

Because of the significant WRF and confusion, our patient underwent temporary hemodialysis for three weeks. She exhibited partial recovery of renal function with a final stable creatinine level of 160 $\mu\text{mol/L}$. At this time, her serum ionized calcium level was 1.2 mmol/L (reference range 1.16–1.32 mmol/L).

In a case series involving 15 patients who underwent revision surgery for prosthetic joint infection using absorbable calcium sulfate beads, three patients developed hypercalcemia (two were transient and asymptomatic, and one had severe hypercalcemia [calcium level of 3.5 mmol/L] on postoperative day 5, requiring intensive care unit [ICU] admission) [2]. Three other cases of clinically significant hypercalcemia in association with calcium sulfate bead utilization have also been reported [3-5]. Interestingly, all these cases presented more than 72 hours following surgery. The total volume of the calcium sulfate beads, dose of antibiotics, and accelerated absorption of the beads were potential risk factors for hypercalcemia related to the absorption of oral calcium sulfate beads.

The present case illustrates the importance of recognizing the impact of a local antibiotic vehicle on clinical outcome in terms of both the efficacy and toxicity associated with the beads themselves. In addition to assessing serum calcium level, elevated antibiotic levels can indicate accelerated absorption of the beads. Previous studies have reported hypercalcemia, but this is the first to also demonstrate super therapeutic systemic levels of antibiotics related to absorption of calcium sulfate beads. This cause of hypercalcemia should be considered when evaluating postoperative kidney injury or confusion.

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

ORCID

Douglas Challener <https://orcid.org/0000-0002-6964-9639>

Omar Abu Saleh <https://orcid.org/0000-0003-4955-5544>

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