Severe Hypercalcemia Following the Implantation of Antibiotic Impregnated Calcium Sulfate Beads for Prosthetic Joint Infection

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Introduction

Prosthetic joint infections are a significant cause of morbidity and mortality, which affect only a small number of joint replacements annually. These infections are very difficult to treat due to the location of the infection and the associated biofilm of the bacteria. Recently, surgeons have begun using spacers as well as antibiotic impregnated beads to help combat these infections. The advantage of this system is to provide local delivery of antimicrobials without systemic absorption, thus limiting toxicities and enhancing treatment of the biofilm present in the infected joint space. This delivery system is believed to be very safe, with limited side effects reported thus far.

We present a case of a patient who developed severe hypercalcemia several days after implantation of calcium sulfate beads during a revision of an infected total knee arthroplasty.

Case Presentation

A 70-year-old male with medical history notable for type 2 diabetes mellitus, essential hypertension, history of deep venous thrombosis and pulmonary embolism on warfarin, hypothyroidism, prostate cancer in remission, and seizures presented to our emergency department due to chief complaint of left knee pain. The patient had previously underwent a left total knee arthroplasty, and had recently completed a course of oral antimicrobials for a possible infection of the joint. The knee was aspirated and found to be infected, thus the patient was admitted in preparation for surgical intervention. Pre-operative labs were within normal limits, including a calcium of 8.7 mg/dL except for a therapeutic INR. The patient was taken for irrigation, debridement and polyethylene exchange of the left total knee arthroplasty on hospital day two. This involved opening up the previous incision, removing the polyethylene liner, debriding the site, using lavage and then, implanting of calcium sulfate beads impregnated with Vancomycin and Tobramycin.

The patient did well post-operatively until approximately 48-72 hours post-operatively, hospital day 4, when the patient was noted to be more lethargic, confused and having a poor appetite. We became involved in this patient's care to find the cause of the symptoms mentioned above.

A workup was initiated for the altered mental status, and the patient was found to be severely hypercalcemic at 14.0 mg/dL, which was confirmed on a repeat specimen. In addition, ionized calcium was found to be 2.02 mmol/L. Upon review of the chart and discussion with the patient, no prior episodes of hypercalcemia were reported. A wide differential diagnosis for acute hypercalcium, which included hyperparathyroidism, vitamin D excess, malignancy, multiple myeloma, hyperthyroidism, medication-induced and impaired renal excretion of calcium was worked up. Sepsis was low on our differential given the absence of a fever, no leukocytosis or vital sign instabilities. For this reason, we did not obtain blood cultures.

Extensive laboratory investigations were obtained in an attempt to find the cause of the hypercalcemia and the associated altered mental status. The results of these tests are found in Table 1, but they did not show an alternative cause to the hypercalcemia and altered mental status. We attributed the altered mental status to the acute hypercalcemia and focused our treatment on resolving it.

Over the next two days, the patient was continued on aggressive fluid hydration with several doses of furosemide given for volume overload. Serum and ionized calcium trended down to normal values. A graph of the serum calcium can be found in Figure 1. The patient's mental status returned to baseline around hospital day five, corresponding to decreasing levels of calcium, and fluids were discontinued. The patient was discharged with a calcium level of 8.8 mg/dL. At follow up approximately two months after hospitalization the patient was doing well with no further episodes of hypercalcemia, and a normal serum calcium of 8.6 mg/dL.

Discussion

This case demonstrates a patient who developed hypercalcemia following implantation of antibiotic impregnated calcium sulfate beads for treatment of prosthetic joint infection. Previously, acute kidney injury as well as antibiotic toxicity have been associated with implantation of calcium sulfate beads. A previous study reported the incidence of heterotrophic bone formation at 1.2% and several patients in this study developed acute renal failure. A case series of 15 patients who underwent revision of prosthetic joints due to infection with implantation of
antibiotic eluting calcium sulfate beads, three patients developed transient hypercalcemia. One of the three aforementioned patients became confused and lethargic. This occurred 48 hours after a revision of infected hip with placement of 40 cc of calcium sulfate beads. He was found to have a serum calcium as high as 14.2 and was treated with aggressive hydration and IV bisphosphonates with resolution over several days.

To our knowledge, this would be the third such case report of this occurring since this product has been utilized. We believe the calcium sulfate beads were the cause of this patient’s hypercalcemia as all of the other common causes of hypercalcemia such as hyperparathyroidism, vitamin D excess, malignancy, multiple myeloma, hyperthyroidism, medication-induced and impaired renal excretion of calcium were ruled out based on laboratory data. The time of the hypercalcemia, plus the acute onset of symptoms and findings lead us to believe that the calcium sulfate beads were the cause of the hypercalcemia.

### Conclusion

This case demonstrates several learning points for clinicians, including primary care physicians who are taking care of an increasing number of surgical patients in the hospital and outpatient settings. It is likely that hypercalcemia is a potential complication of calcium sulfate bead implantation and should be considered in surgical patients. Secondly, the number, size and location of the beads may have some importance to the systemic absorption of the materials. Prompt recognition and treatment is crucial to treat this serious condition. Institutions may consider developing a protocol to monitor calcium levels in the post operative period in these patients to detect and treat hypercalcemia before it reaches severe levels.

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### References