Case Report

SEVERE HYPERCALCEMIA AFTER JOINT ARTHROSCOPY: CALCIUM SULFATE BEADS TO BLAME

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ABSTRACT

Objective: To review the diagnosis and clinical course of a woman with severe, symptomatic hypercalcemia resulting from the use of calcium sulfate beads (CSBs) during orthopedic surgery for knee joint infection.

Methods: Clinical and laboratory data are presented.

Results: This is a unique case report of a woman that developed severe hypercalcemia 6 days after knee joint arthroscopy with CSB placement for knee prosthesis infection. Her laboratory data were unrevealing for alternate causes of severe hypercalcemia. Her symptoms and calcium level improved with intravenous fluids and 1 dose of calcitonin.

Conclusion: This case demonstrates a rare but serious side effect of using calcium-based beads as fillers for orthopedic surgeries. It is important for patients and physicians to be aware that severe hypercalcemia can result from CSBs used during orthopedic procedures. **(AACE Clinical Case Rep. 2019;5:e372-e374)**

Abbreviations:
CSB = calcium sulfate bead; **IV** = intravenous

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INTRODUCTION

Calcium sulfate beads (CSBs) have been used for decades during orthopedic revision surgeries to aid in the treatment of joint infections (1). The calcium-based beads provide dual benefits by acting as a space filler after joint debridement and as a mechanism to deliver local antibiotics to the infected joint (off-label use). Contraindications for use according to the manufacturer include renal compromise, hypercalcemia, severe vascular or neurological disease, uncontrolled diabetes, pregnancy, severe degenerative bone disease, and uncooperative patients (2). Although hypercalcemia is mentioned as a contraindication for use of CSBs, there is minimal literature on the risks of hypercalcemia resulting after use of the calcium-based beads.

Severe hypercalcemia is a rare, but life-threatening, risk after the use of CSBs during joint arthroplasties. We present a case documenting severe, symptomatic hypercalcemia requiring hospitalization after infected joint arthroplasty.

CASE REPORT

A 61-year-old female with a medical history of hypertension, hypothyroidism, pre-diabetes, arthritis, migraines, and knee replacement surgery 6 months prior developed right knee pain and was diagnosed with a septic knee joint based on aspiration fluid cultures growing *Staphylococcus lugdunensis*. She was admitted for septic right knee joint prosthesis and underwent arthrotomy, synovectomy, and pulsatile lavage with 3,000 mL of bacitracin and gentamicin. She also received placement of 10 mL (19.5 g) of CSBs as a bone void filler soaked in tobramycin and vancomycin per manufacturer recommendations.

Preoperative laboratory results were significant for calcium of 8.8 mg/dL (normal range is 8.5 to 10.1 mg/

dL) and albumin of 3.1 g/dL (normal range is 3.5 to 4.8 g/dL), and a corrected calcium level of 9.5 mg/dL. Infectious disease recommended peripherally inserted central catheter line access and 6 weeks of intravenous (IV) cefazolin followed by 6 months of oral cephalexin to treat right prosthetic knee joint infection. After a brief 3-day admission, the patient was discharged home.

Three days later, the patient developed altered mental status, which was attributed to overuse of opioid pain medication. That evening, the patient presented to the emergency room for continued complaints of altered mental status and a fall at home. Physical exam was significant for dry mucus membranes, disorientation, somnolence, and a general ill-appearance. On admission to the intensive care unit, her calcium level was 16.1 mg/dL (normal range is 8.5 to 10.1 mg/dL) with albumin level of 2.4 g/dL (normal range is 3.5 to 4.8 g/dL), with a corrected calcium level of 17.4 mg/dL (Table 1).

Other laboratory results on admission are presented in Table 2 and were significant for creatinine at 1.13 mg/dL (normal range is 0.40 to 1.10 mg/dL) (patient's baseline creatinine was 0.7 mg/dL), potassium at 2.7 mmol/L (normal range is 3.5 to 5.2 mmol/L), alkaline phosphatase at 249 U/L (normal range is 35 to 120 U/L), phosphorus at 1.7 mg/dL (normal range is 2.3 to 4.6 mg/dL), ionized calcium at 2.17 mmol/L (normal range is 1.18 to 1.32 mmol/L), and rapid urine drug screen was negative, including opioids. Computed tomography scan of the head, abdomen, and pelvis were normal. Chest X-ray showed no acute process.

Further evaluation revealed 25-hydroxyvitamin D of 35 ng/mL (normal range is 30 to 100 ng/mL), 1,25-dihydroxyvitamin D of 9.0 pg/mL (normal range is 19.9 to 79.3 pg/mL), intact parathyroid hormone <6.3 pg/mL (normal range is 18.5 to 88.0 pg/mL), and parathyroid hormone-related peptide <2.0 pmol/L (normal range is <3.4 pmol/L). Serum protein electrophoresis suggested the possibility of a faint band and immunofixation electrophoresis resulted with small monoclonal protein present. After altered mentation resolved, the patient denied using over-the-counter medications, tums, or calcium supplementation at home.

The hypercalcemia was treated with IV normal saline, aggressive potassium repletion, and calcitonin at 4 U/kg (280 U) once. After receiving a single dose of calcitonin, the calcium level decreased to 8.4 mg/dL (normal range is 8.5 to 10.1 mg/dL) within 24 hours and then stabilized at the lower end of normal. The patient was started on calcium carbonate replacement. The remaining electrolyte abnormalities normalized and the patient was discharged home after a 6-day hospital stay. During outpatient follow up, her calcium level remained within the normal range without further intervention. Repeat serum protein electrophoresis and immunofixation were normal.

DISCUSSION

Although hypercalcemia is listed as a contraindication for the use of CSBs, the usage of the beads themselves can lead to acute hypercalcemia in the setting of a normal preoperative calcium level. A 2015 case report by Carlson et al (3) documented severe, symptomatic hypercalcemia after use of calcium-based beads for hip arthroplasty. According to the report, the serum calcium level peaked on postoperative day 5 at a value of 14.5 mg/dL and resolved to normal on postoperative day 8 with aggressive IV fluids and 1 dose of calcitonin.

Kallala et al (4) published a case series highlighting the use of CSBs during revision arthroplasty for 15 patients, of which 3 people developed hypercalcemia, 1 of whom required medical treatment. In a 2018 review to assess the safety profile of CSBs, 755 patients underwent joint arthroplasties and 41 of those patients developed hypercalcemia, 2 of which were symptomatic (1).

Rare case reports have noted the hypercalcemia side effect from CSBs, however it remains unclear why this occurs only in specific cases. Kallala et al (1) published the possibility of a dose-dependent relationship between the volume of calcium-based beads used and hypercalcemia. They recommended screening for contraindications to using calcium-based beads and close monitoring of calcium both before and after operation. They further recommend limiting the volume of CSBs to <40 mL per operation. They also note a variety of host factors and surgical variables that likely contribute to the premature breakdown of the CSBs. The grading system accounted for host factors related to immunocompromised state, prolonged steroid use, diabetes mellitus, IV drug abuse, and other active infections (1). Interestingly, our patient received 10 mL CSBs, had a normal preoperative calcium level, and did not have any identified risk factors.

A 10-mL pack of CSBs contains approximately 19.5 g of calcium sulfate, which is 29.4% elemental calcium. Therefore, a 10-mL pack of CSBs contains 5.73 g of

Table 1
Calcium Trend Before and After Surgery

	Albumin (g/dL)	Calcium (mg/dL)	Corrected calcium (mg/dL)
Before surgery	3.1	8.8	9.5
3 days after surgery	2.4	16.1	17.4
4 days after surgery	--	8.4	--

Table 2
Additional Workup

	Patient's lab value	Normal range
Potassium (mmol/L)	2.7	3.5-5.2
Alkaline phosphatase (U/L)	249	35-120
Phosphorus (mg/dL)	1.7	2.3-4.6
Ionized calcium (mmol/L)	2.17	1.18-1.32
25-hydroxyvitamin D (ng/mL)	35	30-100
1,25-dihydroxyvitamin D (pg/mL)	9.0	19.9-79.3
Intact parathyroid hormone (pg/mL)	<6.3	18.5-88.0
Parathyroid hormone-related peptide (pmol/L)	<2.0	<3.4

elemental calcium to be released over 30 to 60 days. For comparison, 1 calcium carbonate antacid tablet contains 0.471 g of elemental calcium. Potential pathophysiologic possibilities to explain the hypercalcemia in our patient include premature breakdown of the CSBs, location of the bead placement near increased vasculature, or more rapid absorption of calcium from the beads. There is very limited data to fully elucidate the cause of hypercalcemia and more prospective studies are needed to further evaluate this adverse reaction to CSBs. Therefore, it is important to maintain a high suspicion for resultant postoperative hypercalcemia in all patients who receive CSBs.

It is vitally important that physicians are aware of the risk of severe symptomatic hypercalcemia resulting from the use of calcium-based beads during surgery. Therapeutic alternatives to the use of CSBs including debridement, prostheses removal, and systemic antibiotics can be considered as treatment pathways to avoid the potential risk of hypercalcemia. Physicians need to be aware of the clinical signs and symptoms of hypercalcemia, including altered mental status, in order to diagnosis this complication. The case presented here documents an additional hospital stay and acute illness resulting from calcium-based bead usage during arthroscopy.

CONCLUSION

This case demonstrates the rare but serious side effect of using calcium-based beads as fillers for orthopedic surgeries. It is important for patients and physicians to be aware that severe hypercalcemia can result from CSBs used during orthopedic procedures.

DISCLOSURE

The authors have no multiplicity of interest to disclose.

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