ACUTE INTRAOPERATIVE REACTIONS DURING THE INJECTION OF CALCIUM SULFATE BONE CEMENT FOR THE TREATMENT OF UNICAMERAL BONE CYSTS: A REVIEW OF FOUR CASES

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ABSTRACT

Unicameral bone cysts can predispose patients to pathologic fracture and deformities of growth. Treatment options vary from continuous decompression with transcortical placement of a cannulated screw to percutaneous aspiration and injection of medical-grade calcium sulfate. From 2005 to 2007, we treated 22 patients with unicameral bone cysts using aspiration and injection of calcium sulfate. Three patients experienced acute laryngospasm and one patient developed tachyarrhythmia, temporarily, associated with injection of calcium sulfate. All reactions occurred in patients under age 18 without predisposing risk factors and resolved spontaneously with supportive care. Although the mechanism is unclear, we hypothesize that these reactions are either due to the nociceptive stimulus of the calcium sulfate injection or a systemic calcium bolus. Clinicians using this product for this indication should be aware that such reactions may occur. We suggest endotracheal intubation and communication to the anesthesiologist about the time of the injection in preparation for these idiopathic responses. Further research is necessary to determine exactly how this reaction occurs and how it can be avoided.

INTRODUCTION

The unicameral bone cyst (UBC) is a benign bone tumor most frequently seen in the pediatric population. The exact etiology is still debated; however, many believe this phenomenon arises from one of three possibilities: 1) An intramedullary synovial cyst, 2) Intramedullary venous congestion, or 3) Disturbances of skeletal development.[1] Whatever the mechanism, these lesions are often asymptomatic and are discovered only incidentally, or they may come to the attention of the orthopaedic surgeon when there is a pathologic fracture through the lesion. Treatment begins conservatively, as these defects sometimes fill in as development progresses. However, there are certain cases where surgical intervention is warranted to prevent progression of an expanding lesion and/or a possible pathologic fracture, especially in locations associated with severe complications (e.g., the femoral neck).

Several interventions have been reported to be successful, but more recently, minimally invasive procedures have become popular.[1] These new techniques are not free of complications. We previously reported several cases of local soft-tissue reactions to Osteoset® surgical-grade calcium sulfate bone graft substitute (Wright Medical Technology).[2] In this study, we report four cases of acute systemic reactions to the injection of calcium sulfate-containing bone substitutes (Pro-Dense Injectable bone graft substitute and Minimally Invasive Injectable Graft – MIIG 115, Wright Medical Technology, Inc., Arlington, TN).

REVIEW OF CASES

Patient 1

An otherwise-healthy 11-year-old male presented to his local physician after being hit in the right wrist by a baseball. Radiographic studies obtained locally were negative for any fracture but demonstrated a lytic lesion in the proximal radius. The patient was referred to our center for further treatment. On our evaluation, we felt the lesion to be most consistent with a unicameral bone cyst, and because of its size and the patient's symptomatology, the indication was made for percutaneous aspiration, irrigation and injection of bone graft substitute.

General anesthesia was induced and the patient was ventilated using a laryngeal mask airway (LMA). After the usual preparation and draping, two large-bore needles were introduced into the lesion. The contents of the lesion were aspirated, confirming the diagnosis of UBC. After irrigation, MIIG 115 calcium sulfate bone graft substitute was injected into the lesion. After several seconds, the patient experienced severe laryngospasm, making ventilation through the LMA impossible. The patient desaturated acutely and required intubation. He was extubated shortly following the procedure, without further complications.

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Patient 2

A 15-year-old, healthy, active male presented to our clinic with pain in the left distal tibia while jogging. Radiographic evaluation of the tibia revealed a lucent lesion and cortical reaction consistent with a non-displaced pathologic fracture through a cyst, possibly UBC versus fibrous dysplasia.

The patient was taken to the operating room for aspiration, irrigation and calcium sulfate injection using two large-bore needles. After aspiration and irrigation, MIIG 115 calcium sulfate was injected. Immediately following injection, the patient had an increase in his airway pressures and became difficult to ventilate with a bag mask. This case of mild laryngospasm resolved without the need for intubation.

Patient 3

An otherwise-healthy, six-year-old male tripped and fell onto his left hip. He complained of persistent pain in the hip and walked with a limp. He underwent radiographic evaluation by his pediatrician, which revealed a lucent lesion in the left femoral neck. He was subsequently referred to our center for further care and the diagnosis of UBC was made.

After an initial trial of non-operative therapy, the patient underwent injection of corticosteroids into the cavity which caused near-complete obliteration of the cyst. However, after about 18 months the cyst recurred, and the decision was made to proceed with aspiration, irrigation and injection of calcium sulfate.

The procedure was uneventful until injection of the MIIG 115 calcium sulfate, when the patient demonstrated increased resistance to ventilation consistent with laryngospasm. His oxygen saturation dropped to a low of 46% during the incident, however, within 30 seconds of the start of the incident his condition improved because of increasing positive pressure ventilation applied by bag mask. There were no further respiratory events and the patient did not suffer any adverse sequelae.

Patient 4

A nine-year-old, otherwise-healthy female presented to our emergency treatment center with pain in the left distal tibia, sustained after a twisting motion. Initial radiographic evaluation revealed a lucent lesion with a pathologic fracture through the medial cortex (Figure 1). The patient's past medical history was unremarkable and she had no significant positive findings on review of systems. This lesion was determined to be consistent with a UBC. She was initially treated in a long-leg cast and although the fracture healed, the UBC enlarged. Furthermore, the patient continually complained of focal pain in the area of the lesion. She was indicated for aspiration, irrigation and injection of calcium sulfate bone graft substitute.

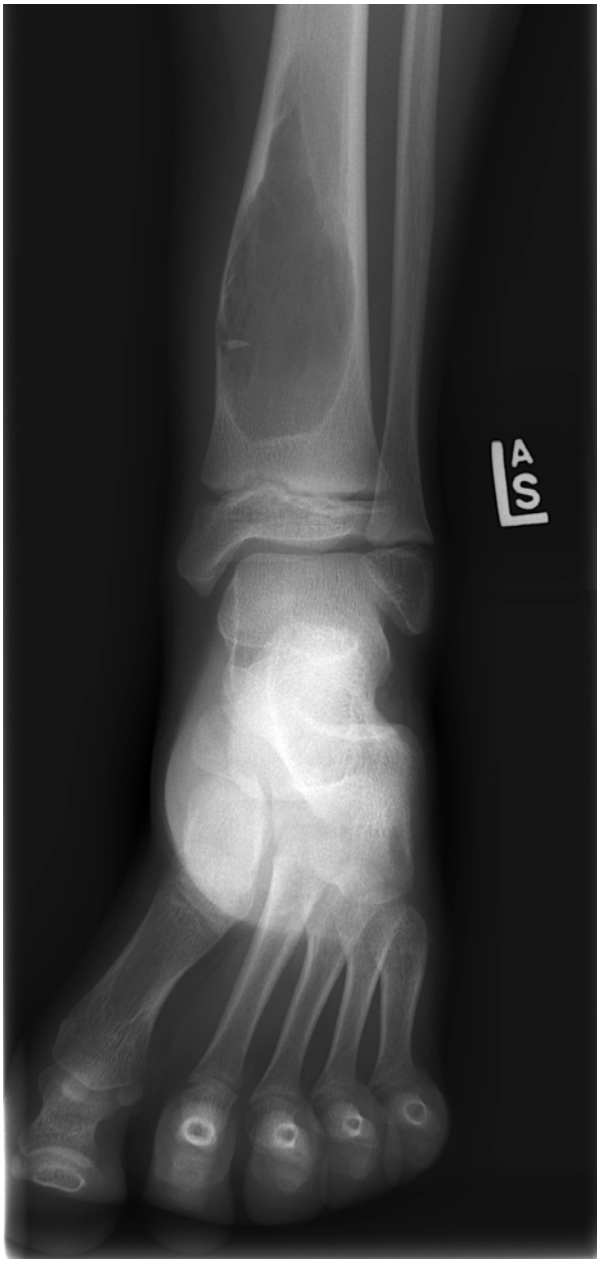

Figure 1. 9-year old female (Case 4) with pathologic fracture through UBC of left distal tibia.

Intraoperatively, the aspirate findings were consistent with UBC. The case initially progressed without complication until the Pro-Dense Injectable calcium sulfate/calcium phosphate cement was introduced. At that time, the patient's heart rhythm changed to a supraventricular tachyarrhythmia with a rate of approximately 120 beats per minute, representing a 40% increase over baseline

Figure 2A.

Figure 2B.

Figure 2. Intraoperative fluoroscopy shots from the same patient demonstrating access ports (Figure 2A) to cyst and post-injection films demonstrating containment of the injected material in the cyst cavity (Figure 2B).

rate. This resolved without intervention and the patient remained hemodynamically stable throughout the incident. The patient was taken to the post-operative care unit and monitored closely, with no further arrhythmias.

DISCUSSION

Treatment of a unicameral bone cyst by aspiration and injection of bone substitute is a well-described technique.[1] This treatment is used mainly for cases recalcitrant to other treatments, or cases in which the lesion is located in an area of high mechanical stress. The goal of therapy is to prevent pathologic fracture and limb deformity in the developing pediatric skeleton.

There are several bone substitute products available. Products composed of calcium sulfate are desirable because they provide an osteoconductive matrix that can be delivered in a slurry form, making the compound amenable to injection through a minimally invasive approach.[4,5] These compounds are approved by the FDA, are widely used, and in our experience have been generally well tolerated and safe in a wide variety of patients and clinical scenarios. Adverse effects due to the application of these products have been described, however.

Reactions have been previously reported with calcium sulfate pellet treatment (OsteoSet®, Wright Medical Technology, Arlington, TN) of benign bone lesions. In a series of 58 patients there was a 13.8% incidence of delayed reactions observed, with no clear risk factors identified to forming a reaction.[2] These delayed reactions consisted of painful, self-limiting soft tissue responses that resolved with symptomatic anti-inflammatory therapy. Similar local reactions have previously been reported with calcium phosphate and calcium sulfate materials.[6,7]

Interestingly, some studies suggest calcium sulfate demonstrates local cytotoxic properties.[8] In addition, it has been reported that injections of calcium-based cement can have a potential for adverse reactions. Krebs et al. demonstrated that intravascular injection of calcium phosphate cement can induce pulmonary embolism in an animal model.[9] This may be clinically important because UBC membranes are very permeable and can allow passage of contrast materials into the circulation.[10]

The mechanisms of the observed reactions in our study are unclear and no such reaction is described in the literature. These patients did not demonstrate any readily identifiable risk factors which would predispose them to such a reaction. At the present time, our best hypothesis to explain these cases would be that the injection of calcium sulfate induced laryngospasm and tachycardia through a pain stimulus which overcame the level of anesthesia. As reported above, these products have some potential for local toxicity, and a dissolution of calcium sulfate is believed to lead to an acidic microenvironment.[8] The MIIG 115 is designed to absorb quickly in soft tissues and synovium to prevent problems with extravasation. It is possible that absorption of calcium sulfate into the soft tissues, and the subsequent local acidic and inflammatory environment, could be a significantly noxious stimulus, enough for the patient to overcome relatively "light" anesthesia usually provided during minor procedures.

Another hypothesis is that rapid systemic dissemination of calcium from the local environment causes these idiopathic reactions. One animal study demonstrated injection of calcium chloride into sheep caused "laboured respiration" and tachycardia.[11] In addition, there have been case reports of intravascular calcium infusion causing vasoconstriction and death.[12] Previous studies performed with calcium sulfate pellets, however, have shown that there is no increase in serum calcium levels when this bone substitute is utilized.[13] It is feasible that the liquid formulation may go into solution more easily, leading to increased calcium levels. Unfortunately, no serum calcium levels were drawn on our patients at the time of their reactions, to confirm or disprove this hypothesis.

Finally, it is possible that the pressure of injection overcame the cyst cavity's ability to contain its contents, leading to vascular dissemination. Fat embolism has been demonstrated in sheep secondary to injection of polymethylmethacrylate during vertebroplasty, resulting in cardiovascular and pulmonary complications.[14] However, this mechanism is unlikely in our cases because first, at the time of injection there were two ports in the cystic cavity, one acting to release pressure (Figure 2A). Second, our cases were done under fluoroscopy and there was no visible evidence of active extravasation (Figure 2B).

In summary, two hypotheses remain to explain these idiopathic reactions: 1) The nociceptive stimulus of local tissue damage associated with injection of calcium sulfate overcoming the light anesthetic, or 2) Systemic dissemination of calcium. To prepare for these possibilities in the future, we have asked our anesthesiologists to provide deeper anesthesia with shorter-acting agents than customarily used, and to be highly cognizant of airway management around the time of injection. Regardless of the etiology, these reactions appear to be self-limiting and were readily managed by proper airway management and supportive therapy. We believe that treatment with surgical-grade calcium sulfate bone graft substitute is safe, but the clinician using this product should be prepared to deal with possible reactions at the time of injection. Further research may be warranted to determine the incidence, risk factors and mechanism for developing these reactions.

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