

A Mimicker: An Acute Phase Reaction from Zoledronate Mimicking Symptoms seen in Opioid Withdrawal



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INTRODUCTION

- Zoledronate, a bisphosphonate, preferred treatment for hypercalcemia when unresponsive to intravenous fluids.¹
- Bisphosphonates can cause transient acute phase reaction consisting of fevers, chills, myalgias, arthralgias, and headaches.^{2,3} Mimic opioid withdrawal symptoms.

Our case highlights cognitive bias involving a patient with opioid use disorder who received zoledronate for hypercalcemia secondary to immobilization and significant bone infection.

CASE PRESENTATION

- 41-year-old male past medical history active intravenous opioid use complicated by group A streptococcal bacteremia with L5-S1 discitis/osteomyelitis, L2-L3 osteomyelitis, left psoas abscess, right sided parapneumonic effusion with septic emboli and cavitary lesions, and left ankle abscess/septic arthritis status post left ankle washout.
- Pain well-controlled by acute pain service (Table 1). Intravenous opioids were discontinued, slightly decreasing opioid regimen.
- A day later, reported tachycardia, diaphoresis, myalgias, and chills, which primary team reconsulted acute pain service for opioid withdrawal

Table 1: Inpatient Multimodal Analgesic Regimen

Day 1 (prior to symptom onset) *Zoledronate Infusion Given	Day 2 (symptom onset)	Day 3 (symptom resolution)
• Discontinued IV Dilaudid 0.5 mg every 6 hours as needed for breakthrough pain • Tylenol 975 mg every 8 hours scheduled • Buprenorphine-Naloxone 2 mg twice daily • Oral Dilaudid 4 and 6 mg every 3 hours as needed for moderate/severe pain • Cyclobenzaprine 5 mg 3 times daily • Gabapentin 600 mg 3 times daily • Naproxen 500 mg twice daily	• Tylenol 975 mg every 8 hours scheduled • Buprenorphine-Naloxone 2 mg twice daily with plan to uptitrate to minimum dose of 8 mg total daily dose prior to discharge • Oral Dilaudid 4 and 6 mg every 3 hours as needed for moderate/severe pain • Cyclobenzaprine 5 mg 3 times daily • Gabapentin 600 mg 3 times daily • Naproxen 500 mg twice daily	• Same as Day 2

Table 2: 24 Hour Opioid Requirements by day

Days	24 Hour Opioid Requirement	Morphine Milligram Equivalents (MME)
Day 1 (prior to symptom onset) *Zoledronate Infusion Given*	1. 36 mg Oral Dilaudid 2. 0.5 mg IV Dilaudid 3. 4 mg Sublingual Buprenorphine-Naloxone	146 MME
Day 2 (symptom onset)	1. 30 mg Oral Dilaudid 2. 4 mg Sublingual Buprenorphine-Naloxone	120 MME
Day 3 (symptom resolution)	1. 30 mg Oral Dilaudid 2. 4 mg Sublingual Buprenorphine-Naloxone	120 MME

- Since total opioid dose decreased slightly, very unlikely any level of opioid withdrawal (Table 2).
- Patient received a zoledronate infusion for hypercalcemia, same day intravenous opioids were discontinued.
- Received normal saline previously for hypercalcemia, which was suspected from prolonged immobilization in setting of severe bone infection. Calcium level did not improve, so a one-time dose of zoledronate was given.
- No other medications known to cause “withdrawal-like” symptoms per chart review.
- Therefore, it was suspected that an acute phase reaction occurred, which is commonly seen within a few days of bisphosphonate use.

DISCUSSION

- Zoledronate well known for acute phase reactions, likely cause of “withdrawal-like” symptoms.
- Acute phase reactions with bisphosphonates mostly occur in the first infusion, and its incidence decreases with subsequent infusions. Symptoms typically occur 24-72 hours post-infusion, and last at most for 72 hours.

Our case emphasizes cognitive bias, and providers should thoroughly investigate potential etiologies and rule out accordingly to provide the best care.

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