

# Hyperkalemia as a Precursor to Daptomycin Induced Muscle Toxicity

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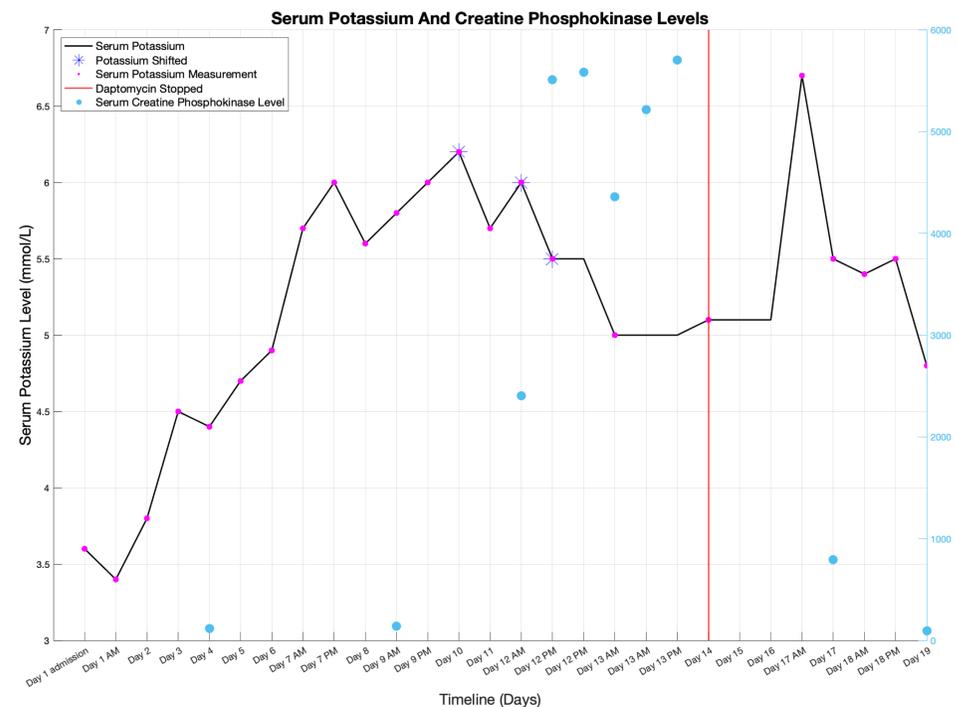


## OVERVIEW

Daptomycin, an antibiotic used to treat gram-positive organisms, can cause muscle toxicity and rhabdomyolysis in some patients. This case report discusses a 26 year old woman on daptomycin for methicillin-resistant *Staphylococcus aureus* (MRSA) infective endocarditis with tricuspid valve replacement, who developed hyperkalemia several days prior to developing an elevated creatine phosphokinase (CK) and rhabdomyolysis thought to be secondary to treatment. After discontinuation of daptomycin, her potassium and CK eventually returned to normal. Daptomycin induced muscle toxicity is a known adverse reaction and can cause hyperkalemia, but it is unusual for hyperkalemia to be a precursor. Rather, hyperkalemia typically develops secondary to rhabdomyolysis. This case demonstrates the importance of monitoring potassium levels while patients are receiving long-term daptomycin therapy as it may be an early signal for the development of rhabdomyolysis.

## Case

- 26-year-old woman with past medical history of intravenous drug use and MRSA tricuspid valve endocarditis status post tricuspid valve replacement with subsequent development of heart block leading to Micra pacemaker placement presented to the hospital with chest pain and shortness of breath
- On week 3 of a 6-week course of daptomycin, ceftaroline and rifampin therapy
- BNP on admission was elevated to 2078 pg/mL, patient was diuresed with furosemide 40mg IV twice daily
- On hospital day 6, her blood cultures grew extended spectrum beta-lactamase *Klebsiella pneumoniae*, initial blood cultures were negative
- PICC line was removed and ceftaroline was switched to meropenem
- On this day, she became hyperkalemic (5.7 mmol/L) and she remained hyperkalemic for much of her hospitalization
- Her creatinine rose to 1.21 mg/dL and a creatine phosphokinase (CK) level was ordered to evaluate for muscle breakdown in the setting of daptomycin use
- On hospital day 7, her CK was normal at 142 U/L, while she remained hyperkalemic
- Her potassium was 6.2mmol/L on day 9, at which time she was given calcium gluconate, insulin and dextrose furosemide, and sodium zirconium cyclosilicate, and she continued to require daily treatment
- On day 12, the patient's CK was elevated at 2,406 U/L, it was repeated and was 5,582 U/L
- Daptomycin toxicity was the most likely cause, and the antibiotic was switched to vancomycin on day 14
- The patient began refusing labs but they were collected as allowed and showed eventual resolution of hyperkalemia and rhabdomyolysis with a potassium of 4.8 mmol/L and CK of 93 U/L on day 19 of hospitalization



This graph represents this patient's serum potassium and creatine phosphokinase levels throughout the course of her hospitalization in relation to daptomycin administration. Values were not obtained on days without a pink or blue marker. There were several days in which labs were obtained multiple times in one day as is depicted by the timeline at the bottom. The purple stars signify days in which the potassium was shifted. The red line is the day Daptomycin administration was stopped.

## Differential Diagnosis

- Pseudohyperkalemia from mechanical trauma during venipuncture can cause hyperkalemia.<sup>7</sup> Venipuncture was repeated several times with hyperkalemia persisting, an arterial blood gas (ABG) was performed, and the potassium remained elevated at 5.3 mmol/L (5.4 later the same day on a comprehensive metabolic panel). If it were due to hemolysis, the ABG potassium would likely have been normal.<sup>7</sup>
- Metabolic acidosis was ruled out as a cause of hyperkalemia as her pH on ABG was 7.4.<sup>7</sup>
- Red blood cell transfusion can cause hyperkalemia<sup>7</sup> but the 2 units of packed red blood cells she received at an outside facility were given 6 days prior to the onset of her hyperkalemia.<sup>7</sup>
- Enoxaparin can cause hyperkalemia,<sup>7</sup> and while the patient had this medication ordered, she refused enoxaparin until day 9, and her potassium became elevated on day 6 making cause unlikely.
- Type IV renal tubular acidosis is another cause of hyperkalemia but was unlikely as she showed no signs of hypoaldosteronism, had normal chloride, and was treated with amlodipine during her hospitalization to normalize her blood pressure which ranged from 170s/120s before treatment and 100-120s/60-80s after treatment.<sup>7</sup>

## Discussion

Daptomycin is used for the treatment of antimicrobial resistant microbes such as vancomycin-resistant *Enterococcus* species and as an alternative treatment for methicillin-resistant *Staphylococcus aureus* (MRSA) infections.<sup>1,2</sup> CK elevation in patients taking daptomycin at high doses ( $\geq 8$  mg/kg/day) has been described at rates of 2.8-3.2%,<sup>3</sup> and up to 5% of patients may also experience rhabdomyolysis,<sup>4</sup> which is characterized by muscle necrosis resulting in the release of intracellular contents into circulation.<sup>4</sup> The release of intracellular contents can cause hyperkalemia which can potentiate fatal arrhythmias if high enough. Therapy should be stopped in patients with CK  $>5x$  the upper limit of normal.<sup>5</sup>

In this case, hyperkalemia presented as a precursor to elevated CK, likely secondary to daptomycin induced muscle toxicity. The Naranjo algorithm is a tool that was developed to help assess the causality for adverse drug reactions. The algorithm consists of 10 questions and scores range from 0 to 13, with higher scores indicating a stronger causal relationship.<sup>6</sup> In this case a Naranjo algorithm score of 6 pointed to a probable adverse drug reaction.

There is sparse data on this topic, but case reports by Ibarra and colleagues, and Budovich and colleagues describe different presentations of this phenomenon.<sup>8,9</sup> This case adds to the literature that hyperkalemia may serve as a precursor to elevated CK levels and rhabdomyolysis in patients on daptomycin therapy.

## Take Home Points

- It is important to monitor serum potassium levels while patients are receiving long-term daptomycin therapy as it may be an early signal for the development of rhabdomyolysis
- In patients with elevated serum potassium, it may be reasonable to monitor CK levels more frequently than once a week to ensure early detection of rhabdomyolysis
- It may be reasonable to consider an alternative antimicrobial to daptomycin in patients with elevated serum potassium levels that are unexplained by other causes

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