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 tricispid 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, cefartoril 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 cefartoril 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

Differential Diagnosis

- Pseudohyperkalemia from mechanical trauma during venipuncture can cause hyperkalemia. 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.
- Metabolic acidosis was ruled out as a cause of hyperkalemia as her pH on ABG was 7.4.
- Red blood cell transfusion can cause hyperkalemia 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.
- Enoxaparin can cause hyperkalemia, 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 hypocalcosteronism, had normal chloride, and was treated with amlopidine during her hospitalization to normalize her blood pressure which ranged from 170s/120s before treatment and 100-120s/60-80s after treatment.

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. CK elevation in patients taking daptomycin at high doses (2-8 mg/kg/day) has been described at rates of 2.8-3.2%, and up to 5% of patients may also experience rhabdomyolysis, which is characterized by muscle necrosis resulting in the release of intracellular contents into circulation. 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.

In this case, hyperkalemia was 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. 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. Hyperkalemia as a precursor to daptomycin induced muscle toxicity is presented by patient as a probable severe adverse reaction.

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

REFERENCES