Cardiology in the Young

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Hypotension associated with azithromycin infusion in children with heart failure: a case report

Dominic Zanaboni and Carolyn Vitale

Division of Pediatric Cardiology, University of Michigan C.S. Mott Children's Hospital, Ann Arbor, MI, USA

Abstract

We report two cases of acute hypotension after intravenous azithromycin administration in children with acute, decompensated heart failure. In each of our reported cases, azithromycin was being used to treat possible *Mycoplasma* myocarditis. In this report, we aim to describe hypotension as a potentially rare adverse reaction to intravenous azithromycin and encourage judicious use in patients with cardiac dysfunction.

Brief Report

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Author for correspondence:
D. Zanaboni, MD, Division of Pediatric Cardiology, University of Michigan C.S. Mott Children's Hospital, 1540 E Hospital Dr, Ann Arbor, MI 48109, USA. Tel: 314-347-6997; Fax: 734-936-9470.
E-mail: zanaboni@med.umich.edu

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Case 1

Patient 1 was a previously healthy 8-year-old female who presented with a 2-week history of gastrointestinal upset. Her exam was significant for hepatomegaly and dry mucus membranes. Laboratory evaluation demonstrated a mild transaminitis and mildly increased blood urea nitrogen. She had a normal white blood cell count, haematocrit, and inflammatory markers. A respiratory viral panel polymerase chain reaction (PCR) was negative, including for *Mycoplasma pneumoniae*. Admission echocardiogram demonstrated biventricular dilation and severely depressed function.

At the time of ICU admission, intermittent furosemide and infusions of milrinone and low-dose epinephrine were started. Nitroprusside was started on day 2 of ICU admission. The patient had multiple short runs of ventricular tachycardia. On day 3, *Mycoplasma* IgM and IgG titre were found to be positive and confirmed by immunofluorescent antibody stain. Without another aetiology of cardiomyopathy, we elected to treat for *Mycoplasma* myocarditis given the positive serologic test. She was given the first intravenous dose of azithromycin 10 mg/kg over 60 minutes and developed an acute decrease in her systolic blood pressure 71 minutes later. She suffered a cardiac arrest within minutes of developing systolic hypotension and was emergently cannulated on to veno-arterial extracorporeal membranous oxygenation. There was no other apparent aetiology for decompensation, including no rhythm change or signs of an allergic drug reaction.

On day 4 of ICU admission, the patient was given a second dose of azithromycin using the same dosage and infusion rate while supported on veno-arterial extracorporeal membranous oxygenation. There was an acute decrease in pulse pressure 90 minutes after the start of infusion with an associated drop in measured central venous saturation and rise in central venous pressure.

Given the temporal association of azithromycin infusion and narrowed pulse pressure, the patient was transitioned from azithromycin to doxycycline on day 5 of ICU admission. After this change, there were no similar instances of haemodynamic changes.

The patient was later found to have a pathogenic variant of Lamin A and ultimately received a heart transplant.

Case 2

Patient 2 was an 11-year-old female with a past medical history significant for global developmental delay and remote history of seizures. She presented with a 1-week history of gastrointestinal upset and activity intolerance. Her exam was normal apart from hepatomegaly. Laboratory evaluation revealed a mild microcytic anaemia, normal white blood cell count, mild transaminitis with elevated total bilirubin, elevated brain-naturetic peptide, and mild increase in C-reactive protein and procalcitonin. A respiratory viral panel PCR was negative, including for *Mycoplasma pneumoniae*. An echocardiogram demonstrated biventricular dilation with severely depressed function. Testing for infectious myocarditis was performed, which included serologic testing for *Mycoplasma pneumoniae*.

Upon ICU admission, she was treated with milrinone infusion, intermittent furosemide and epinephrine infusion. On day 8 of ICU admission, *Mycoplasma* IgM and IgG titres were found to be positive and confirmed by immunofluorescent antibody stain. In effort to treat a possible

reversible aetiology of cardiomyopathy, we elected to start azithromycin and she was given her first dose of 10 mg/kg/dose over 60 minutes. She developed acute hypotension 18 minutes after the initiation of the infusion and suffered a cardiac arrest. She was emergently cannulated on to veno-arterial extracorporeal membranous oxygenation. There was no other apparent aetiology for decompensation, including no rhythm change or signs of an allergic drug reaction.

On ICU days 9 and 10, azithromycin was given at the same dose and infusion rate while supported on veno-arterial extracorporeal membranous oxygenation with an acute narrowing of her pulse pressure and rise in central venous pressure approximately 20 minutes after the infusion was started. On day 10, she was also being treated with a nitroprusside infusion. Azithromycin was transitioned to doxycycline on ICU day 11. The patient continued to have brief periods with a narrow pulse pressure without a clear aetiology, but none as stark as those associated with azithromycin infusion. A unifying diagnosis for her cardiomyopathy was never identified and she ultimately died in the ICU.

Conclusion

We present two patients with acute decompensated heart failure who were treated for presumed *Mycoplasma* myocarditis with intravenous azithromycin and suffered acute hypotension and subsequent cardiac arrests. *Mycoplasma* myocarditis is a rare diagnosis with the estimated incidence among patients with *Mycoplasma* infection to be between 1 and 5%.[1,2] Among the limited description of Mycoplasma myocarditis in the literature, the predominant presenting symptoms are respiratory in nature, with just a select few having primary cardiac manifestations.[1,2] Furthermore, the accuracy of serologic tests, particularly for the acute phase of *Mycoplasma pneumoniae* infection, are quite variable[3–5] making this rare diagnosis more complex if there is not a high pre-test probability. In the absence of other confirmed diagnoses, treatment of *Mycoplasma* may be considered as a reversible cause of acute decompensated heart failure. As such, we elected to treat for potential *Mycoplasma* myocarditis in our circumstance. In both cases, the haemodynamic changes appeared to be intrinsically related to azithromycin infusion, as has been previously reported in by Wong, et al.[6] Neither patient had associated rhythm changes or signs to suggest allergic drug reactions. The volume of infusion in both cases were approximately 4–5 mL/kg given over 1 hour, suggesting that an acute volume load was unlikely. Lastly, macrolide antibiotics can reduce nitroprusside metabolism, resulting in toxicity; however, azithromycin typically does not have this effect in comparison to other macrolides.[7,8]

Overall, *Mycoplasma* myocarditis is a rare and challenging diagnosis. We suggest that in cases of myocarditis, *Mycoplasma* should be considered in the context of presenting clinical symptoms and serologic testing should be corroborated with other means including history, exam, and PCR testing before treating with antibiotics. In cases suspicious for *Mycoplasma* myocarditis, it is important to consider the potential adverse effect of acute hypotension and consider a tetracycline over a macrolide.

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Conflicts of interest. None.

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