

## Concurrent Digoxin Toxicity and BRASH Syndrome

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**Background:** Digoxin toxicity occurs due to excess inhibition of sodium-potassium-ATPase resulting in increased intracellular calcium and arrhythmogenicity, plus increased vagal tone leading to bradycardia. Digoxin has a narrow therapeutic window, and toxicity can result in hyperkalemia and arrhythmias including premature ventricular contractions (PVCs) and bidirectional ventricular tachycardia.<sup>1,2</sup> Digoxin is renally excreted, thus renal impairment is one of the main risk factors for developing toxicity.

The clinical syndrome BRASH (Bradycardia, Renal failure, AV nodal blocking agents, Shock, and Hyperkalemia) shares several features with digoxin toxicity. BRASH syndrome is a self-perpetuating cycle of the effects of hyperkalemia and AV nodal blockers causing bradycardia, which exacerbates renal hypoperfusion.<sup>3,4</sup>

Concurrent clinical suspicion for BRASH syndrome and digoxin toxicity can complicate diagnosis and clinical decision making.

**Case:** A 74-year-old male with a history of non-ischemic cardiomyopathy and heart failure with reduced ejection fraction with implantable cardioverter-defibrillator (ICD), permanent atrial fibrillation, type 2 diabetes mellitus, chronic kidney disease stage III, and recent COVID-19 infection presented with progressive generalized weakness and lethargy. The patient was noted to be bradycardic to 30 beats per minute (bpm) on radial pulse palpation with blood pressure of 95/49 mmHg. His labs revealed potassium of 6.1 mmol/L, creatinine 4.0 mg/dL (baseline 1.6), digoxin level of 2.2 nmol/L, and lactate of 1.0 mmol/L. EKG revealed a heart rate of 55 bpm with ventricular paced complexes and PVCs, with PVCs contributing to underestimation of heart rate on radial palpation. Home medications included carvedilol, digoxin, furosemide, spironolactone, and valsartan.

**Decision-making:** Elderly patients with multiple comorbidities and non-specific presenting symptoms should prompt a broad work up and careful review of home medications. Acute renal failure, decreased oral intake precipitated by recent COVID-19 infection, and use of multiple AV nodal blocking agents were thought to cause BRASH syndrome. Digoxin toxicity was also suspected given his clinical history and elevated digoxin level. The patient's hyperkalemia was of particular concern given the direct correlation between hyperkalemia and mortality in acute digoxin toxicity. Home medications including carvedilol were held, and he received digoxin Immune Fab, judicious fluid resuscitation, and calcium gluconate. ICD back up rate was increased to decrease ventricular ectopy and increase cardiac output. Once renal function and clinical status improved, the patient was restarted on guideline-directed medical therapy including carvedilol without complications. He advised to avoid digoxin in the future.

**Conclusion:** Digoxin toxicity remains an important cause of morbidity and mortality.<sup>5</sup> Digoxin Immune Fab is considered safe and effective treatment for severe toxicity, though it is costly and requires monitoring.<sup>2</sup> In this case, prompt recognition of concurrent BRASH syndrome guided initiation of supportive measures to interrupt the self-perpetuating cycle of bradycardia and renal hypoperfusion and decrease hyperkalemia-related mortality risk in the setting of acute digoxin toxicity.

## References:

1. Cummings ED, Swoboda HD. Digoxin Toxicity. [Updated 2023 Mar 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK470568/>
2. Pincus M. Management of digoxin toxicity. *Aust Prescr*. 2016 Feb;39(1):18-20. doi: 10.18773/austprescr.2016.006. Epub 2016 Feb 1. PMID: 27041802; PMCID: PMC4816869.
3. Saldivar L, Beasley S, Romesser C, et al. BRADYCARDIA, RENAL FAILURE, ATRIOVENTRICULAR NODAL BLOCKING AGENTS, SHOCK AND HYPERKALEMIA: A RARE SYNDROME THREATENING CARDIOVASCULAR COLLAPSE. *J Am Coll Cardiol*. 2023 Mar, 81 (8\_Supplement) 2765. [https://doi.org/10.1016/S0735-1097\(23\)03209-6](https://doi.org/10.1016/S0735-1097(23)03209-6)
4. Sattar Y, Bareeqa SB, Rauf H, Ullah W, Alraies MC. Bradycardia, Renal Failure, Atrioventricular-nodal Blocker, Shock, and Hyperkalemia Syndrome Diagnosis and Literature Review. *Cureus*. 2020 Feb 13;12(2):e6985. doi: 10.7759/cureus.6985. PMID: 32201662; PMCID: PMC7075507.
5. Peters AE, Chiswell K, Hofmann P, Ambrosy A, Fudim M. Characteristics and Outcomes of Suspected Digoxin Toxicity and Immune Fab Treatment Over the Past Two Decades-2000-2020. *Am J Cardiol*. 2022 Nov 15;183:129-136. doi: 10.1016/j.amjcard.2022.08.004. Epub 2022 Sep 9. PMID: 36089419; PMCID: PMC9588603.