Case Report

Pan African Journal of Emergency and Critical Care (PAJEC)

Atrial fibrillation with Slow Ventricular response as a sign of Digoxin Toxicity Secondary to Acute Renal failure

Selome Yewedalsew[1], Estrella Roffe[2], Meron Tesfaye[3], Tilahun Jiru[2], Abaynesh Haftu[2], Abeselom Ashenafi[3], Gemechis Direba[3], Asmamaw Abebe[3], Mohammed Shuaibu[4], Hossein Kalantari[2], Getaw Worku[2*]

Keywords: ECG, digoxin, renal failure, toxicity

1. SUNY Downstate Medical Center, Brooklyn, NY
2. NYMC, Metropolitan Hospital Center, New York, NY
3. Addis Ababa University, Addis Ababa, Ethiopia
4. CityMD, New Yoro, NY
Correspondence: Getaw Worku
Email: getawworku.hassen@nychhc.org

Received: May 9, 2024;
Accepted: August 24, 2024;
Published: October 10, 2024

ABSTRACT

Introduction: *Digoxin is a cardiac glycoside that has been used for centuries for atrial fibrillation (AFib) and congestive heart failure (CHF). Digoxin has a narrow therapeutic index with a potential for toxicity that can be life-threatening. Toxicity can result from accidental or intentional overdose, renal failure, and/or hypokalemia. Cardiac manifestations of digoxin toxicity cause dysrhythmias of different types. Bidirectional ventricular tachycardia is a specific dysrhythmia in the setting of digitalis toxicity, but AFib with slow ventricular response (SVR) is another digoxin toxicity-related dysrhythmia.*

Case report: *Here, we report AFib with SVR as a sign of digoxin toxicity secondary to acute renal failure (ARF).*

Conclusion: *The presence of AFib with SVR should trigger a search for digoxin toxicity. Every effort should be made to thoroughly review the patient's medications by reviewing the medical record and contacting the primary care physician as most patients do not present with their medications or an accurate medication list and the electronic record may not reflect current medications. The digoxin level should be obtained.*

Citation: *Selome Yewedalsew, Estrella Roffe, Meron Tesfaye, et.al. Atrial fibrillation with Slow Ventricular response as a sign of Digoxin toxicity Secondary to Acute Renal failure. PAJEC.2024;2(2): page 26 -31.*

1. Introduction

Digoxin is a cardiac glycoside that has been used for centuries for atrial fibrillation (AFib) and congestive heart failure (CHF). Digoxin exerts its effect by reversibly inhibiting the sodium-potassium adenosine triphosphatase (ATPase) on the cardiomyocyte. This mechanism increases the calcium level and leads to an increased ionotropic effect, hence its use in congestive heart failure (CHF) [1,4,5]. Another effect of digoxin is increased vagal tone, which is utilized to treat AFib [3,8,9]. There is controversy regarding its use for AFib. Digoxin has a narrow therapeutic index with a potential for toxicity that can be life-threatening. Toxicity can result from accidental or intentional overdose, renal failure, and/or hypokalemia. Cardiac manifestations of digoxin toxicity cause dysrhythmias of different types. Bidirectional ventricular tachycardia is a specific dysrhythmia in the setting of digitalis toxicity, but AFib with slow ventricular response (SVR) is another digoxin toxicity-related dysrhythmia.

The mechanisms of toxicity are not fully understood, but several mechanisms have been suggested as contributory pathways [6, 10, 11]. One such mechanism includes increased vagal tone leading to bradycardia and various Atrioventricular blocks [12,13].

2. Case report

A 73-year-old female patient presented at the emergency department ED) for a slow heart rate evaluation. The patient had an increase in liver enzymes and a suspicious mass on a computed tomography (CT) scan of the abdomen and pelvis and was referred for a liver biopsy. The patient presented at the ambulatory surgery office, and a low heart rate triggered the transfer to ED. In the ED, the patient reported mild to moderate and intermittent chest pressure. Pain is non-radiating, but she could not state how long she has had it. The patient also reported mild shortness of breath and generalized weakness due to watery diarrhea for two weeks with poor oral intake. She denied vomiting, abdominal pain, fever, cough, weakness in extremities, speech, or vision changes. The patient has a history of alcohol use disorder and smokes cigarettes. Past medical history included myasthenia gravis, coronary artery disease, liver cirrhosis, diet-managed diabetes mellitus, and AFib. The medication list included 250 micrograms of digoxin oral daily, 50 mg metoprolol oral daily, 40mg omeprazole oral daily, 20mg prednisone oral daily, 300 mg ursodiol two pills oral twice a day, 20 milliequivalent KCL oral daily, 40 mg furosemide oral daily, 2.5mg metolazone oral daily, and 60 mg pyridostigmine oral daily. The patient had no past surgical history but reported a penicillin allergy.

Physical examination in the ED was as follows: vitals BP 119/70 mmHg, HR 33 beats per minute (peripheral heart rate), RR 16 breaths per minute, oxygen saturation of 96% on room air, and finger stick glucose of 130 mg/dL.

The patient had no visible distress, lungs were clear to auscultation bilaterally, irregularly irregular heartbeat with a rate of 33 beats per minute, no murmurs, scleral icterus, (+) 2 bilateral lower extremities edema, no jugular vein distention (JVD). Her ECG showed AFib with an SVR of 38 beats per minute (Figure 1). The patient was given normal saline, external pacemaker pads were placed in case pacing or defibrillation was needed, and a trial with 0.5mg atropine intravenous with minimal increase in the heart rate.

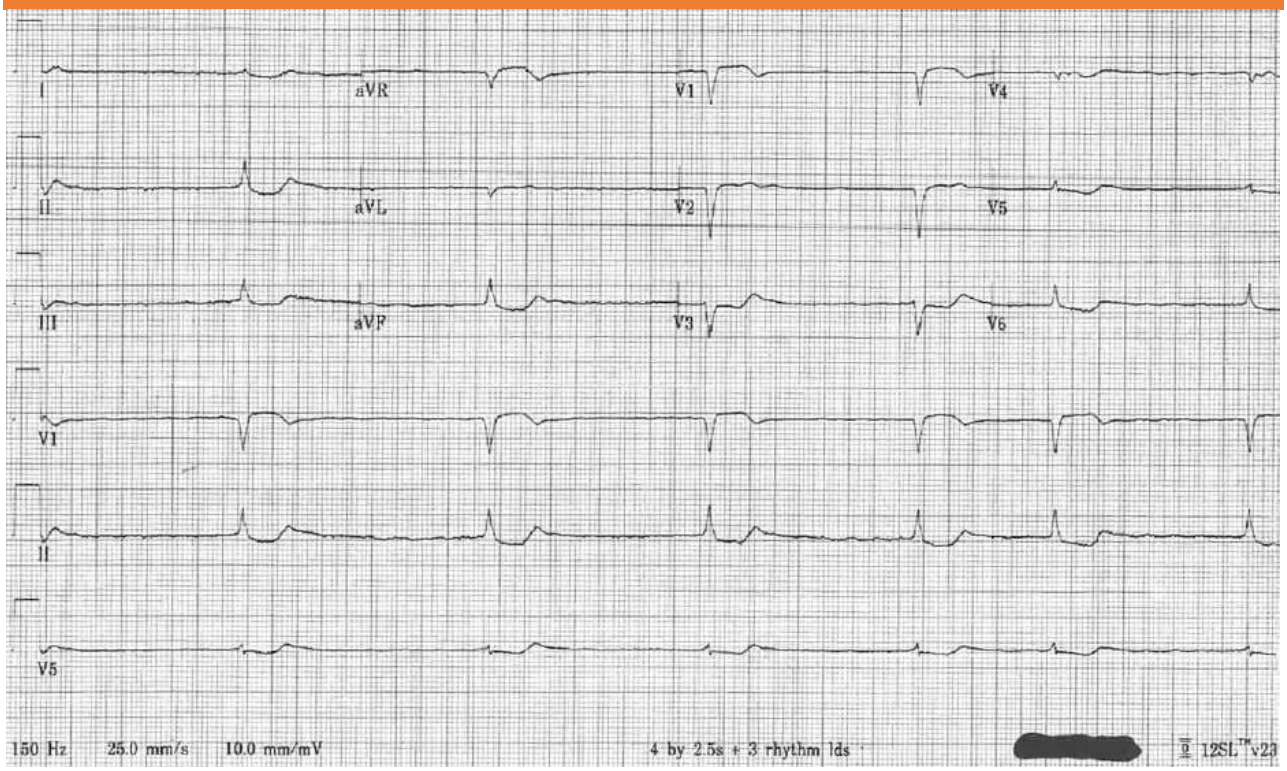

Figure 1: ECG showing atrial fibrillation with a slow ventricular response

Laboratory workup demonstrated creatinine of 3.5 mg/dL, BUN 120 mg/dL, potassium of 4,7 mmol/mL, and digoxin level of 5 ng/mL. Liver function test showed albumin of 2.8 g/dL, total bilirubin 4.7 mg/dL, direct bilirubin 3.0 mg/dL, and international normalized ratio (INR) 1.8. Cardiology and renal services were consulted and supportive care with intravenous fluid, monitoring of electrolytes, and withholding digoxin was recommended without digoxin-specific antibody. During the course of her hospital stay the creatinine improved and the patient was discharged to home in improved condition.

3. Discussion

Digoxin exerts its effect by reversibly inhibiting the sodium-potassium adenosine triphosphatase (ATPase) on the cardiomyocyte. This mechanism increases the calcium level and leads to an increased ionotropic effect, hence its use in congestive heart failure (CHF) [1,4,5]. Another effect of digoxin is increased vagal tone, which is utilized to treat AFib[3,8,9]. There is controversy regarding its use for AFib. The mechanisms of toxicity are not fully understood, but several mechanisms have been suggested as contributory pathways[6,10,11] . One such mechanism includes increased vagal tone leading to bradycardia and various Atrioventricular blocks[12,13].

Digoxin toxicity can occur for several reasons including accidental or intentional overdose, renal failure as a result of fluid loss due to gastroenteritis, or electrolyte imbalance such as hypokalemia[10,14-19]. The renal effect can be worsened in elderly patients with CHF [17,20-22]. The clinical symptoms of digoxin toxicity are nonspecific and may mimic any other disease, but the cardiac effect may give a clue that the patient may have digoxin toxicity. The cardiac effects may manifest as dysrhythmia, such as AFib with SVR or biventricular tachycardia[23].

Our patient was on several antidiuretic medications and had two weeks of diarrhea, which

compromised the renal function, leading to the accumulation of digoxin in the body. The digoxin renal clearance varies linearly with the renal function, leading to toxicity in patients with ARF despite regular digoxin doses. The renal dysfunction can be further exacerbated in the setting of volume depletion and CHF, particularly in geriatric patients.

Treatment of digoxin toxicity includes management of the underlying condition of renal failure and electrolyte imbalance and temporarily holding the digoxin dose. A special digoxin-binding antibody should be given in selected cases of very high digoxin levels, hyperkalemia, hemodynamic instability, and tachyarrhythmia. Indications of Digi bind are hyperkalemia greater than 5mmol/mL, cardiac arrest, life-threatening dysrhythmia, and > 10mg ingestion or digoxin level greater than 12 ng/mL[(24)].

This patient presented with a slow heart rate and her ECG showed AFib. Further, the workup showed acute renal failure with a high digoxin level. The patient was managed medically with a multidisciplinary approach, including cardiology and nephrology consultations, and her renal function improved.

The important point of the case is identifying the low heart rate and the presence of AFib with SVR. Patients are evaluated by different providers with varying experiences, including ECG reading, emphasizing this pathological ECG and its association with digoxin toxicity. Considering bradycardia as just an effect of digoxin and not entertaining digoxin toxicity may lead to further exposure to digoxin and life-threatening dysrhythmia.

4. Conclusions

The presence of AFib with SVR should trigger a search for digoxin toxicity. Every effort should be made to thoroughly review the patient's medications by reviewing the medical record and contacting the primary care physician as most patients do not present with their medications or an accurate medication list and the electronic record may not reflect current medications. The digoxin level should be obtained.

Abbreviation

Afib=Atrial Fibrillation
CHF=Congestive Heart Failure
CT= Computed Tomography
ECG= Electrocardiogram
ED= Emergency Department
INR = International Normalized Ratio
JVD=Jugular Vein Distention
SVR=Slow Ventricular Response

Competing interests

The authors declare that they have no competing interest

References

1) Bauman, J. L., Didomenico, R. J. & Galanter, W. L. Mechanisms, manifestations, and management of digoxin toxicity in the modern era. *Am J Cardiovasc Drugs* **6**, 77-86, doi:10.2165/00129784-200606020-00002 (2006).
2) Bhatia, S. J. & Smith, T. W. Digitalis toxicity: mechanisms, diagnosis, and management. *J Card Surg* **2**, 453-465, doi:10.1111/j.1540-8191.1987.tb00204.x (1987).
3) Blackshear, J. L., Kopecky, S. L., Litin, S. C., Safford, R. E. & Hammill, S. C. Management of atrial fibrillation in adults: prevention of thromboembolism and symptomatic treatment. *Mayo Clin Proc* **71**, 150-160, doi:10.4065/71.2.150 (1996).
4) Ehle, M., Patel, C. & Giugliano, R. P. Digoxin: clinical highlights: a review of digoxin and its use in contemporary medicine. *Crit Pathw Cardiol* 10, 93-98, doi:10.1097/HPC.0b013e318221e7dd (2011).
5) Ponikowski, P. *et al.* 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special

contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail* **18**, 891-975, doi:10.1002/ejhf.592 (2016).
6) Fisch, C. & Knoebel, S. B. Digitalis cardiotoxicity. *J Am Coll Cardiol* **5**, 91A-98A, doi:10.1016/s0735-1097(85)80467-8 (1985).
7) Almarzuqi, A., Kimber, S., Quadros, K. & Senaratne, J. Bidirectional Ventricular Tachycardia: Challenges and Solutions. *Vasc Health Risk Manag* **18**, 397-406, doi:10.2147/VHRM.S274857 (2022).
8) Ferrari, F., Santander, I. & Stein, R. Digoxin in Atrial Fibrillation: An Old Topic Revisited. *Curr Cardiol Rev* **16**, 141-146, doi:10.2174/1573403X15666190618110941 (2020).
9) Theone, S., Carballo, S., Carballo, D. & Marti, C. [Digoxin and atrial fibrillation in 2016]. *Rev Med Suisse* 12, 1758-1760 (2016).
10) Patocka, J., Nepovimova, E., Wu, W. & Kuca, K. Digoxin: Pharmacology and toxicology-A review. *Environ Toxicol Pharmacol* 79, 103400, doi:10.1016/j.etap.2020.103400 (2020).
11) Thacker, D. & Sharma, J. Digoxin toxicity. *Clin Pediatr (Phila)* 46, 276-279, doi:10.1177/0009922806294805 (2007).
12) https://www.uptodate.com/contents/cardiac-arrhythmias-due-to-digoxin-toxicity?search=digoxin%20toxicity&topicRef=319&source=see_link.
13) https://www.uptodate.com/contents/digitalis-cardiac-glycoside-poisoning?search=digoxin%20toxicity&source=search_result&selectedTitle=1~88&usage_type=default&display_rank=1#H7.
14) Kanji, S. & MacLean, R. D. Cardiac glycoside toxicity: more than 200 years and counting. *Crit Care Clin* **28**, 527-535, doi:10.1016/j.ccc.2012.07.005 (2012).
15) Matzke, G. R. & Frye, R. F. Drug administration in patients with renal insufficiency. Minimising renal and extrarenal toxicity. *Drug Saf* **16**, 205-231, doi:10.2165/00002018-199716030-00005 (1997).
16) Shah, M., Palani, A., Hashemi, A. & Shin, J. Bradycardia, Renal Failure, Atrioventricular Nodal Blockade, Shock and Hyperkalaemia Syndrome Involving Digoxin Toxicity: A Case Report. *Heart Int* **17**, 60-62, doi:10.17925/HI.2023.17.1.60 (2023).
17) Shlipak, M. G., Smith, G. L., Rathore, S. S., Massie, B. M. & Krumholz, H. M. Renal function, digoxin therapy, and heart failure outcomes: evidence from the digoxin intervention group trial. *J Am Soc Nephrol* **15**, 2195-2203, doi:10.1097/01.ASN.0000135121.81744.75 (2004).
18) Wells, T. G., Young, R. A. & Kearns, G. L. Age-related differences in digoxin toxicity and its treatment. *Drug Saf* **7**, 135-151, doi:10.2165/00002018-199207020-00005 (1992).
19) Wofford, J. L. & Ettinger, W. H. Risk factors and manifestations of digoxin toxicity in the elderly. *Am J Emerg Med* **9**, 11-15; discussion 33-14, doi:10.1016/0735-6757(91)90161-c (1991).
20) Digiovanni-Kinsley, S., Duke, B., Giovane, R. & Paisley, C. A Case of Digoxin Toxicity Due to Acute Renal Failure. *Cureus* **13**, e17599, doi:10.7759/cureus.17599 (2021).
21) Papadakis, M. A., Wexman, M. P., Fraser, C. & Sedlacek, S. M. Hyperkalemia complicating digoxin toxicity in a patient with renal failure. *Am J Kidney Dis* **5**, 64-66, doi:10.1016/s0272-6386(85)80139-6 (1985).
22) Shah, P. *et al.* The effect of digoxin on renal function in patients with heart failure. *BMC Nephrol* **22**, 349, doi:10.1186/s12882-021-02562-0 (2021).
23) Kelly, R. A. & Smith, T. W. Recognition and management of digitalis toxicity. *Am J Cardiol* **69**, 108G-118G; disc 118G-119G, doi:10.1016/0002-9149(92)91259-7 (1992).
24) Chan, B. S. & Buckley, N. A. Digoxin-specific antibody fragments in the treatment of digoxin toxicity. *Clin Toxicol (Phila)* **52**, 824-836, doi:10.3109/15563650.2014.943907 (2014).