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TEST YOUR KNOWLEDGE

A case of sudden slow heart rate in a patient with atrial fibrillation – what could be the possible cause?

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Abstract

General practitioners regularly encounter atrial fibrillation in their daily practice. A crucial cornerstone of its management includes prescribing anticoagulants and controlling the heart rate. Tachycardia or bradycardia often reflects an ongoing pathological process that should be addressed. Clues are frequently revealed through comprehensive history-taking, complete physical assessment and 12-lead electrocardiogram (ECG) interpretation at the bedside. Thus, early recognition of potential life-threatening arrhythmia in the outpatient setting will lead to appropriate clinical management. In this paper, we illustrate a sudden decrease in the heart rate of a patient with atrial fibrillation. We discuss the ECG interpretation, potential differential diagnoses and approach to clinical management.

Case summary

A 64-year-old woman with underlying conditions including diabetes mellitus, hypertension, bronchial asthma, chronic kidney disease and atrial fibrillation (treated with warfarin) reported experiencing chest discomfort for 2 days. She sought help at a nearby health clinic where an immediate 12-lead electrocardiogram (ECG) was performed (**Figure 1**). She was subsequently referred to the emergency department. Upon arrival, she was alert, and her vital signs were as follows: blood pressure=133/61 mmHg, heart rate=34 beats per minute (bpm), temperature =36.4°C and oxygen saturation=99% on room air. Her respiratory and abdominal examinations revealed no abnormalities. A second ECG was conducted in the emergency department (**Figure 2**).

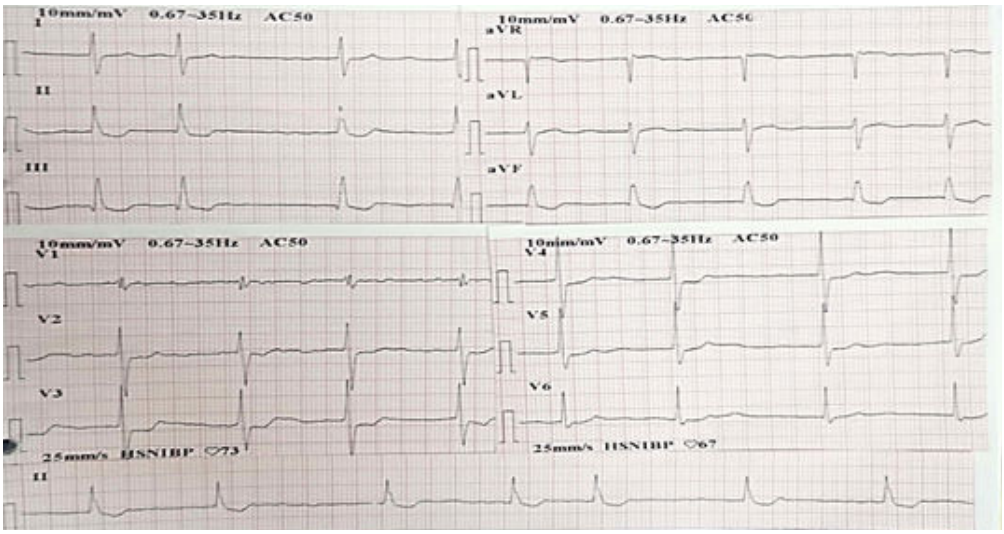

Figure 1. Twelve-lead electrocardiogram at the health clinic.

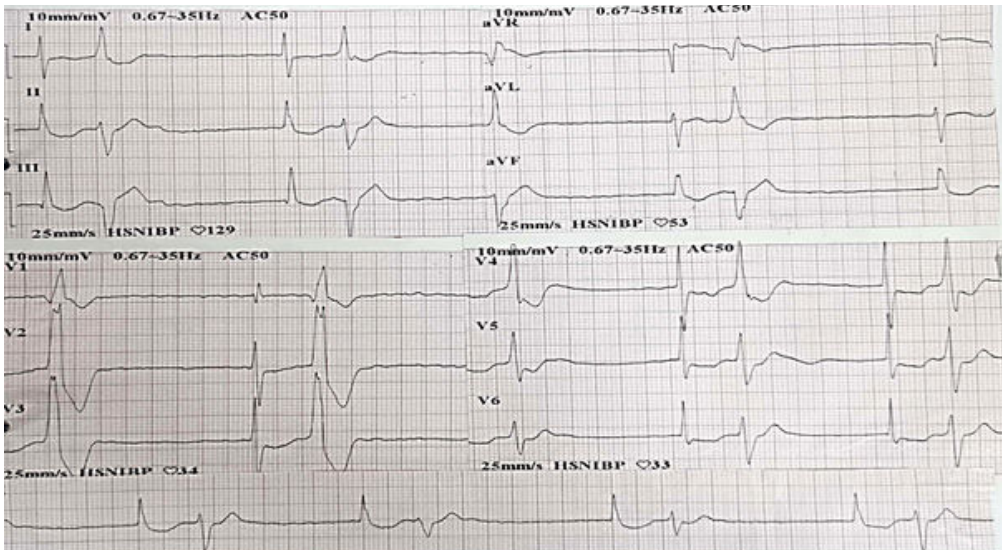

Figure 2. Twelve-lead electrocardiogram in the emergency department.

Questions:

1. Describe the ECG (Figures 1 and 2).
2. What further information should be elicited from the patient?
3. What are the differential diagnoses?
4. Outline the management plan.

Answers with discussion

1. Describe the ECG.
   - **Figure 1**: Atrial fibrillation, heart rate of 60 bpm
   - **Figure 2**: Junctional bradycardia, heart rate of 30 bpm, frequent ventricular ectopic beats with a bigeminy pattern

2. What further information should be elicited from the patient?
   - Gastrointestinal loss symptoms (e.g. vomiting or diarrhoea)
   - Recent history of viral illnesses or sick contacts
   - Detailed medication history

The patient had just recovered from acute gastroenteritis a week prior. She denied any recent exposure to sick contacts or viral infections such as COVID-19. Her medication regimen included perindopril 4 mg once daily, bisoprolol 1.25 mg once daily, digoxin 0.25 mg once daily, warfarin 2 mg once daily, metformin 500 mg twice daily, salbutamol inhaler 200 mcg as needed and budesonide inhaler 200 mcg twice daily. Her medications were not adjusted during follow-up visits. She also denied overuse of any medication.

3. What are the differential diagnoses?
   - Electrolyte imbalance
   - Digoxin toxicity
   - Acute coronary syndrome
   - Acute myocarditis
   - Hypothyroidism
   - Sick sinus syndrome

4. Outline the management plan.
   - Evaluate the patient's airway, breathing and circulation.
   - Check the electrolyte, serum digoxin and cardiac enzyme levels and thyroid function.
   - In instances of symptomatic bradycardia accompanied by haemodynamic instability, intravenous atropine should be administered promptly. A higher degree of heart block (e.g. second or third-degree atrioventricular block) will necessitate temporary cardiac pacing. Excessive ventricular ectopic beats may be treated with intravenous lignocaine.[1]
   - In cases of life-threatening digoxin toxicity, digoxin-specific antibody fragments (Digibind) should be administered as the reversal agent.

Despite the intravenous administration of 3 mg atropine in the emergency department, the patient remained bradycardic. Consequently, intravenous dopamine infusion was initiated to maintain the heart rate within the normal range. The patient was transferred to the coronary care unit for close monitoring. Her electrolyte panel showed the following: sodium level of 137 mmol/L; potassium level, 4.8 mmol/L; urea level, 15.5 mmol/L; creatinine level, 207 mmol/L; glomerular

filtration rate, 30 mL/min/1.73 m^2; magnesium level, 0.57 mmol/L; corrected calcium level, 2.48 mmol/L and phosphate level, 0.92 mmol/L. The serum digoxin level was 2.6 ng/mL, which was above the recommended therapeutic range (<1.2 ng/mL). Both thyroid function and cardiac enzyme level were normal. After consultation with a cardiologist, she received six vials of Digibind (a total of 240 mg) intravenously on the second hospitalisation day. Her heart rate normalised, and intravenous dopamine was gradually tapered off. A repeated ECG showed rate-controlled atrial fibrillation (**Figure 3**). After a 1-week hospital stay, she was discharged in good health. Digoxin was subsequently discontinued from her medication regimen.

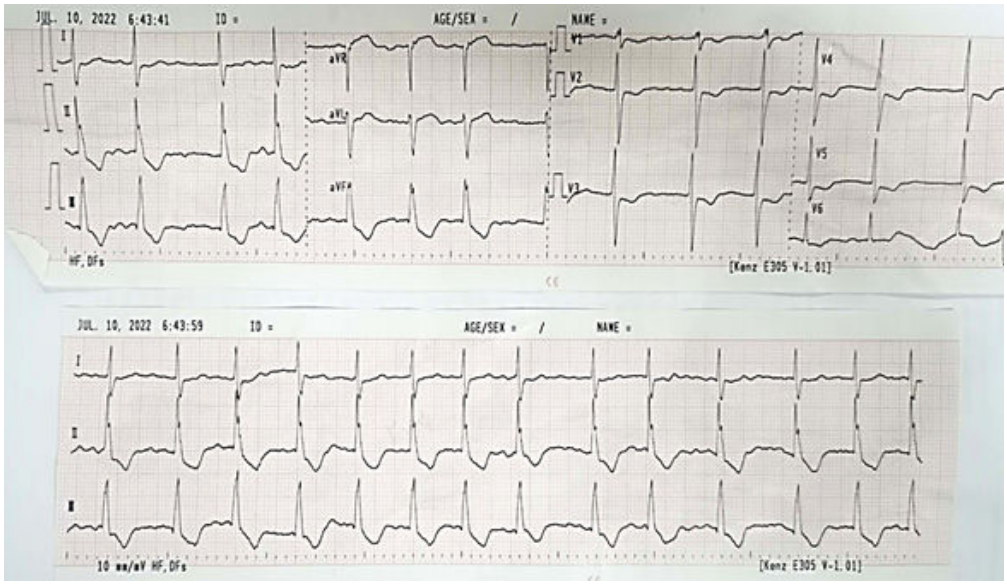

Figure3. Twelve-lead electrocardiogram in the coronary care unit.

Discussion

Digoxin operates through two mechanisms of action. First, it inhibits cardiac myofibril Na+–K+ ATPase, increasing the intracellular Ca2+ level and producing an inotropic effect. Second, digoxin enhances the vagal tone to both sinoatrial and atrioventricular nodes, thereby slowing the heart rate.[2] The Digitalis Investigation Group (DIG) trial published in 1997 concluded that while digoxin did not reduce all-cause mortality, it decreased the hospitalisation rate in patients with reduced ejection fraction.[3] Consequently, digoxin is recommended as an adjunct pharmacological therapy for patients with heart failure and as a rate-controlling agent for patients with atrial fibrillation.[4]

The usage of digoxin has been declining over the years.[5] According to the Malaysian Statistics on Medicine 2015–2016, the rate of digoxin usage in Malaysia is relatively low compared with that in European countries.[6] Accordingly, digoxin toxicity, although less common, can be easily overlooked when it occurs. The serum digoxin level is recommended to be maintained at <1.2 ng/mL. This guideline is based on a post-hoc analysis of the DIG trial, which demonstrated that a serum digoxin level of 0.5–0.9 ng/mL is the optimal therapeutic range for reducing mortality and hospitalisation among patients with heart failure.[7]

Diagnosing digoxin toxicity can be challenging, as the clinical presentation is often non-specific and subtle. The clinical features can be categorised on the basis of the organ systems involved as follows:

- Gastrointestinal: Nausea, vomiting, anorexia and diarrhoea;
- Visual: Yellow–green discolouration, haloes and blurring;
- Cardiovascular: Palpitations, syncope and dyspnoea;
- Central nervous: Confusion, dizziness and delirium.

Notably, there are four ECG findings consistent with digoxin usage: T wave flattening, QT interval shortening, 'reversed tick' pattern in leads V4–V6 and prominent U wave. However, these findings do not necessarily indicate digoxin toxicity. When digoxin toxicity sets in, the hallmark feature of cardiac toxicity is an increase in automaticity coupled with a concomitant delay in conduction. This can result in arrhythmias such as frequent premature ventricular contractions, sinus bradycardia,

slow atrial fibrillation, atrioventricular block, regularised atrial fibrillation and ventricular tachycardia.[8]

In the present case, digoxin toxicity may have occurred owing to acute kidney injury secondary to a recent episode of acute gastroenteritis. Other known precipitating factors include hypokalaemia, hypomagnesemia, hypothyroidism and drug–drug interactions. Concurrent usage of amiodarone, verapamil, macrolide or quinidine can increase gastrointestinal absorption and reduce renal clearance of digoxin.[9]

Digibind is a specific antibody that binds with digoxin molecules and is excreted by the kidneys. Indications for Digibind include life-threatening cardiac arrhythmia, severe hyperkalaemia, steady-state serum digoxin levels exceeding 5 ng/mL and acute ingestion of 0.3 mg/kg digoxin.[1] Haemodynamic instability secondary to junctional bradycardia justified the use of Digibind in the present case.

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Author contributions
JY Goh – conceptualization
CW Siaw - draft writing

Conflicts of interest
The authors declare no conflicts of interest.

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How does this paper make a difference in general practice?
- Clinician able to recognise early on possible digoxin toxicity.
- Early referral to tertiary centres for prompt reversal of digoxin toxicity.
- Avoidance of digoxin prescriptions for patients with risk factors of digoxin toxicity.
- Clinician will be aware of the possible drug–drug interaction for patients taking digoxin

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