Case Report

A Case of Quinine-Induced High Degree Complete Heart Block in a Young Teenage Nigerian Female

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Abstract

Background: Third-degree atrioventricular block occurs when atrial and ventricular activity are autonomous of each other.

Method: This is a case of a 17-year-old lady presenting to the emergency room of the University of Port-Harcourt Teaching Hospital, Rivers State with sudden onset chest tightness and syncope immediately following a dose of intravenous Quinine administration for treatment of malaria at a peripheral clinic. Vital signs on arrival revealed marked bradycardia with a pulse rate of 17 beats per minute with a blood pressure reading of 110/40mmhg. An urgent electrocardiogram done showed a third-degree Atrioventricular (AV) Block with a slow ventricular escape rhythm and complete AV dissociation. She was a previously healthy young teenager with no history of effort intolerance or cardiac disease. There was also no history of cardiac disease or sudden cardiac death in any first degree relative. Drug-induced AV block was diagnosed based on history, clinical presentation, and investigations.

Result: AV block is not uncommon with drug use however, but third-degree AV block is rarely caused by drugs. Quinine use for treatment of malaria should be reviewed due to this life-threatening side-effect especially in a region where centers for temporary pacing are not widely available nor affordable in Nigeria.

Conclusion: Cardiovascular monitoring is essential if Quinine administration is indicated for prompt identification and treatment of cardiac electrical disturbances.

Keywords: Quinine, atrioventricular block, toxicity, Nigeria.

Introduction

Atrioventricular (AV) block is simply defined as a recurrent delay in the transmission of an electrical impulses coming from the atrium to the ventricles and this is usually as a result of a defect in the conducting system. The defect or disruption of the conducting system can either be transient or permanent, with the nature of the conduction being absent, delayed, or intermittent.[1] Commonly used terminology includes:

- First degree AV block where conduction is slowed but there are no missed beats.
- Second degree AV block in which case beats are missed in a regular pattern (e.g., 2:1, 3:2), or other degrees of block, which has been further classified

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into Mobitz type I (Wenckebach) and Mobitz type II AV block.
- Third degree AV block which occurs when no impulse from the atrium reaches the ventricles.[1]

Third-degree atrioventricular block is sometimes called complete heart block. In this condition, atrial and ventricular activity are autonomous of each other. The exact area of the block is ascertained from the escape rhythm. Atrioventricular nodal block can be seen as a narrow QRS complex, having a rate between 40 and 60 beats per minute, whilst a wide QRS escape rhythm at slower rates signifies that the block is in the His–Purkinje system.[2]

Drugs are considered reversible causes of AV block that usually do not require pacemaker implantation.[3] Three different types of bradycardia can be observed during therapy with drugs namely drug induced bradycardia in an essentially normal heart, drug provoked bradycardia in a heart with underlying latent disease (of the sinoatrial node, AV node or infranodal conduction system) and drug associated bradycardia.[4] Clinically, β-blockers, calcium channel antagonist, non-dihydropyridine and digitalis can cause significant bradycardia. Other drugs that can induce bradycardia include carbamazepine, sympatholytic anti-hypertensives, cimetidine, lithium, opioid blockers, anti-depressants, and cocaine.[5] Bradyarrhythmia develops more commonly with amiodarone, propafenone, sotalol, or flecainide than with quinidine, procainamide, or disopyramide; combination therapies of drugs also increases the risk of significant bradycardia.[6,7] Development of drug-induced bradycardia necessitating pacemaker implantation was found in 8% of patients on a variety of anti- arrhythmic drugs used for different indications.[7]

Quinine is used to treat malaria and babesiosis. This is particularly so in the treatment of malaria caused by chloroquine resistant Plasmodium falciparum in the absence of artesunate.[8] As of 2006, Quinine is no longer recommended by the WHO (World Health Organization) as a first-line treatment for malaria.[9] Cardiovascular toxicity of Quinine is similar to quinidine toxicity which includes myocardial depression, peripheral vasodilation, and electrophysiologic effects such as an increase in action potential duration and effective refractory period and a decrease in membrane responsiveness and automaticity.[10]

Case presentation

A 17-year-old female student was rushed to the Emergency room following a 5-minute transient loss of consciousness which occurred 2 hours before presentation. She was referred from a general practitioner (GP) clinic where she presented with a 5-day history of a febrile illness which was associated with headaches and generalized body pains. She was initially treated with oral medications and then subsequently admitted for treatment with parenteral medications-intravenous Quinine as symptoms did not subside. Following the first dose of IV Quinine patient complained of dizziness and IV fluids was given rapidly and patient recovered from dizziness, however, after completion of the second dose of IV Quinine 8 hours later, patient felt sudden chest tightness which was followed by transient loss of consciousness (TLOC) that lasted for about 5 minutes. Patient was subsequently referred to the University of Port-Harcourt Teaching Hospital for further expert management.

On admission into the ER, vital signs checked revealed a pulse rate of 17 beats per minute (bpm) irregular, with moderate volume while the blood pressure reading was 110/40mmg. Her SPO_2 was 99% in room air, lung auscultation demonstrated vesicular breath sounds, however, patient was fully conscious with no ongoing chest pain or dizziness and no focal or global neurological deficit.

There was no prior history of effort intolerance, occasional chest pain, palpitations, pre-syncope or syncopal attack, cough, dyspnea, orthopnea, orthopnea, orthopnea, or paroxysmal nocturnal dyspnea. There was also no prior history of cardiac disease in the patient or cardiac disease/sudden cardiac death in first-degree relatives. There was no oliguria, passage of frothy urine or bipedal swelling.

An urgent electrocardiogram done at presentation showed marked bradycardia with complete heart block as shown in figure 1.

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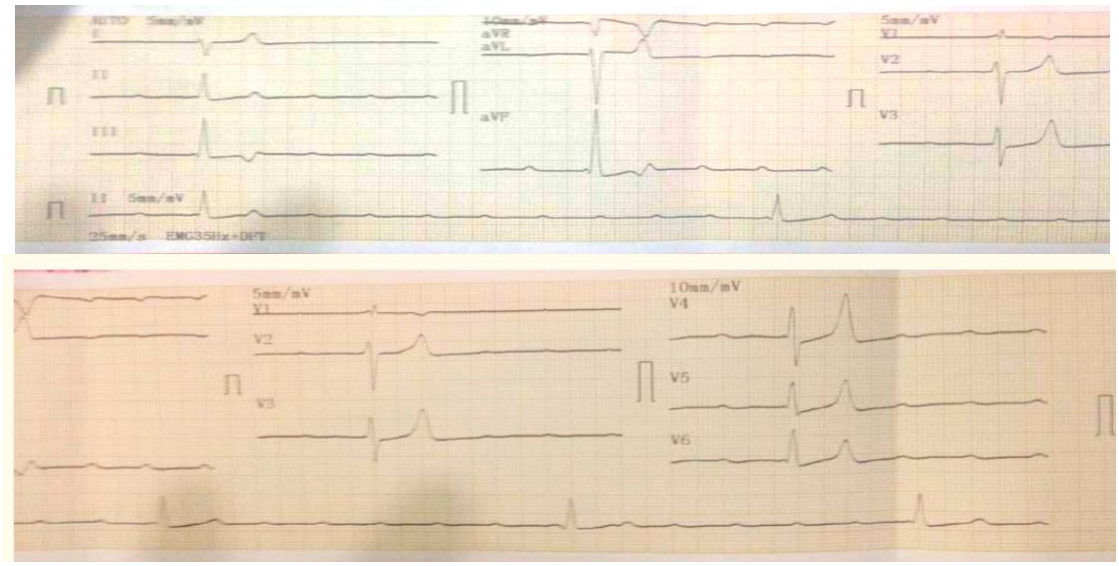

Figure 1: Electrocardiogram done at presentation showed marked bradycardia with complete heart block

The patient was transferred into the high dependency unit (HDU) and connected to a cardiac monitor. An intravenous access was secured with IV normal saline given at 1 liter 8hourly and 100mg of IV hydrocortisone given as a bolus injection. Patient was also placed on supplementary oxygen. The interventional cardiologist was notified for emergency temporary pacing if features of hemodynamic instability were noticed. Samples were taken for an urgent serum electrolyte, urea & creatinine.

Patient had persistent bradycardia for about 9 hours after presentation in the ER after which, pulse rate gradually started improving to 60 then 80bpm with the systolic blood pressure persistently above 110mmHg and adequate urinary output. Repeat ECG after cessation of bradycardia revealed a complete left bundle branch block demonstrated in figure 2

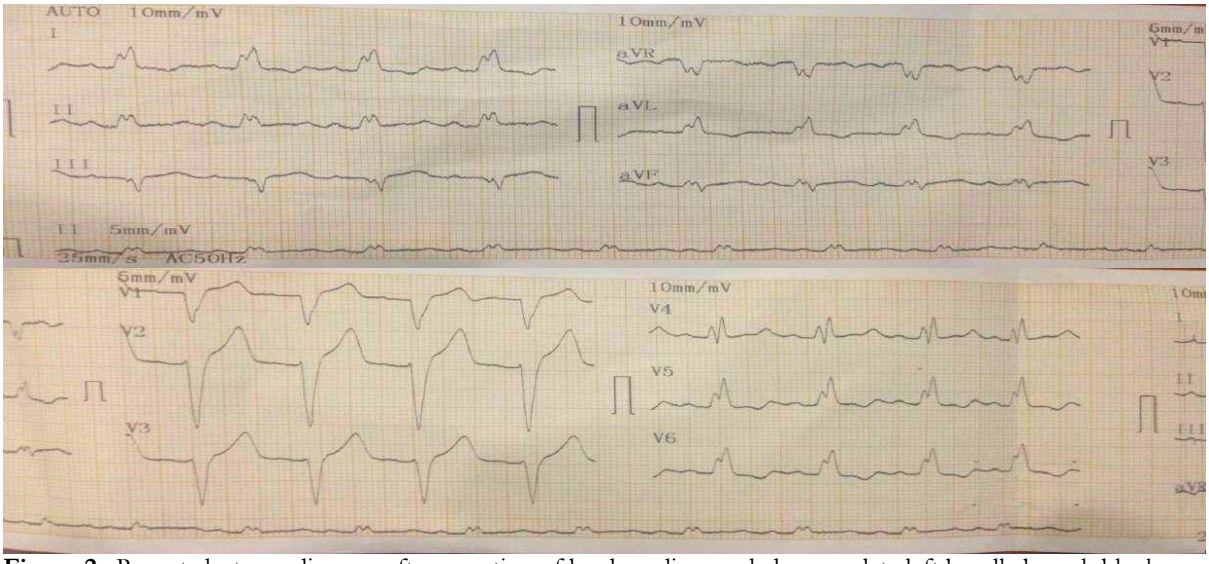

Figure 2: Repeat electrocardiogram after cessation of bradycardia revealed a complete left bundle branch block

Results of initial renal function showed mild azotemia with urea = 8.7mmol/l, creatinine = 205µmol/l and potassium = 5.7mmol/l. A repeat test done the next day showed gross improvement in renal indices.

A transthoracic echocardiogram was performed; however, no structural or functional defects were noted,

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and a pre-discharge ECG done at the third day is shown below (figure 2), the patient was subsequently discharged to be seen in the Cardiology out-patient clinic a week later.

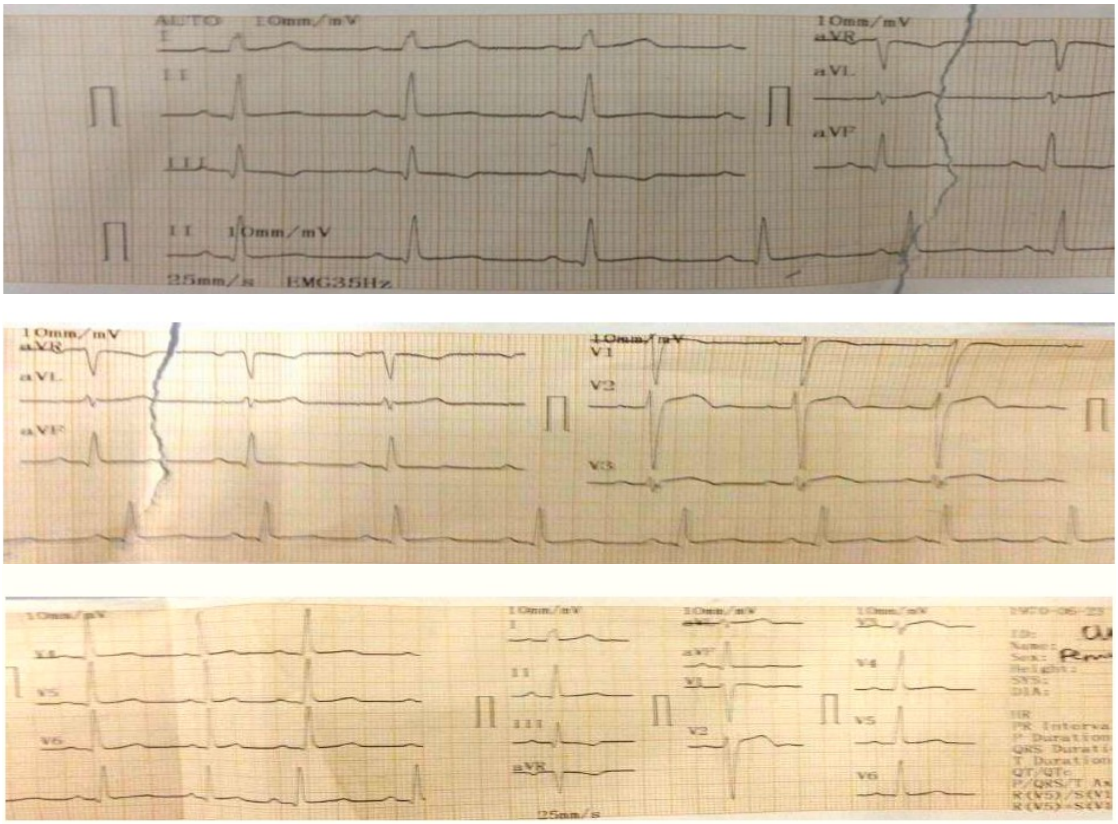

Figure 3: Pre-discharge electrocardiogram done on the third day

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Discussion

The index patient developed a high degree complete AV block following administration of intravenous Quinine used to treat malaria. While quinine is still routinely used in our environment for the treatment of severe malaria or resistant malaria, the WHO no longer recommends its use as first line treatment for severe malaria.[9] Quinine has a good safety profile as long as it is used as prescribed, and the therapeutic dose is not exceeded but, side effects can occur which are reversible and can be managed by discontinuing quinine.[11] Adverse effects on the kidneys and liver are characterized by increased creatinine levels and elevated serum transaminases respectively.[12] The patient had transient elevated creatinine at presentation which normalized thereafter. Hematological adverse effects that are often experienced with the use of quinine include anemia, neutropenia, and thrombocytopenia with microangiopathic hemolytic anemia and disseminated intravascular coagulation occurring in rare cases.[12] With the exception of mild anemia, this patient's complete blood count panel was normal. Quinine has also been noted to have major toxic effects on the nervous system including optic and auditory nerve damage secondary to both vascular and neural injury.[10]

Quinine can cause atrioventricular conduction disturbances.[13] This mechanism has been postulated to be via depressed myocardial excitability with a reduction in pacemaker discharge, increase in the effective refractory period with resultant depression in intraatrial and intraventricular conduction.[10,14] In sensitive patients, such changes can occur with normal dosages given over a prolonged period; however, in most cases cardiac effects are due to overdosage. Electrocardiographic changes, such as prolongation of the QT interval, widening of the QRS complex, and T wave flattening, can be seen with plasma concentrations above 15mg/ml.[13] Pulmonary edema has been reported by various authors at therapeutic doses [15,16] while pericarditis was described by Lim et al.[17] Quinine, and more profoundly quinidine, its diastereomer, can cause ventricular tachycardia, torsade de pointes, and ventricular fibrillation by prolonging the QT interval; with ventricular tachycardia occurring with increased plasma concentrations of quinine.[13]

This young girl had two therapeutic doses of quinine within 24 hours and developed complete AV block. Atrioventricular conduction may be increased via quinine's vagolytic effect but at very high plasma concentrations sinoatrial block or arrest and high-degree atrioventricular block may be seen.[10,14] In patients with acute malaria the volume of distribution of quinine is reduced, and systemic clearance is slower than in healthy subjects; these changes are proportional to the severity of the disease.[18] As a result, plasma quinine levels are higher in patients with malaria, and this may account for effects seen in index patient who developed adverse effects despite administration of therapeutic doses. A diagnosis of third degree (complete) AV block can be made in a patient with suggestive symptoms (e.g., fatigue, dyspnea, presyncope, and/or syncope) by obtaining a surface electrocardiogram (ECG), using a full 12-lead ECG but in some situations, a single-lead rhythm strip is used if a full 12-lead ECG cannot be obtained. For the rare patient with a non-diagnostic surface ECG, invasive electrophysiology studies can definitively diagnose third degree (complete) AV block and accurately identify the level of the block.[1]

The most important clinical determination in a patient presenting with a third degree (complete) AV block is whether the patient is hemodynamically unstable or not due to the resulting bradycardia and reduced cardiac output.[1] Initial management of the patient with third degree (complete) AV block thus depends on the presence and severity of any signs and symptoms related to the ventricular escape rhythm. Unstable patients require immediate pharmacologic therapy and other supportive treatment, in most instances, should also receive temporary pacing to increase heart rate and cardiac output.[1] There are currently no guidelines for the management of drug induced bradycardia, neither are there controlled studies regarding pacing in patients with a drug induced bradycardia, but discontinuation with observation, supportive medical therapy and/or temporary/permanent pacing has been suggested, however, if the drug is to be continued, there may be need for permanent pacing.[19]

The ultimate predictor of the outcome appears to be the degree to which the patient's cardiovascular function is affected.[10] Signs and symptoms of hemodynamic instability include hypotension, altered mental status, signs of shock, ongoing ischemic chest pain, and evidence of acute pulmonary edema.[20] This young lady's systolic blood pressure was persistently above 110mmHg, she was fully conscious with no chest pain, no evidence of pulmonary edema and good urinary output. Hypotension if present, can also be secondary to quinine's alpha-blocking properties which further exacerbates quinine-induced myocardial depression by decreasing coronary perfusion.[10] This patient's quinine sulphate was discontinued, and adequate hydration was maintained to sustain blood pressure. The AV block terminated spontaneously within 12 hours probably after hepatic biotransformation and renal excretion.[18]

Implications of the findings from this case study

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Quinine is still being used routinely by medical practitioners for treatment of malaria infection thus, cardiovascular monitoring is essential if the drug is indicated. The importance of the knowledge of Electrocardiography (ECG) in all medical practitioners for prompt identification and treatment of cardiac electrical disturbances which can be lifesaving cannot be over emphasized.

Conclusion

This case highlights the life- threatening arrhythmia associated with quinine in a young patient with no underlying structural heart condition. Drug- induced complete heart block is not an uncommon entity, however, this condition is more common with patients with underlying heart diseases and in those on anti-arrhythmic medication. The use of Quinine for the treatment of malaria should be reviewed due to this life-threatening side-effect especially in a region where centers for temporary pacing are not widely available nor affordable.

Declarations

Authors' Contribution: Aisha O. Ajala: Case design, Guarantor. Boma Oyan: Manuscript preparation, Literature search. Sotonye Dodiyi-Manuel: Concept, Case design. Jacqueline Ejituwu: Manuscript editing, Literature search.

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