Cardiac dysrhythmia resulting from antibiotic abuse

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ABSTRACT

Antibiotics are commonly used to combat infections and could be used in treating some connective diseases. They are not without side effects especially when used without regard to age, gender, diseases and their severity, comorbidity, and idiosyncrasies. This is more likely to occur when dispensed by unqualified persons to selves or others. Consequences of inappropriate use include various morbidities and in some instances death. This is a report of a middle-aged man with several risk factors for cardiovascular disease, who on the side had chronic osteomyelitis. Wound swab grew organisms sensitive to levofloxacin, and he had the drug prescribed to him by the attending orthopedic surgeon. With reduction in discharge to the point that he no longer bound his foot in bandage, he went on using the drug beyond the duration of prescription without reverting to his orthopedic surgeon until he developed sudden onset palpitation and shortness of breath. With this was an unusual tachyarrhythmia which defied initial measures. This prompted further review of his drug history when he admitted to taking levofloxacin for up to 3 months. Suspecting it to be the culprit, he was advised to discontinue it. With this, his symptoms started to abate, alongside gradual improvement in electrocardiograms till eventual normalization. This report is made to highlight the possibility that some antibiotics have the propensity to induce arrhythmias that can be very serious especially in cardiovascular disease–burdened patients. Such patients then go into heart failure and it becomes difficult to tell which came first, the arrhythmia or the heart failure. Resolving the order of onset assists in proper management. As a result, it is being recommended that patients with unexplained arrhythmias with or without heart failure should have their drug histories evaluated. Uncontrolled prescription and use of antibiotics should also be discouraged.

Key words: Abuse, arrhythmias, levofloxacin, Nigeria

INTRODUCTION

Antibiotics are commonly used pharmacological agents, usually in infections, though newer indications in certain connective tissue diseases are emerging. Under prescription by physicians, rational antibiotic use ensures that choice is determined by age, gender, disease and its severity, comorbidity, or idiosyncrasies. However, in our environment, several classes of people prescribe and dispense antibiotics, including patients themselves, who most times do not have the appropriate training. Hence, it is common place to see antibiotics sold over the counter with no form of control. The dangers are numerous ranging from resistance development, kidney damage, blood dyscrasias, cutaneous lesions, and ultimately even to death. When death results, anaphylaxis is suspected with scant attention paid to cardiac morbidity.

The case reported here is that of a patient who after being put on levofloxacin by his orthopedic surgeon for chronic osteomyelitis persevered on it beyond the duration of prescription, until he presented with a weird cardiac dysrhythmia defying initial action. This prompted a review which included drug history, and suspicion that the abused antibiotic could be the cause. When the suspected offending drug was withdrawn, the heart rhythm gradually

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returned to normal, to the point that patient became well and started skipping clinic appointment for reasons of “no longer having any problem.” Clinicians should be on alert for this, especially in areas where patients and untrained prescribers’ abuse of antibiotic is rife. This is to prevent avoidable deaths from cardiac dysrhythmias.

CASE REPORT

B. U. consulted the author in December 2011 with a sudden onset shortness of breath, palpitations, sweating, and dizzy spells. He had upper abdominal discomfort which he related to his diagnosis of peptic ulcer disease. He was hypertensive, grossly obese but not diabetic. He also suffered from chronic osteomyelitis which at the time was scantily discharging. He came with a chest X-ray that revealed moderate cardiomegaly and unfolded aorta, abdominal ultrasound and viral screen that were normal. He also came with an echocardiographic report of concentric hypertrophy of hypertensive heart disease with left ventricular diastolic dysfunction. Urinalysis showed ketonuria (2+). Osteomyelitis wound swab grew *Staphylococcus aureus*, fasting blood sugar stood at 5.1 mmol/l, full lipid profile result was: Total cholesterol –6.5 mmol/l, high-density lipoprotein-cholesterol –1.2 mmol/l, low-density lipoprotein-cholesterol –4.4 mmol/l, triglycerides –2.0 mmol/l. He was on levofloxacin, aspirin, glyceryl trinitrate, frusemide, aldactone, carvedilol, simvastatin, fenofibrate, clopidogrel, and triple therapy for *Helicobacter pylori* eradication.

On examination, significant findings apart from his obesity were anxiety state and epigastric tenderness. Aspirin and glyceryl trinitrate were discontinued, and he was advised to continue with the other drugs pending review. The diagnoses entertained were Metabolic syndrome and Pickwickian syndrome.

Along the line he developed fever and treated himself for malaria with an artemisinin combination therapy. With palpitations not relenting, he was sent for electrocardiography that initially showed only occasional atrial ectopics. A Holter monitor done revealed, mean heart rate –88/min, highest heart rate –184/min, lowest heart rate –61/min, tachycardia events –0, bradycardia events –0, ST depression – detected, atrial fibrillation – not detected, Asystole – nil, atrial ectopics –1094 in 24 h, ventricular ectopics – 4 in 24 h, multifocal ventricular ectopics –0 in 24 h. His treatment was revised in January 2012 to frusemide 40 mg daily, aldactone 25 mg bd, carvedilol 12.5 mg daily, fenofibrate 160 mg daily, and drug review was embarked upon. He admitted to apart from his current prescription having remained on daily 500 mg levofloxacin which the orthopedic surgeon attending to his chronic osteomyelitis put him on since December 2011. This was before consulting the author. At this point, cardiac dysrhythmia due to levofloxacin abuse was suspected, and a letter was written to his orthopedic surgeon recommending antibiotic discontinuation. With this he started to feel better though not much change was recorded on electrocardiogram. Given his obesity and possibility of gastro-esophageal reflux disease (GERD), omeprazole was reintroduced and amiodarone prescribed. A repeat electrocardiogram in June 2012, though still showing tachycardia was now sinus rhythm. A gradual reduction in dose of amiodarone dose was embarked on above treatment. In April, the palpitations, sweating, and dizzy spells had returned, making him feel very weak. Pulse rate was now 43/min with frequent ectopics and blood pressure had gone down to 74/50 mmHg. Carvedilol was reduced to 6.25 mg daily, lisinopril 2.5 mg daily, aldactone 25 mg bd and fenofibrate 160 mg daily, and drug review was embarked upon. He admitted to apart from his current prescription having remained on daily 500 mg levofloxacin which the orthopedic surgeon attending to his chronic osteomyelitis put him on since December 2011. This was before consulting the author. At this point, cardiac dysrhythmia due to levofloxacin abuse was suspected, and a letter was written to his orthopedic surgeon recommending antibiotic discontinuation. With this he started to feel better though not much change was recorded on electrocardiogram. Given his obesity and possibility of gastro-esophageal reflux disease (GERD), omeprazole was reintroduced and amiodarone prescribed. A repeat electrocardiogram in June 2012, though still showing tachycardia was now sinus rhythm. A gradual reduction in dose of amiodarone dose was embarked upon.
upon and by September 2012, the electrocardiogram had returned largely to normal [Figure 2]. He continued to follow up albeit irregularly and remains normal using only amiodarone 100 mg daily and carvedilol 12.5 mg bd.

**COMMENTS**

Some antibiotics especially macrolides are known to increase cardiac arrhythmogenic risks.\(^2\) Reports have been published in relation to azithromycin.\(^3\) This is said to be commoner in those with high baseline risk for cardiovascular diseases.\(^4\) This prompted the American Food and Drug Administration to issue public safety alerts warning of arrhythmias, especially QT prolongation with such drugs. This was however not the experience in Europe and Norway specifically, where some workers failed to find a higher morbi-mortality from cardiac causes in patients using the same drug.\(^5\) This brings to question the possibility of a genetic bearing.

The patient reported here is a Nigerian male with cardiac morbidities, namely hypertension, obesity, and dyslipidemia. He seemed to be doing well on treatment for his hypertensive heart disease, till his attending orthopedic surgeon put him on levofloxacin (following culture and sensitivity test) for his discharging chronic osteomyelitis. Barely 2 weeks after this he presented with symptoms bordering on cardiac dysrhythmias with hemodynamic consequences. With initial Holter monitoring showing largely atrial ectopics and an electrocardiogram of supraventricular tachycardia, his beta blocker dose was increased. This served no useful purpose as he developed bradycardia and hypotension without assuaging the symptom of hemodynamic consequences of cardiac dysrhythmias.

When his drug history was delved into with the unraveling of protracted use of levofloxacin, the possibility of this as culprit was entertained. This is because it is one of the recorded side effects of levofloxacin in drug formularies. With discontinuation of levofloxacin, he started to gradually feel better. Possibility of GERD, since he was obese and reported a diagnosis of peptic ulcer disease, was also entertained. GERD is also known to precipitate dysrhythmia but was considered unlikely here, because he had used triple therapy for peptic ulcer disease and *H. pylori* eradication. This was at the onset of his cardiovascular symptoms of cardiac dysrhythmias with hemodynamic compromise. Gradually and with the use of amiodarone, his electrocardiogram that lagged behind symptomatic improvement returned to normal.

![Figure 2: Twelve-lead static electrocardiogram of the patient after discontinuation of levofloxacin note (1) normalization of p waves (2) normal P-R interval (3) normocardia](image)

In a study by Wynn,\(^6\) deaths per million antibiotic dispensed at the end of 5–10 days among three antibiotics were worse for levofloxacin. Cumulative incidence of serious cardiac dysrhythmias (inpatient and emergency encounters for cardiac dysrhythmias) for antibiotic type used over 10 days was worse for levofloxacin, and increased with duration of intake. The patient here pushed levofloxacin beyond the duration recommended by his orthopedic surgeon because the discharge from the sinus which caused him unacceptable distress before (he had to have his feet in bandage over a long time) dried up, and he could move about without a bandaged foot.

Levofloxacin and macrolides should still be used rationally for appropriate indications, but this potential side effect should be kept in mind. In other words, risk and benefit profile of antibiotics should be taken into consideration when making decisions regarding antibiotic to use in any given situation. When patients have cardiac co-morbidities such as old age and other cardiovascular risk factors, other options should be considered first. When levofloxacin is deemed appropriate, such patients should be closely monitored, and the drug hardly given beyond 1 week.
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