Bidirectional ventricular tachycardia associated with digoxin toxicity and with normal digoxin levels

Michael Chapman, MBChB, MRCP, * Mark Hargreaves, MD, MRCP, CCDS, † Heiko Schneider, MBChB, MRCP, † Martin Royle, MBChB, MRCP, CCDS ‡

From the *North Tyneside Hospital, Newcastle-upon-Tyne, United Kingdom, †Rochdale Infirmary, Rochdale, United Kingdom, and ‡Whiston Hospital, St Helen’s, Merseyside, United Kingdom.

Introduction

Bidirectional ventricular tachycardia (VT) is a regular tachyarrhythmia of ventricular focus with 2 different QRS morphologies alternating on a beat-to-beat basis.1 The rate typically is between 140 and 180 bpm, with a frontal plane axis varying between −20° to −30° and 110°.

Causes of this rare arrhythmia are limited and include catecholaminergic polymorphic VT, digitalis toxicity, myocarditis, left ventricular hypertrophy, myocardial infarction, herbal aconite poisoning, familial hypokalemic periodic paralysis, and Andersen-Tawil syndrome.1–3 Recently, pulmonary embolism8 and pheochromocytoma9 have also been implicated in causing this arrhythmia.

We present 2 cases of bidirectional VT attributable to digoxin, one of which had a significantly raised serum digoxin level and 1 within laboratory normal limits.

Case reports

Case 1

A 58-year-old woman presented with severe sepsis secondary to community-acquired pneumonia and acute kidney injury approximately 1 year after mechanical aortic and mitral valve replacement for rheumatic heart disease. She previously had been diagnosed with severe mixed mitral valve disease, moderate to severe aortic regurgitation, and pulmonary hypertension with predominantly right-sided heart failure. Coronary angiography was normal, and computed tomography of the chest showed no evidence of thromboembolism.

Other past medical history of note was permanent atrial fibrillation and rheumatoid arthritis. Medication on admission included digoxin, warfarin, ramipril, furosemide, spironolactone, and terbutaline.

Biochemistry tests on admission revealed a urea level of 106 mg/dL (reference range 7–22.4 mg/dL), creatinine 4.41 mg/dL (0.56–1.0 mg/dL), potassium 5.7 mEq/L (3.5–5.0 mEq/L), magnesium 2.16 mg/dL (1.82–2.31 mg/dL), and adjusted calcium 8.08 mg/dL (8.7–10.3 mg/dL). Routine hematology tests showed a white cell count of 10.0 × 10⁹/L and prothrombin time of 314.9 seconds (international normalized ratio 28.9).

Twelve-lead ECG revealed bidirectional VT with right bundle branch block (RBBB) morphology and alternating frontal plane axis (Figure 1). Serum digoxin level, measured at 8 hours, was significantly elevated at 5.87 ng/mL (0–2.0 ng/mL).

Treatment consisted of intravenous fluids, antibiotics, and administration of digoxin-specific antibody fragments. Interestingly, this resulted in cardioversion to sinus bradycardia (Figure 2). The patient’s renal function normalized, and digoxin was discontinued because of the occurrence of this arrhythmia and restoration of normal sinus rhythm.

Case 2

An 86-year-old man presented with acute onset of palpitations and dyspnea. He had multiple comorbidities including previous lung carcinoma with lobectomy in 1975, chronic obstructive pulmonary disease, permanent atrial fibrillation, congestive cardiac failure with severe left ventricular systolic dysfunction, previous cerebrovascular accident, type 2 diabetes mellitus, peripheral vascular disease with previous femoral–popliteal bypass, and prostate carcinoma.

His regular medications were digoxin, perindopril, warfarin, furosemide, amiloride, gliclazide, beclometasone inhaler, and salbutamol inhaler. There was no family history of arrhythmia or sudden cardiac death, and there had been no recent change to his medication doses.

Routine biochemistry testing on admission showed potassium 4.6 mEq/L, urea 16.8 mg/dL, creatinine 0.89 mg/dL, and corrected calcium 9.76 mg/dL. Hematology testing on admission was unremarkable. Serum digoxin level, measured at just over 6 hours, was within normal limits at 0.58 ng/mL.
The patient was noted to be hypotensive with a blood pressure of 85/62 mmHg and tachycardic. His admission ECG (Figure 3) confirmed bidirectional VT that, as in case 1, had an RBBB morphology and alternating frontal plane axis.

Immediate direct current cardioversion resulted in atrial fibrillation with partial left bundle branch block (LBBB) and left-axis deviation (Figure 4). Digoxin was discontinued because it was the only recognized trigger of bidirectional VT in this patient. Diltiazem was later commenced for rate control.

**Discussion**

Digitalis toxicity can produce a diverse set of arrhythmias because of its effect on intracellular calcium leading to delayed afterdepolarizations and enhancement of vagal tone on the atrioventricular node (AVN). These arrhythmias can include premature atrial or ventricular contractions, varying degrees of AVN block, accelerated junctional rhythms, paroxysmal atrial tachycardia with block, and bidirectional VT. When digitalis toxicity is suspected, the serum glycoside
level is of considerable value, especially when it is assayed 6 hours post dose. Levels > 2 ng/mL are generally considered toxic; however, there is considerable overlap. Toxic manifestations can be seen with levels < 2.0 ng/mL but can be absent in others cases with levels > 3 ng/mL. Observational studies have evaluated the clinical characteristics of patients with arrhythmias attributable to digoxin. Other than serum digoxin level, statistically significant differences have been found with regard to age, elevated blood urea nitrogen level, presence of coronary artery disease, and acute or chronic pulmonary disease. Retrospective analysis of 73 patients presenting with arrhythmias attributable to digoxin also found serum digoxin levels to be significantly lower in those patients who were hypokalemic compared to those who were normokalemic.

During bidirectional VT, the surface ECG most often shows a tachycardia with RBBB morphology and alternating QRS axis best seen in the inferior limb leads. However, there
are cases of LBBB morphology bidirectional VT as well as alternating LBBB and RBBB morphology, leading to some debate regarding the exact mechanism.

Current understanding is thought to be related to elevated intracellular calcium causing delayed afterdepolarization in anatomically separate parts of the conducting system. In 2011, a model by Baher et al. based on rabbit ventricles was able to produce the ECG characteristics of bidirectional VT. They proposed that for this arrhythmia to initiate, 2 separate foci with different rate thresholds for delayed afterdepolarization–induced ventricular bigeminy needed to be present. Because the ventricular rate exceeded the lower threshold, ventricular bigeminy would develop. This would effectively double the heart rate, taking the overall ventricular rate above the second threshold. Once this had developed, the 2 competing sites would simply alternate on a beat-to-beat basis. The authors proposed that this mechanism would explain why the rhythm is often of RBBB morphology with alternating frontal axis (where the 2 foci are in the anterior and posterior fascicles of the left bundle branch). It also explains why cases have been reported with alternating LBBB and RBBB morphology (with foci in the left and right bundles) and why this arrhythmia may progress to polymorphic VT (where ≥ 3 foci develop).

Both of our cases were attributable to digoxin and remarkably were admitted within 2 weeks of each other. The finding of this arrhythmia in the presence of a therapeutic serum digoxin level serves to further highlight the arrhythmic properties of digoxin within normal laboratory limits. Patient 2 was elderly with severe left ventricular systolic dysfunction, both of which have been shown to lead to increased risk of digoxin toxicity. This may explain the occurrence of this arrhythmia with a normal digoxin level.

References