ELECTROCARDIOGRAPHIC MANIFESTATIONS: DIGITALIS TOXICITY

Gene Ma, MD,* William J. Brady, MD,† Marc Pollack, MD,‡ and Theodore C. Chan, MD*

*Department of Emergency Medicine, University of California San Diego Medical Center, San Diego, California; †Department of Emergency Medicine, University of Virginia Health System, Charlottesville, Virginia; and the ‡Department of Emergency Medicine, York Hospital, York, Pennsylvania

Reprint Address: Theodore Chan, MD, Department of Emergency Medicine, UCSD Medical Center, 200 West Arbor Drive #8676, San Diego, CA 92130-8676

Abstract—Toxicity from the digitalis family of cardiac glycoside medications remains common. Successful treatment depends on early recognition; however, the diagnosis of potentially life-threatening toxicity remains difficult because the clinical presentation is often nonspecific and subtle. The hallmark of cardiac toxicity is increased automaticity coupled with concomitant conduction delay. Though no single dysrhythmia is always present, certain aberrations such as frequent premature ventricular beats, bradydysrhythmias, paroxysmal atrial tachycardia with block, junctional tachycardia, and bidirectional ventricular tachycardia are common. Treatment depends on the clinical condition rather than serum drug level. Management varies from temporary withdrawal of the medication to administration of digoxin-specific Fab fragments for life-threatening cardiovascular compromise. © 2001 Elsevier Science Inc.

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INTRODUCTION

The objective of this article is to review the electrocardiographic manifestations of digitalis toxicity, particularly as they relate to the pathophysiology and management of this potentially lethal poisoning. Despite the introduction of new classes of drugs in the management of congestive heart failure (CHF) and atrial fibrillation, many patients presenting to Emergency Departments (EDs) continue to be managed with cardiac glycosides. Cardiotoxicity from cardiac glycosides, known as a class as digitalis, ranges from obvious with nausea, vomiting, and hypotension, to more subtle presentations with nonspecific symptoms. The difficulty in diagnosing patients with digitalis intoxication can be attributed to several factors, including: 1) the signs, symptoms and electrocardiogram (EKG) manifestations often can be attributed to the underlying disease process for which the drug is prescribed; 2) a narrow therapeutic window of digoxin resulting in marked variability in the sensitivity of individuals to the drug; and 3) the lack of any dysrhythmia diagnostic of toxicity (1–3). It is believed that chronic toxicity occurs in 4–10% of patients on digitalis, yet is suspected in only 0.25% of the cases (4,5).

CASE PRESENTATIONS

Case 1

A 50-year-old man presented to the ED complaining of shortness of breath, nausea, and palpitations. He had a history of atrial fibrillation and congestive heart failure and was taking digoxin. His primary physician had increased his dose of digoxin the week prior from 0.125 mg to 0.25 mg per day because he was having increasing episodes of palpitations.
The patient was a middle-aged man who appeared in moderate distress. Vital signs included a pulse rate of 148 beats/min, blood pressure of 96/52 mmHg, and respiratory rate of 18 breaths/min. Chest examination revealed bilateral clear breath sounds. Cardiac examination revealed a regular tachycardia without murmurs or rubs. Extremities revealed 1+ pitting edema at the ankles bilaterally.

An EKG was obtained (Figure 1). The patient was diagnosed with a bidirectional tachycardia most likely as a result of digoxin toxicity. Because of intermittent episodes of hypotension, the patient was treated with digoxin-specific antibody fragments (Fab) and admitted to the coronary care unit. A subsequent digoxin level was reported at 3.7 mg/dL. Ten hours after therapy, the patient reported feeling remarkably improved, and a repeat EKG was obtained (Figure 2). The patient was subsequently discharged from the hospital 2 days later after an unremarkable course.

Case 2

A 59-year-old man presented to the ED with a 4-h history of palpitations. The patient denied chest pain or discomfort or any respiratory symptoms. The patient had a history of atrial fibrillation as well as longstanding hypertension and was currently medicated with digoxin 0.25 mg per day. The patient denied any recent changes in his dose.

On examination, the patient was a middle-aged man in minimal distress. Vital signs revealed a regular pulse rate of 140 beats/min, blood pressure of 156/94 mmHg, and respiratory rate of 12 breaths/min. The remainder of the patient’s examination was unremarkable.

An EKG was obtained (Figure 3), which revealed a junctional tachycardia. The patient was initially treated with i.v. fluids. Laboratory values revealed a digoxin level of 4.3 mg/dl. The patient was admitted to telemetry for observation. By the next morning, the patient’s symptoms had resolved and repeat EKG revealed atrial fibrillation with controlled ventricular response (Figure 4).

Case 3

A 90-year-old woman was referred from a clinic to the ED for 1 day of confusion. The change in mentation was preceded by 3 days of nausea and vomiting. The patient had a history of congestive heart failure and was taking
digoxin 0.25 mg per day, with no recent change in her medication regimen.

On examination, the patient was an elderly woman who appeared in moderate distress with altered senso-
rium. Vital signs were notable for a pulse rate of 30
beats/min, blood pressure of 78/42 mmHg, and respira-
tory rate of 24 breaths/min. The chest examination re-
vealed bibasilar rales and cardiac examination revealed a
regular bradycardia with no murmurs. The extremities
were cool to touch with pitting edema bilaterally.

An EKG was obtained, which revealed third-degree atrio-ventricular (AV) block (Figure 5). The cardiac rhythm deterioriated into a ventricular tachycardia and sinusoidal pattern from which she did not respond to initial ACLS therapy (Figure 6). The family requested no

further intervention and the patient died at that time. Subsequent post-mortem laboratory tests revealed a
digoxin level of 5.0 mg/dL and a potassium level of 7.9.

**DISCUSSION**

Digitalis derivatives are found in several plants, includ-
ing oleander, foxglove, and lily of the valley. They are
used therapeutically as digoxin or digitoxin primarily for
their ability to slow conduction through the atrioventric-
ular (AV) node in disease states such as atrial fibrillation
and flutter. These agents act by inhibiting the sodium-
potassium adenosine triphosphatase (ATP-ase) pump
and increasing intracellular calcium concentration at the

![](image-url1)

Figure 3. Junctional tachycardia.

![](image-url2)

Figure 4. Atrial fibrillation with well-controlled ventricular response.
level of cardiac myocyte. As a result, digitalis medications increase myocardial contractility.

In terms of conduction, these intracellular changes impair conduction through the AV node and simultaneously increase cardiac automaticity, particularly in the Purkinje fibers. The end result is an increased propensity toward automaticity while at the same time slowing conduction through the AV node. Understanding this concept is paramount to recognizing the EKG manifestations of digitalis poisoning.

Digoxin is well absorbed after ingestion and intravascular concentrations may rise rapidly after oral overdose. Yet tissue distribution may be delayed due to a very large volume of distribution of 5–10 liters/kg. Peak effects occur after 6–12 h, and the elimination half-life is 30–50 h. Over 60% of digoxin is excreted unchanged by the kidney.

The signs and symptoms of digoxin intoxication depend on whether the poisoning is acute or chronic. In an acute ingestion, nausea and vomiting are prominent along with evidence of cardiotoxicity. In chronic intoxication, nonspecific symptoms such as malaise and weakness predominate, in addition to the classic, although rare, visual disturbances (yellow halos around lights). In many patients, however, the sole evidence for digitalis toxicity is the appearance of a cardiac dysrhythmia. Moreover, hypokalemia and hypomagnesemia from concomitant diuretic use can po-
tentially worsen any toxic dysrythmias resulting from digoxin.

**EKG Manifestations of Therapeutic Digoxin**

Emergency Physicians are all too familiar with the computerized interpretation of the EKG stating “probable digitalis effect” (Figure 7). What this refers to are the four findings on EKG that are consistent with the presence of digitalis, yet do not correlate with toxicity. These findings can be seen at levels well within normal therapeutic range.

The earliest finding is that of T-wave changes of virtually any form, from flattening and inversion (that can simulate acute ischemia or pericarditis) to other abnormal waveforms such as those with peaking of the terminal portion (seen in about 10% of patients) (9). The second finding is QT-interval shortening from a decrease in ventricular repolarization time. The third finding is the classic sagging or “scooped” appearance of the ST-segment with concomitant ST-segment depression. This finding is more pronounced in leads with tall R waves, such as the lateral leads. Lastly, one may find an increase in the U-wave amplitude.

In patients with ventricular hypertrophy or bundle branch block, the above repolarization abnormalities may be masked. However, a definite sagging of the ST segment with an upward concavity is still highly suggestive of digitalis effect even in this setting. Additionally, in left bundle branch block or left ventricular hypertrophy where the QT interval is prolonged, a shortened or normal interval suggests digitalis effect (10). In addition, digitalis can result in PR interval prolongation as a result of slowing conduction through the AV node.

**EKG Manifestations of Digitalis Toxicity**

Digitalis can produce virtually any type of cardiac dysrhythmia, although rapid atrial fibrillation/flutter and bundle branch block are rare. The key to the diagnosis of digitalis as the culprit is recognizing that the medication increases automaticity, delays conduction, and often, both at the same time. Though the actual frequency of digitalis induced dysrhythmias is debatable, the most complete data describing the incidence of the various dysrhythmias come from work by Irons and Orgain (Table 1) (11).

**Increased automaticity.** As a result of increased automaticity, ectopy is a common manifestation of digitalis toxicity. Premature ventricular beats (PVCs), both unfocal and multifocal, are often the earliest dysrhythmia associated with digitalis intoxication, and account for half of the dysrhythmias associated with digitalis. In fact, the finding of frequent PVCs is the most common dysrhythmia associated with digoxin toxicity. Nevertheless, wide complex beats in the setting of atrial fibrillation may not be PVCs from toxicity, but may represent aberrant conduction such as occurs with Ashman’s phenomenon (12).
Conduction block. Depressed conduction is a predominant feature of digitalis toxicity. In a patient with a known history of atrial fibrillation who presents with an apparent regularization of the rhythm, the reflexive presumption is that the patient has returned to a sinus rhythm with a well-controlled rate. However, a detailed examination of the EKG may reveal a persistently fibrillating atrium with AV nodal escape rhythm. In fact, any marked slowing in the ventricular response to atrial fibrillation in a patient on digoxin should suggest the possibility of cardiac toxicity (Figure 8).

Conduction block in this setting can be of any degree from first degree AV block to complete heart block, though Mobitz type II is considered rare. In addition, sinus bradycardia, from increased vagal tone, and other bradydysrhythmias are very common. Sinoatrial (SA) arrest has been reported, although rarely. Digitalis has little effect on the bundle branches and consequently, bundle branch block is not believed to be attributable to digitalis (3).

Other manifestations. Along with increased ventricular ectopy and conduction block, the three classically described dysrhythmias that should immediately suggest digitalis intoxication include paroxysmal atrial tachycardia (PAT) with block, junctional (AV nodal) tachycardia, and ventricular tachycardia (VT) (7).

PAT with block. Although not as common, PAT with block is thought to be nearly pathognomonic for digoxin toxicity. The frequency of PAT with block was initially described by Lown et al., who estimated that in hospitalized patients with this dysrhythmia, digitalis was responsible in 73% of the cases (13). Newer evidence suggests the actual incidence is lower, and that the term paroxysmal is actually a misnomer (10). More recent observations have suggested this dysrhythmia occurs

![Figure 8. (a) Atrial fibrillation with slow ventricular response. (b) Sinus bradycardia](image-url)
progressively rather than being sudden in onset. The atrial rate is usually between 150 and 250 beats per minute, and the degree of AV block varies, with second degree and Wenckebach being the most common forms (Figure 9).

**Junctional tachycardia.** AV junctional escape rhythms result when digitalis suppresses impulse formation at the sinoatrial node to the degree that the inherent AV pacemaker cells outpace the SA nodal cells (14). The escape rhythm usually manifests with a regular ventricular rate of 40–60 beats per minute, but accelerated junctional rhythms are common, often with varying degrees of block (Figure 3).

Impulses originating from the AV junction commonly result in a right bundle branch pattern. On rare occasion, aberrant conduction occurs through the two divisions of the left bundle resulting in an alternating QRS axis, or bidirectional tachycardia (15). Digitalis toxicity is the most common cause of bidirectional tachycardia.

**Ventricular tachycardia.** As noted previously, frequent PVCs during atrial fibrillation in a patient with a previously well-controlled rate on digoxin is highly suggestive of toxicity (10). Bigeminal and trigeminal rhythms should always raise a concern for digitalis toxicity. While rare, ventricular bigeminy and bidirectional ventricular tachycardia with alternating left and right bundle branch block aberration are considered pathognomonic for digitalis toxicity (Figure 1) (16). Ventricular fibrillation and Torsades de Pointes can also occur with digitalis poisoning, though ventricular fibrillation is usually a late manifestation.

**Management**

The key to successful treatment is early recognition. Choice of treatment depends on the EKG findings, clinical presentation, and cardiovascular status of the patient. When the patient is hemodynamically stable, many of the common manifestations, such as first- and second-degree heart block, bradycardia, and ventricular ectopy, can be treated with only temporary withdrawal of the medication and close monitoring (17).

Patients with evidence of clinical deterioration and hemodynamic instability require more aggressive treatment and ALS guidelines apply with a few caveats. Temporary pacemaker may be required for significant bradycardia and heart block unresponsive to atropine. Ventricular tachydyssrhythmias may respond to lidocaine, but quinidine, procainamide and bretyllium should be avoided. Calcium channel blockers are contraindicated because they may increase digoxin levels, and β-blockers must be used with caution as they can worsen conduction block. Cardioversion is relatively contraindicated as it can result in asystole or ventricular fibrillation.

Careful attention to correcting potassium and magnesium derangements is critical as electrolyte imbalances often exacerbate digoxin-related dysrhythmias. Hyperk-
lemia should not be treated with calcium as this may worsen ventricular dysrhythmias and precipitate VT or ventricular fibrillation. Decontamination with charcoal has been proven to be highly efficacious, while hemodialysis or hemoperfusion is ineffective due to the large volume of distribution (15).

The introduction of digoxin-specific Fab fragments has revolutionized the treatment of the severely toxic patient. When given i.v., Fab fragments rapidly reverse conduction disturbances, restore contractility, and re-establish sodium-potassium ATP-ase activity by binding digoxin (18). The efficacy of Fab fragments has been prospectively validated in a multicenter trial for acute, life-threatening digitalis toxicity (19,20). It has also proven efficacious in severe cardiac glycoside poisoning from plants.

The use of Fab fragments should be reserved for patients who present with life-threatening digitalis toxicity, as evidenced by severe cardiac toxicity (such as ventricular tachycardia) with hemodynamic compromise. Treatment also may be indicated in cases of refractory dysrhythmias in the setting of severe hyperkalemia. In general, as toxicity correlates with intracellular rather than serum drug levels, the use of Fab fragments should not be based solely on the serum digoxin level (though some authors recommend treatment with markedly elevated levels) (21). As Fab fragments reverse the effects of digoxin, both toxic and therapeutic, treatment can result in worsening CHF, tachydysrhythmias and hypokalemia. In addition, Fab fragments may exponentially elevate digoxin levels (because most assays measure total serum digoxin levels, including those bound to Fab), making serum level monitoring difficult.

Dosing of Fab fragments is based either on amount of digoxin ingested (acute poisoning) or on calculated total body digoxin load. Alternatively, Digoxin Fab can be initially given at a dose of 5 to 10 vials and titrated incrementally based on clinical manifestations and response (21). In patients with chronic toxicity who are dependent on digoxin, half-doses of Fab can be administered to avoid completely reversing the clinical benefits of the medication. Additional doses of Fab can be given later depending on the clinical condition of the patient. Digoxin should be withheld in patients until manifestations of toxicity have resolved (usually a minimum of 24 h), and restarted when clinically indicated at appropriate doses.

**CONCLUSION**

Although digoxin continues to be a common medication utilized by patients presenting to the ED, the nonspecific signs and symptoms make the diagnosis of toxicity difficult to establish. The key to successful management is early diagnosis. Though no single dysrhythmia is always found, certain aberrations such as PAT with block, junctional tachycardia, and bidirectional ventricular tachycardia are common. The hallmark of digitalis toxicity is increased automaticity with concomitant conduction delay, even in the setting of a normal digoxin level. Digoxin specific Fab fragments have revolutionized the treatment of digitalis toxicity and should be considered early in the severely poisoned patient.

**REFERENCES**