Atrial Flutter Secondary to Digitalis Toxicity

Report of Three Cases and Review of the Literature

By ABNER J. DELMAN, M.D., and EMANUEL STEIN, M.D.

The Rarity of atrial flutter due to digitalis toxicity has been emphasized frequently. The present paper describes three cases of atrial flutter as a manifestation of digitalis intoxication. The clinical characteristics of this entity are reviewed.

Case Reports

Case 1
A 50-year-old man was admitted to Montefiore Hospital on July 10, 1961, with a supraventricular tachycardia. There was a 35-year history of recurrent attacks, frequently documented by electrocardiograms. He was on no drug therapy. The apical pulse rate was 200 per minute and regular, and the blood pressure was 155/110. Physical examination was otherwise normal. An electrocardiogram showed a supraventricular tachycardia with a rate of 200 per minute (fig. 1a). During the next 16 hours, the patient received 3.0 mg. of lanatoside C intravenously and intramuscularly. At this time, he became nauseated; an electrocardiogram showed atrial tachycardia with varying block (fig. 1b). Another 0.6 mg. of lanatoside C was given in the next 6 hours; then an electrocardiogram revealed atrial flutter with varying block (fig. 1c). Digitalis was discontinued, and there was spontaneous reversion to regular sinus rhythm in 30 hours (fig. 1d). No further digitalis was given. He was discharged in regular sinus rhythm on quinidine, 0.2 Gm. four times daily.

Comment. Massive digitalis overdosage in this patient resulted in unequivocal digitalis toxicity manifested by nausea and atrial flutter with varying block, and high degree of atrioventricular block (4:1).

Case 2
A 69-year-old man with a history of two myocardial infarctions and chronic, slow atrial fibrillation was admitted to Montefiore Hospital on December 27, 1954, with a 6-hour history of palpitations. He was on no medication. Admission blood pressure was 120/60. The heart was irregular at 150 per minute and was moderately enlarged to the left. There were no signs of congestive heart failure. An electrocardiogram revealed atrial fibrillation with a rapid ventricular rate (fig. 2a). Within 40 hours he received lanatoside C, 1.2 mg. intravenously, digitoxin, 1.4 mg. orally, and digoxin, 1.5 mg. orally. At this time he developed nausea and vomiting, and an electrocardiogram revealed atrial flutter with varying block (fig. 2b). Digitalis was stopped, and in 4 days, rhythm reverted to atrial fibrillation with a ventricular rate of 60 per minute (fig. 2c). He was

Figure 1

a. Lead II, supraventricular tachycardia, July 10, 1961, 8:30 p.m. b, Lead II, paroxysmal atrial tachycardia with varying block, July 11, 1961, 12:30 p.m.

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Comment. Greater-than-average maintenance digitalis dosage plus probable increased digitalis sensitivity due to hydrochlorothiazide (with possible hypokalemia) resulted in digitalis toxicity manifested by atrial flutter with varying block, slow ventricular rate (80 per minute) and 4:1 atrioventricular block.

Discussion

The first case of atrial flutter due to digitalis toxicity was reported by Wedd in 1924. By 1959, 21 more cases were reported. In 1959, Coffman and Whipple listed the following criteria for atrial flutter due to digitalis intoxication: development of the arrhythmia

Figure 2

a, Lead V₁, rapid atrial fibrillation with aberrant ventricular conduction, December 27, 1954, 5:00 p.m. b, Lead V₁, atrial flutter with varying block, ventricular rate 70 per minute, 4:1 atrioventricular block, December 29, 1954, 9:00 a.m. c, Lead V₁, slow atrial fibrillation, January 1, 1955, 9:00 a.m.

given digoxin, 0.25 mg. orally twice daily 3 days later and was discharged.

Comment. Significant digitalis overdosage in this patient caused clearcut digitalis toxicity manifested by nausea, vomiting, and atrial flutter with varying block, with a slow ventricular rate (80 per minute) and 4:1 atrioventricular block.

Case 3

A 63-year-old man with a history of arteriosclerotic heart disease with regular sinus rhythm (fig. 3a) and moderate congestive heart failure had been on maintenance digoxin, 0.75 mg. per day, and hydrochlorothiazide, 50 mg. (after initial digitalization with digoxin, 3.0 mg. orally, in 2 days) per day, for 2 months. On examination January 13, 1962, his blood pressure was 140/90 and his pulse irregular. Examination was otherwise unremarkable, with no signs of congestive heart failure. An electrocardiogram revealed atrial flutter with varying block (fig. 3b). Digoxin and hydrochlorothiazide were discontinued, and the rhythm reverted spontaneously to atrial fibrillation (fig. 3c), then to regular sinus rhythm (fig. 3d). He was subsequently restarted on digoxin, 0.25 mg. per day, and remained in regular sinus rhythm.

Figure 3

during digitalis therapy; absence of other drugs that cause arrhythmias; and clearing of arrhythmia after omission of digitalis.

Using these criteria, they reviewed the previously reported 22 cases, accepted 15 cases and added a sixteenth case. Since then, two additional cases meeting these criteria have been reported.16, 17

The rarity of atrial flutter and its mechanism of development in digitalis intoxication is unexplained. The indirect or vagal effect of digitalis on the innervated atrial muscle is a decrease in the refractory period, with an increase in muscle excitability. It has been postulated that the vagal effect of digitalis may predispose to ectopic atrial foci and lead to atrial flutter during toxicity.3, 8, 14, 15, 17

Digitalis is usually used in the therapy of atrial flutter. Failure to recognize its causative role in atrial flutter may result in disaster when even more digitalis is given at a time when discontinuance is indicated.1

Analysis of the 16 cases (including our three cases) in which information was available suggests certain clinical clues useful in establishing the diagnosis (table 1).

Seven patients were over 60 years of age. Eight patients were in severe congestive heart failure. Twelve patients had severe heart disease. Five patients had a significant preceding diuresis. Two patients had azotemia. Advanced age,4, 7, 18 severe congestive heart failure,2, 7 severe heart disease,18 preceding diuresis,4, 8, 18 and azotemia4, 18 are all factors that may increase digitalis sensitivity. The 12 patients with severe heart disease had two or more of these associated factors.

The type of digitalis preparation or the route of administration was not significant, since toxicity occurred with oral, intramuscular, and intravenous administration, and with digoxin, digitoxin, whole digitalis leaf, tincture of digitalis, and lanatoside C. However, 14 patients received significantly greater than the accepted dosage range of these specific preparations.2, 19 One of the two patients on

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<td><strong>Clinical Data in Sixteen Patients</strong></td>
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<table>
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<tr>
<th>Age Range</th>
<th>30-39</th>
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<th>50-59</th>
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<td>Number</td>
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**Sex:**
- Male—11
- Female—5

**Type of heart disease**
- Normal
- Arteriosclerotic
- Rheumatic
- Syphilitic
- Patent ductus arteriosus
- Constrictive pericarditis

**Congestive heart failure**
- None
- Mild to moderate
- Severe

**Significant digitalis overdose**

**Previous rhythm**
- Regular sinus rhythm
- Atrial fibrillation

**Ventricular rate** (14 cases recorded)
- 40-100/minute
- 120/minute
- 150/minute

**Ratio of atrioventricular block**
- Ratio
  - 2:1
  - 3:1
  - 4:1
  - 8:1
  - Varying
- Number
  - 3
  - 4
  - 6
  - 3
  - 10

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doses of digitalis within the accepted dosage range had severe heart disease. Of the three patients with no heart disease, two received massive overdosage of digitalis, and the third, significant overdosage.

Thirteen patients had symptoms usually associated with digitalis toxicity, i.e., nausea, vomiting, diarrhea, confusion, and scotomata.

The recorded ventricular rate in 14 patients ranged from 40 to 150 per minute, and was 100 or less per minute in 11. The degree of atrioventricular block ranged from 2:1 to 8:1 in the 16 patients, and was 3:1 or greater in 13. Two patients had a ventricular rate of 150 per minute, and both had frequent premature beats of the ventricle.

In spontaneous, untreated atrial flutter, the degree of atrioventricular block is usually 2:1, with a ventricular rate of 130 to 160 per minute, and frequent premature beats of the ventricle are unusual. Ten patients had atrial flutter with varying block. Paroxysmal atrial tachycardia with varying block secondary to digitalis toxicity is well known. Whether atrial flutter with varying block or atrial tachycardia with varying block will occur in digitalis toxicity may depend on the rate of discharge of an ectopic atrial focus, as first postulated by Prinzmetal et al. Our first patient progressed to atrial tachycardia with varying block and then to atrial flutter with varying block during massive digitalis therapy. It has been recently suggested that atrial flutter with varying block in a patient on digitalis is a contraindication to further digitalis. If the drug is continued, severe atrioventricular block or complete heart block with Stokes-Adams attacks may develop. The appearance of atrial flutter with varying block in a patient on digitalis may be as useful a sign of digitalis intoxication as the development of atrial tachycardia with varying block.

Therapy in atrial flutter due to digitalis toxicity consists of discontinuation of the drug. The arrhythmia will clear when the toxicity subsides. If a rapid ventricular rate is present, a trial of oral or intravenous potassium may be attempted, particularly if potassium deficiency is suspected. Prompt dissolution of the flutter points strongly toward digitalis intoxication as the cause.

Summary and Conclusions

Three cases of atrial flutter due to digitalis toxicity are presented and the world literature is reviewed. Sixteen cases are analyzed for clinical and electrocardiographic features. Significant digitalis overdosage, severe heart disease with associated factors sensitizing to digitalis, and symptoms of digitalis toxicity are characteristic. Two of the three patients with no heart disease had massive overdosage. Thus, toxicity can be strongly suspected in this arrhythmia on clinical grounds. In addition, every patient had one or more of the following: a slow ventricular rate (less than 90 per minute), a high degree of atrioventricular block (3:1 or more), varying atrioventricular block, or frequent premature ventricular beats with a rapid ventricular rate. The presence of any combination of these electrocardiographic features in a patient suspected of digitalis toxicity by clinical criteria is highly suggestive of intoxication. The diagnosis can be made only in patients who develop the arrhythmia while receiving digitalis, and who are receiving no other drugs that can cause the arrhythmia. Diagnosis is confirmed by clearing of the arrhythmia on cessation of digitalis, with or without potassium therapy. Atrial flutter with varying block occurred in 10 patients. It may be as useful a sign of digitalis toxicity as atrial tachycardia with varying block.

Acknowledgment

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References
ATRIAL FLUTTER FROM DIGITALIS TOXICITY

William Withering

At first Withering used a decoction of the foxglove leaves which he soon discarded in favor of an infusion. Gradually he gave this up and came to depend almost entirely on the powdered leaves. He recommended gathering the leaves just before blossoming time, removing the midrib, and using only the powdered leaf blade. This was dried either in the sun or before a fire and then rubbed down to a "beautiful green powder" which weighed about one-fifth of the original weight of the undried leaf. The dose for an adult was one grain twice a day. He gave this powdered leaf either alone, or made with a pill with soap or gum ammoniac as an excipient, with sometimes aromatics added. He did not believe in giving digitalis oftener than twice a day. Time should be allowed for each dose to act. He continued the drug until it acted upon the "kidneys, the stomach, the pulse, or the bowels; let it be stopped upon the appearance of any one of these effects."

Withering not only used digitalis extensively himself, keeping careful case reports and notes, but he spread the gospel of its use among his medical friends with the result that it soon became known and quite generally used.—Louis H. Roddis, M.D. William Withering: The Introduction of Digitalis Into Medical Practice. New York, Paul B. Hoeber, Inc., 1936, p. 57.
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