T Wave Inversion Associated with Severe Theophylline Toxicity

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Adverse cardiovascular effects are commonly seen in severe theophylline poisoning. Primary ST-T wave changes have not been described previously. We report T wave inversion associated with severe theophylline toxicity in a 33-year-old woman with no evidence of organic heart disease. The T wave inversion resolved after treatment. Physicians should be alerted to possible T wave abnormalities in patients with severe theophylline poisoning. (Chest 1989; 96:429-31)

Theophylline is a widely used agent in the treatment of bronchospastic disorders. Toxicity generally occurs at levels greater than 25 µg/ml.† Severe theophylline poisoning is characterized by cardiac arrhythmias, seizures, hypotension and cardiovascular collapse.** To our knowledge, primary T wave abnormalities have not been reported previously in connection with theophylline toxicity. We report T wave inversion associated with severe theophylline toxicity.

CASE REPORT

A 33-year-old white woman with a history of asthma since childhood presented to Hahnemann University Hospital on February 1, 1986. The night prior to admission she developed progressive dyspnea and wheezing, and took a total of 2,400 mg of theophylline over eight hours in an attempt to ameliorate her symptoms. The patient then became nauseous, tremulous, and experienced palpitations which brought her to the emergency room. She denied chest pain or dizziness. Her only medication was theophylline 300 mg twice daily. She smoked one pack of cigarettes daily. There is no history of intravenous drug use, but the patient admits to occasional cocaine use, which she claimed to have last taken two weeks prior to admission.

On presentation, she was afebrile with blood pressure of 94/60 mm Hg. The pulse rate was 80/min with a respiratory rate of 28/min. She appeared anxious, but was alert, oriented and in no respiratory distress. Physical examination was remarkable only for a fine resting tremor and symmetric hyperreflexia.

The admission theophylline level was 50.4 µg/ml. Serum potassium, calcium, phosphorus, and magnesium levels were normal. A room air arterial blood gas determination revealed a pH of 7.50; PCO₂, 29 mm Hg; and PO₂, 100 mm Hg. Her chest x-ray film revealed only slight hyperinflation. The ER electrocardiogram revealed normal sinus rhythm at 62/min with T wave inversion in leads 2, 3, aVF, and V₁ through V₃ (see Fig 1). No dysrhythmia occurred during emergency room cardiac monitoring.

Eighteen hours after treatment with activated charcoal and magnesium citrate, her theophylline level had decreased to 1.9 µg/ml. A repeat electrocardiogram at that time revealed almost complete resolution of the initial T wave inversion (Fig 1). Serial cardiac enzymes were negative for an acute myocardial infarction. Findings from a two-dimensional echocardiogram including Doppler was normal. Pulmonary function testing revealed normal spirometry, but a decreased FEF 25-75% suggesting small airways disease.

A test for urinary benzylisoquinine (metabolite of cocaine) was negative. Follow-up ECGs remained unchanged. Three days after admission, the patient was asked to hyperventilate, during which time simultaneous ABC analysis and ECG were performed. There were no significant ST-T wave changes at a pH of 7.48 and Pco₂ 32 mm Hg. During treadmill exercise tolerance testing, the patient exercised into stage 3 of the Bruce protocol achieving only 60 percent of her predicted maximum heart rate. The exercise electrocardiogram showed normal physiologic ST-T wave changes without arrhythmia. Coronary arteriography revealed normal coronary arteries.

COMMENT

Studies of the electrophysiologic effects of theophylline have shown that it decreases both sinoatrial conduction time and His-Purkinje conduction interval. 6 These changes may be caused by direct action of theophylline or by associated increases in sympathetic tone,7 but were not associated with T wave abnormalities.

Primary T wave inversion has been associated with myocardial ischemia, drug effect, electrolyte imbalance, central nervous system disease and hyperventilation.8,9 Hyperventilation is unlikely to be the cause of T wave inversion in our patient since an electrocardiogram performed during hyperventilation showed no significant T wave changes. Central nervous system disease can be associated with marked ECG waveform abnormalities, which are thought to be due to altered autonomic tone or centrally induced structural cardiac changes.10,11 Electrical stimulation of the animal brain has resulted in inversion and increased amplitude of the T wave.12 It is possible that the central nervous system effects of toxic levels of theophylline are responsible for the T wave changes seen in our patient.

It is interesting that our patient did not have tachycardia while theophylline toxic. We postulate that our patient may have underlying sinus node dysfunction or perhaps had relative autonomic dysfunction secondary to chronic cocaine use. Chronic cocaine use has been associated with decreased tyrosine hydroxylase activity and decreased beta-adrenergic
It is possible that these effects of chronic cocaine use may have: 1) prevented the increase in catecholamine release by theophylline, and 2) blunted the chronotropic effect of the circulating catecholamines. Avakian and Manna\textsuperscript{17} have demonstrated in animals that chronic cocaine use will blunt the positive chronotropic and arrhythmogenic effects induced by epinephrine.

Theophylline toxicity is not an uncommon occurrence and, to our knowledge, primary T wave changes have not been reported. We postulate that the usual tachycardia associated with theophylline toxicity may mask these possible ECG changes. In this case, the relative bradycardia could have unmasked centrally induced repolarization abnormalities due to theophylline toxicity. One should therefore be alerted to possible electrocardiographic changes in severe theophylline toxicity.

References

17) Avakian EV, Manneh VA. Cardiac responsivity to epinephrine following chronic cocaine administration. Proc West Pharmacol Soc 1987; 30:281-84

Myocardial Infarction Complicating Cardiovascular Stress Testing with Normal Coronary Arteriography*

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A patient with normal coronary arteriography who experienced a non-Q myocardial infarction is described. The temporal relationship of ischemic symptoms, ECG changes, and rise in creatine phosphokinase (CPK) support a relationship to an exercise treadmill test.

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It is estimated that over 500,000 cardiovascular stress tests are performed annually in this country.1 Complications

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Figure 1. Coronary angiograms obtained 22 h following exercise testing. A (upper) normal right coronary artery in the RAO projection. B (lower) normal left anterior descending and left circumflex coronary arteries in the LAO projection.