Procainamide-Induced Sinus Node Dysfunction in Patients with Chronic Renal Failure

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Two patients with chronic renal failure developed transient sinus node dysfunction requiring insertion of a temporary pacemaker while receiving procainamide to control ventricular arrhythmias. Blood levels of procainamide were found to be elevated, although at these levels, sinus node dysfunction has not previously been reported. Following discontinuance of procainamide, sinus rhythm returned. A combination of factors, including elevated levels of N-acetyl procainamide, the metabolite of procainamide with anti-arrhythmic properties, are suggested as possible contributory causes for the ECG findings. Thus, procainamide may produce electrophysiologic features of “sick sinus syndrome” in patients with chronic renal failure even when blood levels of this substance are being monitored.

A variety of drugs have been found to produce sinus node dysfunction. Although various ECG manifestations of procainamide-induced cardiotoxicity have been reported, abnormalities of sinus node function have not been emphasized. The purpose of this report is to describe the occurrence of transient sinus pauses and marked sinus bradycardia in two patients with chronic renal failure who were receiving low doses of procainamide for treatment of ventricular arrhythmias.

**Case Reports**

**Case 1**

A 46-year-old black man with chronic renal failure who was receiving maintenance hemodialysis for one year was admitted because of chest pain. He had been receiving clonidine, 0.2 mg twice per day, for hypertension, and digoxin, 0.25 mg once per day, for congestive heart failure. The ECG showed normal sinus rhythm, left ventricular hypertrophy, left atrial enlargement, and frequent ventricular premature beats. Procainamide, 375 mg, taken orally four times per day, was given for frequent ventricular premature beats. Digoxin blood level at time of admission was found to be 1.4 ng/mL. Six days after beginning procainamide therapy, marked sinus bradycardia and long sinus pauses were observed for the first time (Fig 1). Procainamide blood levels at the time of the episode was 15.3 μg/mL, digoxin, 0.95 ng/mL, and serum potassium was 6.3 mEq/L. Three days after discontinuance of procainamide, when there was no discernible procainamide present in the blood, normal sinus rhythm returned. Subsequently, therapy with clonidine and digoxin was reinstated without recurrence of sinus node dysfunction even when serum potassium level was found to be between 6 and 7 mEq/L.

**Case 2**

A 73-year-old woman with chronic renal failure was admitted because of palpitations and chest pain. She had a history of angina pectoris for which she was receiving propranolol, 20 mg per day, and nitroglycerin, and she had symptoms of congestive heart failure for which she was receiving digitoxin, 0.1 mg three days per week, and furosemide, 40 mg once per day. On examination, she was found to have atrial fibrillation with a rapid ventricular response. The ECG showed a left bundle branch block pattern and abnormal left axis deviation. Shortly following admission, atrial fibrillation converted to sinus rhythm. However, because of the appearance of frequent ventricular premature beats, she was given procainamide, 500 mg orally every six hours, and digitoxin was withheld. Six days after admission, when digitoxin, and propranolol had been discontinued, the ECG showed for the first time sinus bradycardia at a rate of 40/min, periods of sinus arrest, and prolongation of P-R interval, as demonstrated in Figure 2. At this time, procainamide blood level was 18.6 μg/mL, BUN value was 53 mg/100 mL, and serum potassium level was 5.3 mEq/L. Because of prolonged sinus pauses, a temporary transvenous pacemaker was inserted. After discontinuance of procainamide, normal sinus rhythm returned.

**Discussion**

The present report demonstrates that procainamide can produce cardiotoxicity in patients with chronic renal insufficiency even when reduced doses are administered. Both patients received procainamide for suppression of frequent ventricular premature beats. One patient, who was receiving maintenance hemodialysis, developed marked sinus bradycardia and periods of sinoatrial arrest while receiving 1.5 g/m per day of procainamide that resulted in a blood level of 15 μg/mL; the other patient, whose BUN level was 54 mg/100 mL at the time of procainamide toxicity, had similar ECG findings while receiving 2 gm per day and had a blood level of 18.8 μg/mL. Although sinus node dysfunction following procainamide administration has been reported previously, and suggested experimentally, its occurrence has not been described at the blood levels found in these pa-
Figure 1. Case 1, ECG recorded after insertion of pacemaker and rhythm strip (Rgl) at time of cardiotoxicity, demonstrating sinus pauses with pacemaker and A-V junctional escape beats. Rhythm strip consistent with 2:1 SA block.

Figure 2. Case 2, ECG and rhythm strip (Rgl) at time of cardiotoxicity demonstrating marked sinus bradycardia and/or episodic 2:1 SA block with AV junctional escape beats. The ECG also shows an LBBB pattern, complete, and abnormal left axis deviation.
patients. It is likely that other factors present in these patients contributed to the development of the bradyarrhythmia. Mildly elevated potassium levels might have lowered the transmembrane action potential in the SA node and/or perinodal atrial tissues which would have potentiated the effects of procainamide. Also, clonidine, which one patient was receiving, and/or digitalis, may have had contributory effects. Clonidine and digitalis, even at the normal blood levels found in these patients, by their autonomic effects, can by themselves produce findings similar to those found in this report. That procainamide was a necessary factor was demonstrated by the observation that following cessation of procainamide, when procainamide levels were no longer elevated, normal sinus rhythm returned. Also, when one patient was rechallenged with clonidine for control of blood pressure at doses considerably higher than those administered at time of cardiotoxicity, and when both patients were given digitalis for congestive heart failure, neither patient developed recurrence of bradyarrhythmia. The possibility that these patients had latent sinus node dysfunction which became manifest after procainamide therapy must also be considered.

Another possible cause for the observed procainamide toxicity is elevation in N-acetyl procainamide, the metabolite of procainamide with similar arrhythmogenic actions. Since marked elevations of this substance have been reported in patients with renal failure who rapidly acetylate procainamide, it is possible that N-acetyl procainamide might have been a factor in one or both patients. Thus, in patients with chronic renal failure, procainamide can produce cardiac toxicity even when reduced doses are administered. Procainamide should therefore be avoided in these patients or used cautiously. Early signs of sinus node dysfunction should be looked for especially when other factors are present that might potentiate the effects of procainamide, since manifestation of "sick sinus syndrome" might be observed even before the QRS complex or the QT interval is appreciably altered.

Esophageal Compression in Association with Silicosis and Mycobacterium Intracellulare*

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An enameler with dysphagia was found to have extrinsic compression of the esophagus by enlarged mediastinal lymph nodes. Scalen lymph node biopsy revealed silicosis, and tissue cultures grew Mycobacterium intracellulare. We believe our patient is the first reported to have dysphagia due to silicotic adenopathy complicated by an atypical mycobacteriosis.

Dysphagia due to extrinsic compression of the esophagus by enlarged lymph nodes occurs infrequently in association with granulomatous diseases. Sarcoidosis and mediastinal granuloma have been reported to cause extrinsic esophageal compression.1-3 Silicosis has previously been shown to cause esophageal diverticulum, and when complicated by Mycobacterium tuberculosis, direct involvement of the esophageal wall.3,4

The relationship between silicosis and tuberculosis is well known. Also, mycobacteria such as M kansasii and M intracellulare often occur in association with pneumoconiosis.5,6 We report a patient with dysphagia due to extrinsic compression of the esophagus by silicotic mediastinal adenopathy complicated by M intracellulare.

CASE REPORT

A 44-year-old black man was seen in consultation by the medical chest service for a two-month history of dysphagia for solid foods and cough productive of yellow sputum. He denied recent weight loss, dyspnea, wheeze, chest pain, hemoptysis, use of tobacco, and previous tuberculosis. For the past 15 years, he had worked at an enamel factory where he was exposed to silica dust. He had past history of hypertension and diabetes mellitus. Physical examination showed a well-developed, 100 kg man with temperature 37.2°C, pulse rate of 84 beats per minute, and blood pressure of 140/100 mm Hg. The only abnormal physical finding was a small lymph node palpable in the left axilla.

Laboratory investigation showed the following: hemoglobin level, 9.1 gm/100 ml; hematocrit reading, 31.7 percent; white blood cell count, 4,200/cu mm, with one metamyelocyte, nine bands, 38 segmented neutrophils, three eosinophils, one basophil, 44 lymphocytes, and four monocytes; erythrocyte sedimentation rate, 90 mm per hour; serum iron value, 20 μg/100 ml (60 to 150); iron binding capacity, 222 μg/100 ml (270 to 380); and fasting blood glucose value, 159 mg/100 ml. The chest roentgenogram showed bilateral pulmonary reticulonodular shadows, bilateral hilar adenopathy, and cardiomegaly (Fig 1).

REFERENCES

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