Transient Global Amnesia Associated With Cardiac Arrhythmia and Digitalis Intoxication

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Abstract:

Transient global amnesia (TGA), an important organic altered mental state with a striking clinical presentation, may be the only manifestation of cerebral ischemia. It is sufficiently uncommon that its victims may be incorrectly considered hysterical or psychotic despite showing clinical features unique to this condition. TGA most commonly involves patients in the fifth or later decades of life and occurs without warning. During the attack profound loss of recent memory and remarkable attenuation of immediate recall appear with sparing of remote memory and all other modalities of intellect. Initially the patient may be amnesic for a period before and after the attack encompassing a few hours or as long as 48 to 72 hours. Subsequently, the span of altered memory shrinks from both ends until memory is completely normal except that there is no recollection of the TGA itself. During the attack the patient is alert, appropriately concerned, and aware something is amiss. He asks the same questions repeatedly (“What happened?,” “What is going on?,” etc.), immediately forgetting both the answers and asking the questions. A single cause has not been identified, but TGA often occurs under circumstances compatible with transient cerebral ischemia and hypoperfusion of the hippocampus, brain stem reticular formation and other structures served by the vertebrobasilar-posterior cerebral arterial systems. It has complicated aortic and cardiac catheterization and has occurred in persons without and with angiographical evidence of occlusive cerebrovascular disease. Causes of cerebral hypoperfusion other than atherosclerosis alone have been sought, including episodic reduction of cardiac output. Although cardiac arrhythmias have been suggested as a possible cause, the occurrence of arrhythmias in close association with TGA has not been documented, nor has attention been drawn to the possibility that a potentially dangerous or iatrogenic cardiac arrhythmia may present as TGA.

Case Report

A 54-year-old hypertensive black woman had good neurological health until the day of admission when she arose, dressed, conversed with her family and was considered normal in every way. She arrived at work without difficulty, but failed to recognize her fellow workers. She approached several persons asking what she was to do and, after receiving instructions, returned within a few minutes to ask the same question. Her employers became concerned about her behavior, found her confused, and brought her to the hospital.

For the past 15 years she had had hypertension in the range of 170 to 200 systolic and 100 to 125 diastolic mm Hg. She took reserpine, 0.25 mg, and hydrochlorothiazide, 100 mg, daily and a potassium supplement occasionally. Fifteen months before admission she began digitoxin, 0.1 mg daily, for mild left ventricular failure due to hypertensive heart disease.

On examination the patient was an alert, anxious, afebrile, middle-aged woman. She weighed 91.6 kg and her...
The hematocrit was 35%, white blood cell count was 5,500 per cubic millimeter with normal differential, and erythrocyte sedimentation rate was 38 mm per hour. The serum sodium was 144, potassium 3.2, chloride 99, and CO₂ combining power 32 mEq/L. The serum calcium was 10, phosphate 3.8, and blood urea nitrogen 16 mg %. The glucose, cholesterol, total protein, albumin, glutamic oxaloacetic transaminase and creatine phosphokinase were normal, and the latter two serum enzymes did not rise on serial determinations. The serum uric acid was elevated at 7.1 mg %. The serum digoxin level was 12.2 ng per milliliter (normal range 10 to 20). Electrocardiogram (ECG) showed sinus bradycardia at 48 per minute with intermittent A-V dissociation (fig. 1). There were occasional ventricular premature beats and S-T and T changes of digitalis treatment. The chest x-ray showed an enlarged heart. Electroencephalograms were obtained on the day of admission and the second and third hospital days. The initial recording revealed brief, generalized theta slowing, at times more prominent over the left hemisphere. A second tracing showed decrease in the amount of theta slowing, and a third was normal.

The patient was believed to be in the midst of an episode of TGA and to have digitalis-related bradycardia exacerbated by both reserpine treatment and hypokalemia and hypomagnesemia induced by thiazide diuretic treatment. The cardiac rate increased to 60 to 70 per minute after intravenous atropine treatment, and potassium chloride was begun, but intermittent A-V dissociation persisted. Amnesia improved, but did not clear. On the second hospital day intramuscular injection of magnesium sulfate was followed by prompt return of normal sinus rhythm at a rate of 66 to 80 per minute. Coincident with permanent restoration of sinus rhythm, the patient’s immediate recall and recent memory returned except that she remained amnesic for a period of two hours on the day of admission. Sinus rhythm persisted, although the rate occasionally fell as low as 58 per minute. Memory remained intact. During the subsequent two years, no episodes of amnesia occurred, and no congestive heart failure supervened after withdrawal of digitalis glycosides. Despite a prescribed diet, she has failed to lose weight. The hypertension persists intermittently, but under better control with hydrochlorothiazide, guanethidine, diazepam, and alpha methylldopa in various combinations. The blood pressure has fluctuated from 140/90 to 200/100 mm Hg.

In the past ten years, there have been six other patients...
with TGA recognized at this hospital. In two patients, ECGs obtained during or soon after the episode of TGA showed sinus bradycardia at rates of 53 and 55 per minute, respectively, with the latter patient having a rate of 60 per minute after TGA cleared. No other ECG abnormalities were present. ECGs were not obtained in two patients whose rate and rhythm were normal during TGA. Two additional patients underwent surveillance with a 24-hour Holter ECG recording without detection of arrhythmia. In none was the ECG obtained at the onset of TGA.

Discussion

Damage to hippocampal formations during temporal lobectomy may produce permanent total loss of immediate recall and recent memory without impairment of consciousness, remote memory or intelligence.12-14 A similar clinical state may follow bilateral posterior cerebral artery occlusion with hippocampal infarction.6, 8 The hippocampal formations, particularly Ammon's horn, are especially vulnerable to hypoxia, leading many investigators to suspect that TGA represents reversible ischemia of this portion of the brain.10, 16, 17 TGA has been reported in a variety of situations capable of compromising cerebral blood flow: hypertension,5, 9, 14, 15 migraine,9, 18 temporal arteritis,14 aortic valve prosthesis and bicuspid aortic valve with aortic insufficiency,19 long-standing atrial fibrillation,10 coronary angiography with suspected arterial embolization,20 cerebral angiography,3 and carotid stenosis.3 Also, there are reports of TGA during events stressful to the cardiovascular system: sexual intercourse,2 hot baths,4, 11 swimming in cold water,2, 11 spinal anesthesia,20 and hyperventilation followed by prolonged Valsalva maneuver.11

Both digitalis and hypomagnesemia have been implicated in confusional states. Before the advent of cardiac monitoring, digitalis intoxication was thought to produce confusion, the so-called digitalis delirium,21-24 but not a memory deficit in an otherwise intact patient. Digitalis-induced bradyarrhythmia with cerebral hypoperfusion secondary to altered cardiac output is now felt to be the explanation rather than a direct, central effect of the drug. Hypomagnesemia also is associated with confusion, seizures, and tetany25-27 and may be responsible for prolongation of the Wernicke-Korsakoff syndrome despite thiamine therapy,28 but it is not associated with amnesia alone. Reserpine itself has not been reported to cause TGA.

The patient reported here had digitalis-induced bradyarrhythmia contributed to by reserpine treatment and by hypokalemia and hypomagnesemia induced by thiazide diuretic treatment. Depletion of either or both minerals and the parasympathetic predominance resulting from sympathetic depression during reserpine treatment promote cardiac sensitivity to digitalis glycosides24, 29-32 and hence to the observed bradyarrhythmia and ventricular ectopy.

The only subjective accompaniment of this potentially dangerous arrhythmia was TGA. Its course coincided with the arrhythmia and resolved only upon the patient's permanent return to normal sinus rhythm. None of the more common manifestations of cardiac arrhythmias such as palpitation, syncope, dyspnea, or chest pain occurred. In two of our TGA patients, sinus bradycardia was present, raising the possibility of a more severe bradyarrhythmia at the time TGA began. The course of these patients suggests that cerebral hypoperfusion caused by bradyarrhythmia may be etiological. Arrhythmias should be suspected and excluded in every patient with TGA.

References

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