Possible Encainide-Induced Hypoproteinemia

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Encainide is a class IC antiarrhythmic agent that is used in the treatment of life-threatening ventricular arrhythmias. Although a number of minor laboratory abnormalities have been reported with encainide therapy,[1,2] hypoproteinemia has not been among them. Reported here is a case of hypoproteinemia and associated pedal edema that developed in a patient during encainide therapy. The hypoproteinemia may be associated with encainide therapy, since other causes of hypoproteinemia were ruled out, and the patient's edema resolved within 1 to 2 weeks of the termination of the drug.

CASE REPORT

A 53-year-old man was admitted to the hospital on October 15, 1987, with a chief complaint of "indigestion." Earlier in the day, he noted that his substernal discomfort became more severe and was associated with diaphoresis, numbness in his fingers, and weakness, but no nausea, vomiting, or radiation of the discomfort. Upon arrival of the ambulance, he was noted to have multifocal premature ventricular contractions, and was administered lidocaine 75 mg intravenously and placed on oxygen.

During transport to the hospital, the patient developed ventricular fibrillation and was countershocked three times and given intravenous atropine. These maneuvers returned the patient to normal sinus rhythm. Upon arrival at the hospital, he was still complaining of indigestion, and was given sublingual nitroglycerin and intravenous morphine sulfate. An electrocardiogram (ECG) revealed marked ST segment elevation. A cardiac catheterization revealed a complete occlusion of the right coronary artery and mild distal left anterior descending artery stenosis, as well as inferior ventricular wall akinesis. His left ventricular ejection fraction was determined to be 29%. An attempt to lyse the right coronary artery occlusion using both intravenous and intracoronary streptokinase was unsuccessful.

In the coronary care unit, the patient was noted to have frequent premature ventricular contractions and couplets. He was placed on mexiletine; however, this treatment failed to reduce the number of premature ventricular contractions. The mexiletine was discontinued, and he was subsequently placed on encainide, 25 mg every 8 hours, which resulted in a dramatic reduction in the number of premature ventricular contractions. A 24-hour Holter ECG revealed only occasional premature ventricular contractions, no complex arrhythmias, and an episode of asymptomatic bradycardia (46 beats per minute). In addition, the patient was noted to have a low blood pressure, though he remained asymptomatic.

The patient was discharged on October 26, 1987, on encainide, 25 mg every 8 hours, aspirin 325 mg daily, and sublingual nitroglycerin as needed.

RELATIONSHIP OF SERUM PROTEIN CONCENTRATION TO ENCAINIDE THERAPY

The time course of the patient's encainide therapy, serum protein concentrations, and symptoms of edema are presented in Table 1. At admission to the hospital, his total protein and albumin levels were 56 g/L (5.6 g/dL) and 38 g/L (3.8 g/dL), respectively. A follow-up visit on February 2, 1988, revealed a total protein and albumin of 44 g/L (4.4 g/dL) and 25 g/L (2.5 g/dL), respectively. The patient noted that he had had some pedal edema since January but no other symptoms of congestive heart failure. Subsequent visits revealed persistent hypoproteinemia, but no evidence of proteinuria (<0.15 g/d [<150 mg/24 h]) or renal insufficiency (creatinine clearance = 1.25 mL/s [75 mL/min]).

Encainide was discontinued in this patient on May 4, 1988. A follow-up serum protein analysis performed on October 27, 1988, revealed a total protein of 68 g/L (6.8 g/dL) and an albumin of 41 g/L (4.1 g/dL).

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TABLE 1. TIME COURSE OF ENCAINIDE THERAPY, HYPOPROTEINEMIA, AND PEDAL EDEMA

Date	Total Protein (g/L)	Albumin (g/L)	Comment
10/15/87	56	38	
10/16/87	57	36	
10/18/87			Encainide started
01/88			Patient complains of pedal edema
02/02/88	44	25	
02/16/88	46	27	
05/04/88			Encainide discontinued
10/27/88	68	41	

DISCUSSION

This case presents an interesting differential diagnosis for hypoproteinemia and mild pedal edema developing in a postmyocardial infarction patient receiving encainide. The edema was attributed to the decreased plasma oncotic pressure resulting from a low serum albumin concentration.

Hypoproteinemia may be the result of urinary loss of protein (eg, nephrotic syndrome), decreased hepatic synthesis (protein malnutrition, liver disease), or, rarely, loss of protein from the gastrointestinal tract. In this patient, no evidence was found that hypoproteinemia was the result of any of these causes. There was no history of anorexia, nausea, vomiting, or diarrhea. On history and physical examination, the patient had no documented weight loss, and there was no evidence of malnutrition, congestive heart failure, or liver disease. Laboratory studies revealed no abnormalities in urine contents, mean corpuscular volume, hematocrit, cholesterol, or liver enzymes. While there was no documented total protein and albumin levels shortly after discontinuation of encainide, the patient reported that the edema resolved within 1 to 2 weeks of this event. A subsequent protein determination 6 months after discontinuing the encainide revealed a normal total protein and albumin concentration. During this time, the patient remained clinically stable and asymptomatic.

Hypoproteinemia has not been reported in the literature as an adverse effect of encainide therapy. In subjecting this patient's case to an algorithm for determining the likelihood of drug-induced adverse drug reactions,[3] it appears that encainide was a "possible" cause of this patient's hypoproteinemia and associated pedal edema.

Pedal edema has been reported to occur in 1% to 2% of patients receiving encainide,[2] though the cause is unclear. Worsening congestive heart failure is unlikely, since this patient experienced no other signs of congestive heart failure. The possibility is therefore raised that encainide was the cause of hypoproteinemia in this patient, given the absence of any evidence suggestive of other causes.

References

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