

> THE PATIENT

44-year-old man

> SIGNS & SYMPTOMS

- Elevated total cholesterol
- Chest pains
- Ketogenic diet

> THE CASE

A 44-year-old man with a history of morbid obesity reestablished care in our clinic. He had been treated in our health care system about 5 years previously, and prior lab testing showed a total cholesterol of 203 mg/dL; triglycerides, 191 mg/dL; high-density lipoprotein (HDL), 56 mg/dL; and low-density lipoprotein (LDL), 109 mg/dL. At that time, he weighed 299 lbs (BMI, 39.4). He then started a strict ketogenic diet and a regular exercise program (running ~ 16 miles per week and lifting weights), which he maintained for several years. He had experienced remarkable weight loss; upon reestablishing care, he weighed 199 lbs (BMI, 26.33).

However, lipid testing revealed a severely elevated total cholesterol of 334 mg/dL; LDL, 248 mg/dL; HDL, 67 mg/dL; and triglycerides, 95 mg/dL. He was advised to start statin therapy and to stop his ketogenic diet, but he was hesitant to take either step. He elected to have his lab work reevaluated in 6 months.

About 4 months later, he presented with new and increasing burning pain in his mid chest and upper abdomen. He rated the pain 6/10 in severity and said it occurred during exertion or at night when lying down. Resting would relieve the pain. Reduced intake of spicy foods and caffeine had also helped. He denied dyspnea, diaphoresis, palpitations, or nausea.

The patient was a nonsmoker but did have a strong family history of cardiovascular disease. His vital signs and physical examination were unremarkable, apart from mild epigastric and periumbilical tenderness on palpation.

THE DIAGNOSIS

The patient's chest pain had features of both gastroesophageal reflux disease (GERD) and coronary artery disease (CAD) with exertional angina. His high-fat diet, nightly symptoms, and the partial relief he achieved by cutting back on spicy foods and caffeine suggested GERD, but the exertional nature of the chest pain and gradual relief with rest was highly suggestive of angina, so an outpatient electrocardiogram treadmill stress test was ordered.

The stress test was markedly abnormal, showing worsening ST depressions and T-wave inversions with exertion, and he experienced chest pain during testing. An urgent left heart catheterization was performed, showing severe multivessel CAD. He subsequently underwent 3-vessel coronary artery bypass grafting. A familial hypercholesterolemia panel failed to reveal any significant variants.

As a result of these findings, the patient received a diagnosis of severe ketogenic diet-associated hypercholesterolemia and early-onset CAD.

DISCUSSION

Low-carbohydrate (low-carb) and ketogenic diets have grown in popularity throughout the United States over the past decade, particularly for weight loss, and the diet has entered the popular consciousness with several celebrities publicly supporting it.¹ Simultaneously, there also has been a growing interest in these diets for the treatment of chronic diseases,

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➤ **The severe worsening of this patient's LDL levels was likely related to his ketogenic diet and was a factor in the early onset of CAD.**

such as type 2 diabetes.² However, the long-term cardiovascular effects of low-carb diets are not well studied, and there is significant heterogeneity among these diets.

■ **Low-carb vs low-fat.** Multiple meta-analyses comparing low-carb diets to low-fat diets have found that those following low-carb diets have significantly higher total cholesterol and LDL levels.^{3,4,5} The National Lipid Association's review of evidence determined that LDL and total cholesterol responses vary in individuals following a low-carb diet, but that increasing LDL levels in particular were concerning enough to warrant lipid monitoring of patients on low-carb diets.⁶ Another meta-analysis evaluated the difference in estimated atherosclerotic cardiovascular disease (ASCVD) risk between low-carb and low-fat diets, finding those following a low-carb diet to have a lower estimated ASCVD risk but higher LDL levels.⁷

■ **Weighing the benefits and harms.** Since our patient's dramatic weight loss and greatly increased exercise level would be expected to lower his LDL levels, the severe worsening of his LDL levels was likely related to his ketogenic diet and was a factor in the early onset of CAD. The benefits of low-carb diets for weight loss, contrasted with the consistent worsening of LDL levels, has prompted a debate about which parameters should be considered in estimating the long-term risk of these diets for patients. Diamond et al⁸ posit that these diets have beneficial effects on "the most reliable [cardiovascular disease] risk factors," but long-term, patient-oriented outcome data are lacking, and these diets may not be appropriate for certain patients, as our case demonstrates.

■ **A reasonable strategy** for patients contemplating a low-carb diet specifically for weight loss would be to use such a diet for 3 to 6 months to achieve initial and rapid results, then continue with a heart-healthy diet and increased exercise levels to maintain weight loss and reduce long-term cardiovascular risk.

■ **Our patient** was started on a post-operative medication regimen of aspirin 81 mg/d, evolocumab 140 mg every 14 days, metoprolol tartrate 25 mg bid, and rosuva-

statin 10 mg/d. A year later, he was able to resume a high level of physical activity (6-mile runs) without chest pain. His follow-up lipid panel showed a total cholesterol of 153 mg/dL; LDL, 53 mg/dL; HDL, 89 mg/dL; and triglycerides, 55 mg/dL. He had also switched to a regular diet and had been able to maintain his weight loss.

THE TAKEAWAY

Growing evidence suggests that low-carb diets may have a significant and detrimental effect on LDL levels. The long-term safety of these diets hasn't been well studied, particularly regarding cardiovascular outcomes. At a minimum, patients who initiate low-carb diets should be counseled on general dietary recommendations regarding saturated fat and cholesterol intake, and they should have a follow-up lipid screening to evaluate for any significant worsening in total cholesterol and LDL levels. **JFP**

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