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Case Report

The Impact of Dietary Cholesterol on Low-Density Lipoprotein: Lessons in Absorption and Overconsumption

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Abstract

This case describes a 58-year-old woman with past medical history of ulcerative colitis, hyperlipidemia, and radiological evidence of atherosclerosis without prior cardiovascular disease who presented for management of hyperlipidemia. At baseline, her lipid panel in 2015 noted a calculated low-density lipoprotein (LDL-C) of 125 mg/dL (3.2 mmol/L). Over the course of the next 5 years, she developed severe LDL elevations to >400 mg/dL (>10.3 mmol/L) following the addition of 1600 mg dietary cholesterol daily achieved through 9 eggs. Following cessation of this intake she had dramatic improvements in LDL, which was later further augmented significantly by initiation of ezetimibe. The impact of dietary cholesterol on lipid profiles has long been an area of controversy, and, for the average American, current guidelines do not recommend egg restriction as an effective tool for LDL lowering. However, as highlighted in this case, certain individuals may be more prone to high LDL when consuming high cholesterol diets. Further study on how to better identify these susceptible individuals could help improve nutritional and medication treatment plans for patients with dyslipidemia.

Key Words: lipid metabolism, nutrition, dietary cholesterol, low-density lipoprotein

The impact of dietary cholesterol on lipid profiles have long been a debated topic of both scientific study and layperson media. This was highlighted by alterations in the 2015 to 2020 American Heart Association dietary guidelines abolishing the prior dietary cholesterol limit of 300 mg/day [1]. Eggs often are the example cited in this debate as they are a rich source of dietary cholesterol without comparative high levels of saturated fat [2] of which the effects on low-density lipoprotein (LDL) cholesterol are better established. Most recently, the inclusion of eggs as a protein source in a balanced diet are maintained in the 2020-2025 American Heart Association dietary guidelines [3].

Eggs specifically have been investigated looking at both direct LDL effects [2, 4] and cardiovascular disease risk [5] with mixed results. Recent research investigating these discrepancies and controversy supports interindividual variability in LDL response to dietary cholesterol as a likely explanation.

Griffin et al highlighted the various mechanisms that may account for this interindividual variability including heterogeneity in the reciprocity between cholesterol synthesis and absorption [6]. Particularly of interest in relation to cholesterol absorption are identified polymorphisms in the Neiman-PickC1-like-protein-1. Identification of numerous genetic variants in the protein, including inhibition mutations that lead to decreases in LDL concentration [7], may ultimately suggest a wide spectrum of absorption phenotypes.

These data propagate the questions of how best to identify interindividual differences in clinical practice and furthermore if intraindividual variability also exists across the lifespan [8].

Case Presentation

A 58-year-old woman presented to the lipid clinic in August 2020 for management of hyperlipidemia.

Her medical history at that time was notable for a long-standing history of ulcerative colitis (UC). Her most recent treatment regimen, starting in 2015 through the time of presentation, involved vedolizumab infusion every 8 weeks. She does not have prior history of cardiovascular disease; however, atherosclerosis was incidentally noted on abdominal computer tomography imaging in March 2016. She has no history of smoking. She denies use of alcohol or recreational drugs. She reports walking for exercise at varied frequencies over the past several years. She had previously walked up to 30 minutes daily, reported walking less than this near time of initial lipid clinic evaluation. She underwent total hysterectomy/oophorectomy at age 37 and reportedly took estrogen replacement with an outside provider until approximately age 55.

Her family history is notable for coronary artery disease in her father with a history of myocardial infarction and bypass in his 60s. Her mother has a history of hypertension and hyperlipidemia. Furthermore, her maternal grandfather also has history of coronary artery disease.

Diagnostic Assessment

On initial evaluation, review of prior diagnostic evaluations demonstrated the following lipid panel trends. At baseline, her first lipid panel recorded on file in 2015 noted a calculated

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LDL (LDL-C) of 125 mg/dL (3.2 mmol/L) with high-density lipoprotein (HDL) 66 mg/dL (1.7 mmol/L), triglycerides (TG) 184 mg/dL (2.1 mmol/L) and total cholesterol 228 mg/dL (5.9 mmol/L).

In 2017, repeat LDL-C was 255 mg/dL (6.6 mmol/L), prompting treatment at that time with atorvastatin. Following initiation of atorvastatin, LDL-C improved to 137 mg/dL (3.5 mmol/L). However, on atorvastatin, she experienced dermatitis and underwent dermatologic evaluation/biopsy. Medication reaction was favored as the etiology and atorvastatin was discontinued. Of note, the patient reports that, in addition to atorvastatin, she reportedly took cholestyramine in 2014 for 1 to 2 weeks but could not tolerate it secondary to constipation/UC flare.

On January 14, 2019, off atorvastatin, LDL-C was 162 mg/dL (2.4 mmol/L). From approximately 2015 until this time the patient consumed a strict vegan diet. Her weight ranged between 93 to 103 lbs (body mass index approximately 16 kg/m^2) throughout this period. Later in 2019, she began incorporating 9 eggs per day (1600 mg dietary cholesterol) into her diet. She denied consumption of other animal products or notable cholesterol-containing foods.

In August 2019, LDL-C was 378 mg/dL (9.8 mmol/L). Lipoprotein (a) measurement in January 2020 was 176 mg/dL (reference range <29 mg/dL). She reports maintaining a consistent intake through 2019 to 2020 with a corresponding repeat peak LDL-C measurement of 420 mg/dL (10.9 mmol/L) in August 2020. Clinical follow-up and treatment for this severe LDL elevation was reportedly delayed due to patient-related illness (UC flares, urinary tract infection) and the COVID-19 pandemic.

Treatment

On evaluation in August 2020, given data to date, she was advised that her goal LDL was 100 mg/dL (2.6 mmol/L) or less. She was advised to limit her egg yolk consumption to 4 per week (approximately 100 mg/day of cholesterol).

On a subsequent visit following this counseling, dietary recall included a transition from whole eggs to egg whites. Additional intake included olive oil, beans, and potatoes. The patient cited concerns for exacerbation of gastrointestinal symptoms as a primary motivator for a rigid diet program. She continued to avoid all other animal products. In October 2020, without addition of medications or other notable lifestyle changes, her LDL-C decreased from 420 mg/dL (10.9 mmol/L) to 204 mg/dL (5.3 mmol/L). In January 2021, her LDL-C decreased further to 130 mg/dL (3.4 mmol/L). Body mass index remained stable during this time. Apart from one TG outlier of 358 mg/dL (19.9 mmol/L) in early 2019, TG and HDL values remained comparatively stable throughout the described timeline (Table 1).

Outcome and Follow-up

During subsequent follow up in August 2021, her LDL-C was 142 mg/dL (3.7 mmol/L). Ezetimibe 10 mg daily was then added with reduction in LDL-C to a near-target of 103 mg/dL (2.7 mmol/L) (Δ 27%) within 4 months. On annual follow-up in August 2022 while following the same medication and diet regimen her LDL-C was 61 mg/dL (1.6 mmol/L). She has remained without changes to other medications or nutritional intake.

Discussion

For the average American, current guidelines do not recommend egg restriction as an effective tool for LDL-C lowering. However, as shown in this case, certain individuals may be more prone to high LDL-C when consuming high-cholesterol diets.

The patient's ability to achieve near normal LDL concentrations both prior to and after various lifestyle interventions effectively rules out an etiology of more commonly identified genetic predispositions (ie, familial hypercholesterolemia) that can be associated with the severity of the patient's peak measurements. The greater than average LDL-C reduction on ezetimibe despite already limiting dietary cholesterol intake also supports evidence of a unique hyperabsorption phenotype. Given the patient's presenting history of atherosclerosis, family history of cardiovascular disease, and dietary changes, a genetic predisposition to hyperabsorption is highly favored.

Notably, prior to reported egg consumption, she did experience an increase in LDL-C from 125 mg/dL (3.2 mmol/L) in 2015 to 255 mg/dL (6.6 mmol/L) in 2017. While likely multifactorial, the cessation of her estrogen replacement correlates with this increase, a change consistent with observational data showing increases in LDL during menopause [8]. Other potential contributors not well documented during this time include short-term medication use (ie, glucocorticoids), exercise changes, and unaccounted-for vegan dietary sources high in saturated fat.

Table 1. Patient BMI and lipid panel data

Date of collection	August 18, 2015	January 23, 2017	August 2, 2018	January 14, 2019	August 27, 2019	August 11, 2020	October 9, 2020	January 8, 2021	August 19, 2021	December 9, 2021	August 23, 2022
BMI (kg/m^2)	16.5	15.9	15.9	16.6	15.7	16	15.9	15.9	15.7	16.4	16.1
Total cholesterol (mg/dL, <199)	228	377	257	320	495	549	318	253	233	197	172
Triglyceride (mg/dL, <149)	184	134	167	358	140	139	90	185	93	159	117
HDL (mg/dL, <50)	66	95	86	87	90	101	96	86	72	62	88
LDL-C (mg/dL, 1-129)	125	255	137	162	378	420	204	130	142	103	61

Abbreviations: BMI, body mass index; HDL, high-density lipoprotein; LDL-C, calculated low-density lipoprotein.

UC is associated with lower LDL cholesterol as compared with the general population, a finding often attributed to the "lipid paradox" of inflammatory states [9]. Treatment of UC with glucocorticoid and Janus kinase inhibition (ie, tofacitinib) is associated with increases in LDL but not with the extreme levels that our patient experienced. In a recent meta-analysis [9], an inverse relationship between C-reactive protein levels and total cholesterol, HDL, and LDL was identified. This supports a hypothesis that suppression of inflammation in general partially explains the LDL increases seen with all inflammatory bowel disease treatment, although significant variability in the degree of these changes between the drug classes does remain.

A review of the literature to date did not find that vedolizumab was associated with lipid abnormalities both in general and specific to LDL [9]. In contrast, mouse models suggest a potential for improvement in metabolic parameters with the mechanism of this medication [10].

Overall, the interplay of UC disease state and associated treatment regimens is an important aspect of lipid management; however, in this case the relative stability of these factors throughout the described timeline limits the potential influence.

This case highlights the importance of establishing careful dietary history in clinical practice before diagnostic or treatment decisions. Further study on how to better identify these susceptible individuals could help improve nutritional and medication treatment plans for patients with dyslipidemia.

Learning Points

- The impact of dietary cholesterol on LDL concentration can vary significantly among individuals.
- Nutritional assessment and counseling are an important part of clinical lipid management, which should be tailored to patient specific needs.
- Further study is warranted to better understand and identify the varying phenotypes of hyperlipidemia in clinical practice.

Contributors

All authors made individual contributions to authorship. M.P.: Involved in the diagnostic review and manuscript submission. M.W.: Involved in the diagnosis and clinical management of this patient. All authors reviewed and approved the final draft.

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Disclosures

None declared.

Informed Patient Consent for Publication

Signed informed consent obtained directly from the patient.

Data Availability Statement

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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