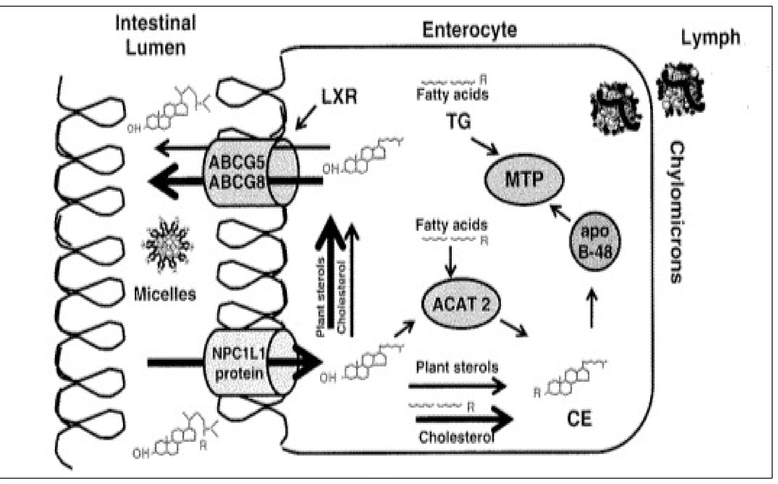
A rare cause of hyperlipidemia: Precision medicine used in a direct primary care clinic to diagnose heterozygous sitosterolemia

John D. Jovan III, B.S.[1], Vasanth Kainkaryam M.D., MS, FAAP, FACP, DABOM [1,2]
[1]Frank H. Netter, M.D. School of Medicine, Quinnipiac University, North Haven, CT
[2]4 Elements Direct Primary Care & Wellness Space, South Windsor, CT

Introduction

- Hypercholesterolemia is a common condition encountered in primary care.
- Rare etiologies may pose a difficult challenge, manifesting as resistance to first line lipid lowering agents.
- Sitosterolemia is a rare autosomal recessive lipid disorder caused by increased absorption of plant sterols, hypercholesterolemia and premature atherosclerosis.
- Only around 100 cases of sitosterolemia have been reported with some estimates showing that it may be much more common with a prevalence of 1:50,000.[2]



Case History

The subject of this case study is a 67-year-old woman with a history of osteopenia who presented for an initial intake evaluation and physical exam. On presentation she had no acute concerns.

Family history was notable for hypertension, lung disease, and chronic kidney disease but no known history of premature ASCVD. The patient described her diet as "borderline vegan." She denied ever smoking and admitted to consuming 2-3 alcoholic drinks per week. She stated her exercise consisted of walking one mile daily and going to the gym twice weekly.

Review of systems was negative for any visual changes, neck swelling, chest pain, shortness of breath, or skin changes.

On physical exam, vitals showed an elevated blood pressure and BMI. Patient was well-appearing with no focal neurologic deficits. Neck exam was without thyromegaly, cardiac exam revealed a regular rate and rhythm with good perfusion, and skin exam was without suspicious lesions.

Differential Diagnosis

Primary HLD

- Genetic (FH, Sitosterolemia)

Secondary HLD

- Metabolic Syndrome
- Obesity
- Diabetes
- Obstructive liver disease
- Nephrotic Syndrome
- Hypothyroidism

Diagnostic Labs

- Cardiometabolic testing (Table 1 and Table 2)
- HbA1c at 5.7%
- Further genetic testing revealed a ***heterozygous mutation*** in the **ABCG8 gene**
- Rosuvastatin started (June 2023)
- Ezetimibe started (December 2023); Rosuvastatin discontinued due to patient preference
- Referred to Dietician (February 2024)
- Coronary Artery Calcium score (July 2024): 31st percentile

	Initial Presentation (June 2023)	1st Follow Up (Dec 2023)	2nd Follow Up (Feb 2024)	3rd Follow Up (May 2024)
Total cholesterol	291 mg/dL	243 mg/dL	199 mg/dL	213 mg/dL
ApoB	156 mg/dL			
Direct LDL-c	211 mg/dL	164 mg/dL	114 mg/dL	132 mg/dL
LDL-p	2567 nmol/L			
Triglycerides	204 mg/dL	86 mg/dL	156 mg/dL	115 mg/dL
Lp(a)	22 mg/dL			

Table 1. Laboratory results

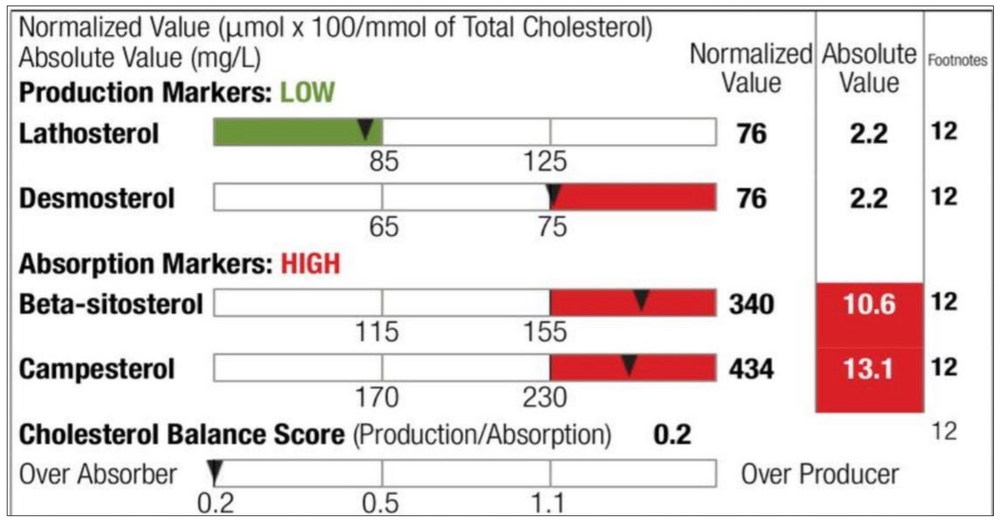


Table 2. Cholesterol Balance Testing

Discussion

Sitosterolemia

- This case highlights a rare genetic cause of hyperlipidemia found by applying precision medicine concepts in a direct primary care clinic.
- Workup for sitosterolemia should be considered in patients with hyperlipidemia who do not respond to initial statin therapy.
- Heterozygous sitosterolemia may present with an elevated LDL, increasing a patient's risk of ASCVD.
- Pharmacotherapy with ezetimibe, which inhibits the NPC1L1 protein, thereby decreasing cholesterol and plant sterol absorption by enterocytes, is the preferred treatment of sitosterolemia. Statins are subsequently added based on the patient's ASCVD risk.
- Lifestyle change for an individual with sitosterolemia is unique and consists of limiting monounsaturated fats, polyunsaturated fats and plant-based sterols. These are typically considered "healthy fats" that are recommended to patients with classic hyperlipidemia.
- Diet should avoid nuts, vegetable oils, shellfish, avocados, and chocolate.
- Multidisciplinary care involving a dietician and nutritionist are critical in the long-term management of patients with sitosterolemia.

References