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CASE REPORT | COLON

Tangier Disease: An Unusual Cause of Chronic Diarrhea

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ABSTRACT

Tangier disease is a rare autosomal recessive disease resulting in cholesterol deposition in different organs. We report a case of a 52-year-old white man who presented for chronic diarrhea without significant findings on noninvasive testing. Subsequent colonoscopy revealed endoscopically normal mucosa, with random biopsies remarkable for foamy macrophages in the lamina propria. Genetic testing showed adenosine triphosphate–binding cassette transporter gene mutation with low high-density lipoprotein and low low-density lipoprotein. To the best of our knowledge, this is the first report of chronic diarrhea in a patient with Tangier disease without any other clear etiology.

INTRODUCTION

Tangier disease, also known a hypoalphalipoproteinemia, is an extremely rare autosomal recessive disease that leads to significant derangement in cholesterol metabolism. In homozygote patients, cells are unable to remove cholesterol, leading to deposits of cholesteryl esters in many organs, including the liver, spleen, and gastrointestinal tract. Patients with Tangier disease have a severe reduction in high-density lipoprotein (HDL) and hypertriglyceridemia. We report a case of a 52-year-old white man with chronic diarrhea found to have xanthomatosis on colonic biopsies, lipid panel demonstrating undetectable HDL level and hypertriglyceridemia, and with subsequent genetic testing confirming the diagnosis of Tangier disease.

CASE REPORT

A 52-year-old white obese man (nonsmoker) with no medical history presented for a second opinion for chronic diarrhea. He described having 5-7 loose stools per day for the past 15 years. He denied bleeding, abdominal pain, nausea/vomiting, weight loss, and fever/chills. He denied a family history of gastrointestinal conditions. Infectious stool studies including ova and parasites were negative. Fecal elastase was normal. Previous colonoscopies revealed normal-appearing mucosa, and histology of colonic biopsies demonstrated xanthomatosis. Given ongoing symptoms, he underwent esophagogastroduodenoscopy which was notable for mild duodenal erythema. Histology of duodenal biopsies showed mucosa with xanthoma. Colon and terminal ileum appeared normal on colonoscopy. However, pathology revealed foamy macrophages within the lamina propria and submucosa consistent with xanthomatosis (Figure 1). Given extensive xanthomatosis on intestinal biopsies, a lipid panel was obtained, and it showed a total cholesterol of 85 mg/dL with HDL less than threshold of analyzer, low-density lipoprotein (LDL) 11 mg/dL, and triglyceride level 568 mg/dL. Apolipoprotein A-1 level was 60 mg/dL. He subsequently underwent genetic testing with adenosine triphosphate–binding cassette transporter gene sequencing that established the diagnosis of Tangier disease. He was recommended to maintain an active lifestyle and adopt a low-fat diet. He was initially treated with loperamide 2–4 mg twice daily. After lifestyle modification, he noticed an improvement in his diarrhea without the ongoing need for antidiarrheal medications. He was advised to encourage his siblings to undergo evaluation for Tangier disease.

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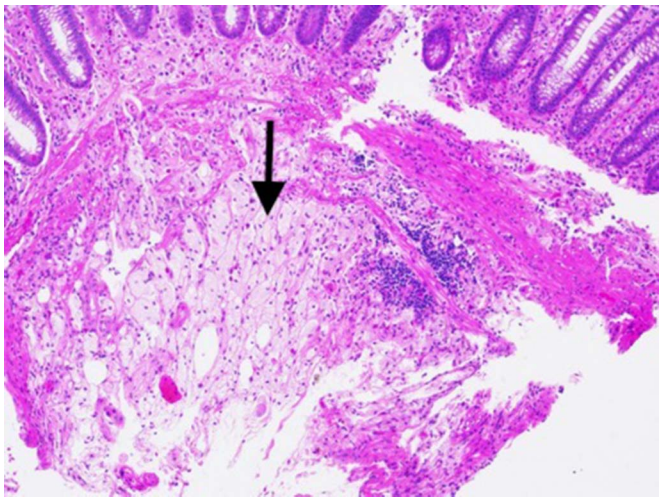

Figure 1. Dense collection of foamy macrophages (arrow) within submucosa, biopsy taken from colon.

DISCUSSION

Tangier disease is an extremely rare autosomal recessive disease that leads to significant derangement in cholesterol metabolism. Patients with homozygotes have undetectable HDL levels, and those who are heterozygotes would have serum HDL that is typically half lower limits of normal. It was first identified in a pair of siblings on an island off the coast of Virginia 60 years ago. Since then, there have only been approximately 100 cases identified worldwide. The genetic basis of the disease involves mutations in the adenosine triphosphate–binding cassette transporter gene on chromosome 9q31, which encodes the cholesterol efflux regulatory protein.[1,2] This cell surface protein enables cholesterol to move extracellularly to apolipoprotein AI, which is the major protein of HDL. As such, cells cannot efflux cholesterol, leading to deposits of cholesteryl esters in many organs, reticuloendothelial cells (foam cells), tonsils, liver, spleen, gastrointestinal tract, lymph nodes, bone marrow, and Schwann cells.[3] Focal deposits in the intestinal and rectal mucosa may be seen on colonoscopy but typically do not cause symptoms.[4] The most pervasive gastrointestinal manifestation is hepatosplenomegaly. A study by Serfaty-Lacrosniere et al reviewed cases of 51 patients with homozygous Tangier disease. Compared with 3,130 controls, they noted that the most common clinical symptom was peripheral neuropathy (54% vs <1%).[5] There is no pharmacotherapy approved for Tangier disease. Although typical cholesterol-lowering agents, such as gemfibrozil, niacin, or statins, may lower LDL or triglycerides in these patients, they typically have no or minimal effect on HDL. A low-fat diet may reduce the overall cholesterol burden and can be associated with symptomatic improvement in neuropathy.

DISCLOSURES

Author contributions: G. Ritaccio wrote the manuscript, reviewed the literature, revised the manuscript for intellectual content, and approved the final manuscript. B. Asif and U. Wong wrote the manuscript and approved the final manuscript. H. Yfantis revised the manuscript for intellectual content and approved the final manuscript. U. Wong is the article guarantor.

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