Journal of Clinical Lipidology (2018) ■, ■–■

Journal of Clinical Lipidology

Clinical Lipidology Roundtable Discussion

Roundtable discussion: Familial hyperchylomicronemia syndrome: Diagnosis and management

Q17 William Virgil Brown*, Ira Goldberg, MD, Barton Duell, MD, Daniel Gaudet, MD, PhD
Q1

Q2 *Emory University School of Medicine, Atlanta, GA, USA(Brown); Department of Medicine, Langone – NYU Medical*
Q3 *Center(Goldberg); Division of Cardiovascular Medicine, School of Medicine, Oregon Health Sciences University(Duell); and Université de Montréal(Gaudet)*

KEYWORDS:
Hyperchylomicronemia;
Triglycerides;
Clinical management;
Lipoprotein lipase;
Apolipoprotein;
APO C-III;
Volasenorsen

Abstract: Plasma triglyceride concentrations are normally below 150 mg/dL in the fasting state. However, these lipids can reach values of several thousand mg/dL. Elevations in this range are due to a massive retention of chylomicrons and usually result from multiple genetic variants with superimposed influences such as diabetes and immune disorders. Less commonly, major gene defects in lipoprotein metabolism can be the cause. These may present soon after birth with strong evidence of familial penetrance. The causes of this syndrome have been discussed in a Roundtable published in the most recent issue of this Journal. The polygenic etiology may also have a familial presentation with similar clinical import. The diagnosis and management of these disorders is of importance since they can lead to critical clinical syndromes including death from acute hemorrhagic pancreatitis. The chronic management requires a dedicated medical team and a patient committed to an effective regimen. We are joined in this discussion by Dr P. Barton Duell, University of Oregon Health Sciences Center, and Dr Daniel Gaudet of the Université de Montreal, Montreal, Quebec. All have had extensive personal experience in the diagnosis and management of patients with familial chylomicronemia. This Roundtable was recorded on November 11, 2017, during a meeting of the National Lipid Association in New Orleans, Louisiana.

Plasma triglyceride concentrations are normally below 150 mg/dL in the fasting state. However, these lipids can reach values of several thousand mg/dL. Elevations in this range are due to a massive retention of chylomicrons and usually result from multiple genetic variants with superimposed influences such as diabetes and immune disorders. Less commonly, major gene defects in lipoprotein metabolism can be the cause. These may present soon after birth with strong evidence of familial penetrance. The causes of this syndrome have been discussed in a Roundtable published in the most recent issue of this Journal. The polygenic etiology may also have a familial presentation with similar clinical import. The diagnosis and management of these disorders is of importance since they can lead to critical clinical syndromes including death from acute hemorrhagic pancreatitis. The chronic management requires a dedicated medical team and a patient committed to an effective regimen.

We are joined in this discussion by Dr P. Barton Duell, University of Oregon Health Sciences Center, and Dr Daniel Gaudet of the Université de Montreal, Montreal, Quebec. All have had extensive personal experience in the

Q4 * Corresponding author. Emory University School of Medicine, Atlanta, GA, USA.
E-mail address: wbrow925@bellsouth.net

1933-2874/© 2018 Published by Elsevier Inc. on behalf of National Lipid Association.
https://doi.org/10.1016/j.jacl.2018.02.018

diagnosis and management of patients with familial chylomicronemia.

This Roundtable was recorded on November 11, 2017, during a meeting of the National Lipid Association in New Orleans, Louisiana.


web 4C/FPO

Dr Brown

Dr Brown: Dr Duell, how do you make the clinical diagnosis of familial chylomicronemia syndrome? What are the clinical signs and historical findings that may lead to this diagnosis?

Dr Duell: The presence of milky plasma and triglycerides well over 1000 mg/dL is the hallmark. The retina often reflects this change in blood color with lipemia retinalis identified on ophthalmologic examination. Recurrent crops of raised red and tender lesions with white centers are often found on the extensor surfaces of the extremities and buttocks. These we call eruptive xanthomata. Hepatosplenomegaly with a tender liver edge on palpation is characteristic. A moderate elevation of both ALT and AST is often found. Many people present with recurrent abdominal pain that is intermittent. In the more extreme form, acute pancreatitis can appear and become life threatening. Unfortunately, it is pancreatitis that brings such patients to medical attention with the initial identification of chylomicronemia as the potential etiology.


web 4C/FPO Q5

Dr Goldberg

Dr Brown: When patients are discovered to have hyperchylomicronemia, when would a doctor send you a patient like this?


web 4C/FPO

Dr Duell

Dr Duell: Well, some recognize the importance of plasma triglycerides at values of several thousand mg/dL with the characteristic findings on examination; but in my specialty practice, it is most often after pancreatitis has occurred.

The second most common reason for referral might be a rash after a dermatologist has recognized eruptive xanthomata. Less commonly, they are referred because of a workup for hepatosplenomegaly and elevated triglycerides have been discovered.

Dr Brown: The pink blood or creamy plasma is not a common reason for the evaluation?

Dr Duell: Usually, people don't look at it. In the clinic, we look for lipemia retinalis, and we draw the blood and spin it to show the patient, so they can understand what's going on in their blood. But I think that's rarely done these days.

Dr Brown: Do you think most doctors would look for hyperchylomicronemia in cases of pancreatitis? Is that a common cause?

Dr Duell: Yes and no. I do get referred patients who have had pancreatitis with triglycerides that are greater than 5000. And they often have been put on a low-carbohydrate diet and a statin, for example, atorvastatin 80 mg a day. With this, the triglycerides don't come down, and so they will get referred in that setting.


web 4C/FPO

Dr Gaudet

Dr Gaudet: From our experience, it is amazing that many people have had recurrent acute pancreatitis (RAP) without this cause being discovered.

Dr Brown: This is a real problem. A major purpose of this Roundtable is to remind our colleagues of this treatable etiology for pancreatitis.

Dr Duell: I agree. However, there is an occasional false positive diagnosis. That is, pancreatitis is attributed to triglyceride levels of less than 500 mg/dL. The importance of having a very high plasma chylomicron triglyceride concentration is not appreciated.

Dr Brown: This is an important point. What is the concentration of triglycerides above which it is potential cause of pancreatitis?

Dr Gaudet: First of all, just for convenience, I want to use the term familial chylomicronemia syndrome (I rather prefer primary chylomicronemia) to refer to single genetic causes and multifactorial chylomicronemia for all the others. The diagnosis of chylomicronemia is shared by both conditions. Having said that, chylomicronemia is just descriptive of blood triglyceride levels when chylomicrons dominate. Chylomicrons definitively become the dominant circulating triglyceride-rich lipoprotein at levels over 1000 mg/dL, but they are present at 500. One thousand is said to be the threshold where we see an increased risk of pancreatitis. But, I've never seen 1 single patient having a pancreatitis at this level. The level varies with other influences including diet, and I'm sure it's more than 2000 mg/dL at the onset of pancreatitis in virtually every patient. Having said that, however, the notion of risk must be stratified according to findings in each patient.

Chylomicronemia, by nature, this is a postprandial disease. When we're measuring triglyceride in fasting blood samples, we underestimate, in general, what's going on postprandially in terms of the chylomicron population because so much of the postprandial triglycerides have cleared. We can assume that if the patient has a triglyceride level of 500 in the fasting state, he or she likely has significant postprandial chylomicronemia.

The risks associated with severe hypertriglyceridemia can be multiple. It is by far more complex than with cholesterol. Indeed, cholesterol (particularly LDL-cholesterol) risk is linear across its distribution. For triglyceride, it depends on the involved lipoproteins. The risk of acute pancreatitis is specifically linked to the chylomicron population and the triglyceride concentration in these particles, not in the endogenous VLDL particles.