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Familial Chylomicronemia Syndrome: Improving Recognition and Diagnosis

Announcer:

You're listening to *On the Frontlines of Familial Chylomicronemia Syndrome* on ReachMD. Here's your host, Dr. Steve Jackson.

Dr. Jackson:

This is *On the Frontlines of Familial Chylomicronemia Syndrome* on ReachMD, and I'm Dr. Steve Jackson. Today, we'll learn about effective identification and diagnosis of familial chylomicronemia syndrome, also known as FCS, with Dr. Nivedita Patni. She's an Associate Professor of Pediatrics and the Program Director of the Pediatric Endocrinology Fellowship at UT Southwestern Medical Center in Dallas. Dr. Patni, welcome to the program.

Dr. Patni:

Thank you, Dr. Jackson. I'm truly honored to be here and grateful for the opportunity to join today and discuss familial chylomicronemia syndrome.

Dr. Jackson:

And we're very grateful to have you. So, Dr. Patni, let's jump right in. We know that FCS often goes under-recognized in clinical practice. Can you tell us a bit about why it's so challenging to identify?

Dr. Patni:

So there are, I would say, several factors that cause it to be such a challenging diagnosis. First—and the most important one, I think—is it is extremely rare. The most recent data is saying that the prevalence is about one in 300,000 individuals. And when some syndromes and diseases are this rare, it's uncommon for physicians to diagnose them right away because of the sheer rarity of it.

The second is that there's a substantial overlap between the more common multifactorial chylomicronemia syndrome and FCS. Both of them can present with severe hypertriglyceridemia and can have similar symptoms. But MCS is more common, so that is a thought process that most physicians have.

Also, I think the age of diagnosis and presentation is so variable. All of these together, I feel, causes it to be an under-recognized disease.

Dr. Jackson:

And knowing that, what are the consequences of diagnostic delay for patients and what opportunities are missed when the condition goes unrecognized?

Dr. Patni:

Delayed diagnosis causes significant clinical and psychosocial consequences because FCS—due to its etiology—is caused by genetic variants in genes that are responsible for digestion of chylomicron. So underdiagnosed or misdiagnosed patients do not respond to the known therapies, present with recurrent acute pancreatitis, and miss access to the targeted therapies that are specific for this syndrome.

It adds to a lot of quality-of-life burden, because a lot of patients experience these chronic abdominal pains, unrecognized pancreatitis, fatigue, and cognitive impairment. There's something called brain fog that a lot of patients feel. And then they develop anxiety about pancreatitis and other things that come with it.

Dr. Jackson:

Now, with that context in mind, when you evaluate a patient with severe hypertriglyceridemia, what clinical features or patient

characteristics raise your suspicion that FCS may be the underlying cause?

Dr. Patni:

So the clinical characteristics are usually recurrent pancreatitis and lipemia retinalis, which is more of an examination finding of physicians when they look at the back of your eye. The chylomicrons in the blood vessels in the retina shine, and they look very white. Xanthomas are a very important sign. Hepatosplenomegaly, because the fatty deposits happen there. And in very young infants and neonates, they have very nonspecific symptoms like discomfort with abdominal pain or pancreatitis. Some of them can have anemia and GI bleeds as well.

So, as I said, these are nonspecific symptoms. But all of this, in association with ineffective treatment with conventional triglyceride-lowering therapy, should increase the suspicion of FCS.

Dr. Jackson:

For those just joining us, this is *On the Frontlines of Familial Chylomicronemia Syndrome* on ReachMD. I'm Dr. Steve Jackson, and I'm speaking with Dr. Nivedita Patni about challenges and opportunities in diagnosing FCS.

Dr. Patni, once FCS is suspected, what does a clinically confirmed diagnosis involve, and how do you distinguish it from other causes of severe hypertriglyceridemia?

Dr. Patni:

There is something called the North American Familial Chylomicronemia Score that we recently came up with to help with the diagnosis. So when somebody presents with the classical characteristics—fasting triglycerides over 880 milligram per deciliter or greater than 10 millimoles per liter at a younger age, absence of any secondary factors that can cause NCS, lack of response to conventional therapies, history of recurrent pancreatitis, and very high triglyceride with a ratio of total triglyceride to cholesterol of greater than 10, along with ApoB—you should try to get that score going.

So it is available on multiple websites, like MDCalc. You can go look up North American FCS Score. So that score helps get an initial idea of gauge. Is it FCS or MCS? Any score of 60 is pretty consistent. And then anything between 40 to 60 is suggestive. If we have a biochemical diagnosis of high triglycerides, low ApoE, ApoBs, and high triglyceride to TG ratios, get the score and then send for genetic testing.

Dr. Jackson:

Yes, let's talk about genetic testing now. Where does it fit into the diagnostic workup, and how can it complement a clinically confirmed diagnosis?

Dr. Patni:

FCS is an autosomal recessive disorder, which means you need to have two hits to cause it. So there are five common genes that, at this point, we know. Lipoprotein lipase deficiency is seen in about 90 percent—maybe even more than APOC1, APOC2, GPHBP1, and LMF1. These are the other four genes that, if we have autosomal recessive hits in any of these five, you get FCS.

Now, again, being a Mendelian disorder and autosomal recessive inheritance, genetic testing usually seals the deal. But there are so many practicalities that come with it, including insurance coverage and being able to get it done. And so that's why we came up with the FCS score, which can help guide us clinically if this is truly FCS versus MCS. But if access is there, and if we can get genetic testing, it confirms it.

Dr. Jackson:

And finally, Dr. Patni, as awareness of FCS continues to grow, what practical steps can clinicians take to improve identification, streamline diagnosis, and ensure patients are referred appropriately?

Dr. Patni:

I think the most important thing is, when anybody walks into the clinic with high triglycerides, make sure that you look into any of the secondary factors. They can control diabetes, hypothyroidism, alcoholism, renal disease, and severe medication use, like chronic steroids. So any of these, once they've been ruled out, can then confirm the persistence of high triglyceride.

There should be at least two—if possible, three—fasting triglycerides that are in the high triglyceride range or hypertriglyceridemia range. Then, if they've been treated, response to the therapy is something very important that has to be seen. So if there is no response, a lipid specialist should definitely follow them up to help do the further workup. And if there is even a slight response, do the FCS score, and if there is a suggestion of it being FCS, sending to a lipid specialist should be the next step.

Dr. Jackson:

With those takeaways in mind, I want to thank my guest, Dr. Nivedita Patni, for sharing her insights on how we can improve the recognition and diagnosis of FCS. Dr. Patni, it was great having you here today.

Dr. Patni:

Thank you so much for having me.

Announcer:

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