A JOINT EXPERT CLINICAL CONSENSUS BY THE NATIONAL LIPID ASSOCIATION (NLA) AND THE AMERICAN SOCIETY FOR PREVENTIVE CARDIOLOGY (ASPC)

Recognition and Management of Persistent Chylomicronemia

Purpose of Statement:

This consensus statement reviews the metabolism of triglyceride-rich lipoproteins, the epidemiology of chylomicronemia, and clinical and diagnostic differences between familial chylomicronemia syndrome (FCS) and multifactorial chylomicronemia syndrome (MCS), and presents the rationale for a new diagnostic approach and shift in paradigm for defining adults with persistent chylomicronemia (PC) along with alarm features for risk stratification and recommendations on management options.

Frequency of Occurrence:

Extreme hypertriglyceridemia, defined as fasting triglyceride (TG) levels ≥1000 mg/dL (i.e., chylomicronemia), affects 1 in ~500 adults in the United States and is associated with an increased risk of pancreatitis and other morbidities.

Approach to Assessment & Treatment of PC:

- Treatment of chylomicronemia should begin with management of any secondary causes (including TG-raising medications), lifestyle modifications (targeting obesity, excessive alcohol intake, dietary habits, inactivity), and first-line TG-lowering drugs (fibrates and/or omega-3 fatty acids).
- Patients with PC (TG ≥1000 mg/dL in more than half of measurements) can be classified into 4 subtypes: genetically documented FCS, clinical FCS, PC with alarm features, and PC with no alarm features.
- PC patients should be treated with intensified lifestyle modification, multidisciplinary care, and combination lipid-lowering therapy.
- PC patients in the first 3 subtypes are at very high risk for acute pancreatitis and warrant consideration for newer medications such as apo C-III inhibitors

Highlights:

- Chylomicronemia is currently categorized only as familial (FCS) or multifactorial (MCS).
- Chylomicronemia can be categorized by TG course as intermittent or persistent (PC).
- Most chylomicronemia cases can be managed with lifestyle and conventional drugs.
- Patients with PC and alarm features have very high risk of acute pancreatitis, similar to that in FCS.
- Patients with PC and very high risk may need novel therapies like apoC-III inhibitors.

Risks:

- Extreme TG elevation is the third most common cause of acute pancreatitis.
- Acute pancreatitis risk appears to be proportional to TG elevation.
- Chylomicronemia-induced acute pancreatitis is associated with worse clinical outcomes, including longer hospital stays, pancreatic necrosis, persistent organ failure, and higher mortality rates, compared with other causes of acute pancreatitis.
- The strongest risk factors for PC-induced acute pancreatitis—history of recurrent TG-induced acute pancreatitis, recurrent hospitalizations for severe abdominal pain without another identified cause, childhood pancreatitis, family history of TG-induced pancreatitis, and/or post-heparin LPL activity <20% of normal—are considered alarm features and identify PC patients at very high risk for acute pancreatitis.

Conclusion:

The current diagnostic approach for chylomicronemia focuses on genotypic categorization of chylomicronemia patients into FCS and MCS. Genetic testing can still be a valuable tool, provided it is feasible, affordable, and performed with informed consent. However, our understanding has expanded beyond genetic classifications to incorporate details about the severity of the clinical phenotype. We have described in detail the rationale for proposing the term persistent chylomicronemia (PC), which identifies adult patients with chylomicronemia with a high disease burden and increased risk of pancreatitis. While further research is needed to refine and better characterize the risk factors for chylomicronemia-induced pancreatitis, the current proposal is a template for transitioning classification of chylomicronemia from genetic criteria to more practical and clinically focused criteria by introducing alarm features that can identify PC cases with similar risk of pancreatitis to that in patients with FCS.

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