6/16/18 B'H

Dear Jeff,

It was a pleasure to have the opportunity to speak with you last week. Just to review some of the key points of our discussion including your history:

You relate a history of familial hypertriglyceridemia, spinal stenosis, pseudohyperparathyroidism with elevated PTH, normal calcium and negative thyroid nodules and repeated bouts of angioedema. You report success on a low carb diet and statins for your triglyceride elevation but these have been difficult to maintain based upon cognitive side effects.

You have had a recent MRI of the LS spine which demonstrates significant spinal stenosis with venous engorgement. Currently, you do not have motor weakness but do have neurogenic claudication and paresthesias. You have had surgical opinions but are concerned and reticent about surgical interventions.

Regarding the angioedema, you have had several episodes that were unprovoked by any identifiable food antigens.

Your family history is remarkable for both parents having heart disease and renal disease

You mentioned that you had 23andMe gene testing and that there were genes identified with abnormal triglyceride metabolism.

Otherwise you are in good health but want my opinion about whether these conditions are related and how to approach them in the safest, alternative way.

My impression:

1) familial hypertriglyceridemia
2) rule out MCAS
3) pseudo hyperparathyroidism

1) Recommendations:
   Regarding elevated triglycerides, high TG content up-regulates tumor necrosis factor-alpha, thereby inducing vascular cell adhesion molecules and are therefore potentially proinflammatory. TGs increase

atherosclerosis and inflammation and requires further management. Chylomicron accumulation in association with elevated triglycerides can cause pancreatic inflammation and is associated with increased risk of acute pancreatitis.
CV risk is higher in patients with elevated triglycerides and VLDL and LDL elevations with apoC3, than merely assessing cholesterol and LDL . Regarding management, several labs including Boston heart can provide this type of in depth analysis.

Potential therapies include Omacore(ethyl EPA) which is approved for hypertriglyceridemia. . Dietary changes should be considered including a low carbohydrate diet with the addition of the amino acid acetylcarnitine 500 mg 3X day. Niacin and fibrates are sometimes used but can be associated with flushing and elevated liver enzymes and are not advisable in my opinion. Intestinal microflora were recently recognized as another source of inflammatory mediators. Consider appropriate follow up regarding your microbiome analysis.

Off label pharmacological management for elevated triglycerides include Lomitapide, which interferes with apoB-containing lipoprotein assembly in the apoB100 and apoB48 pathways, thus reducing both chylomicron and VLDL secretion. It is currently available for the management of homozygous Familial hypercholesterolemia and should be discussed with your cardiologist if other measures are unable to lower your triglycerides.

Regarding MCAS, Signs and symptoms range from nausea to abdominal cramping and diarrhea, from mild pruritus, nasal congestion to anaphylaxis, tachycardia and hypotension, with increase in tryptase levels within 4 hours of symptoms. Most sensitive markers are 24-hour urinary histamine metabolites, and 24-hour urinary levels of PGD. It is unclear whether you have this syndrome but based upon your symptoms, it may be important to have these urinary studies done by your primary care physician. If they are elevated, Cromolyn sodium is a safe anti histamine that can be used on a preventive bases.

Spinal stenosis can be managed conservatively with weight loss, pool exercises to strengthen your abdominal muscles and manual techniques.

However, in the event you develop urinary hesitancy, weakness or atrophy, surgical approaches may be warranted at some date.

With best wishes,
Dr. Jay Lombard