Metabolic-Dysfunction Associated Steatotic Liver Disease in a Patient with Novel Familial Hypobetalipoproteinemia APOB Mutation

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Background

Familial hypobetalipoproteinemia (FHBL) is a rare autosomal codominant lipid disorder affecting approximately 1 in 10,000 people in the United States. It is characterized by abnormally low levels of low-density lipoprotein cholesterol (LDL-C and its main components apolipoprotein B (apoB). FHBL mutations are highly variable and clinical presentation depends on mutation type. It can be associated with hepatic steatosis as a result of impaired very low-density lipoprotein (VLDL) secretion leading to hepatic triglyceride accumulation. It is essential for different genetic presentations of FHBL to be characterized and followed.

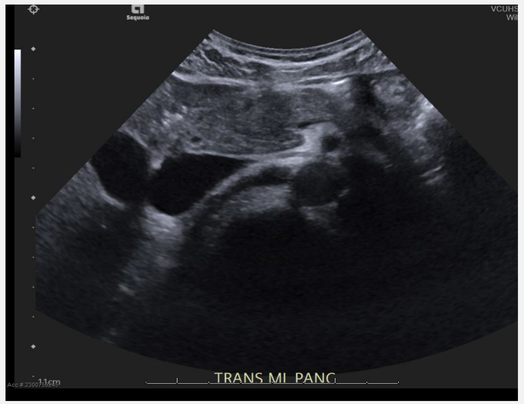
Case Description

Here we present a case of novel p.Y3680* mutation familial hypobetalipoproteinemia. A 28-year-old male presents to a Complex Lipid Management Clinic due to abnormal lipid panel results:

Cholesterol/HDL Ratio 1.5	AST 30 U/L
Triglycerides 62 mg/dL	ALT 32 U/L
Apolipoprotein B 14 mg/dL ↓	Alkaline Phosphatase 74 U/L
Lipoprotein (a) mg/dL <3 ↓	Cholesterol 105 mg/dL
Vitamin D, 25-Hydroxy 36.7 ng/mL	**LDL Calculated 21 mg/dL** ↓
Vitamin A 52.2 ug/dL	Cholesterol HDL 70 mg/dL
Vitamin E (Gamma Tocopherol) 5.2 mg/L	Non-HDL 35 mg/dL

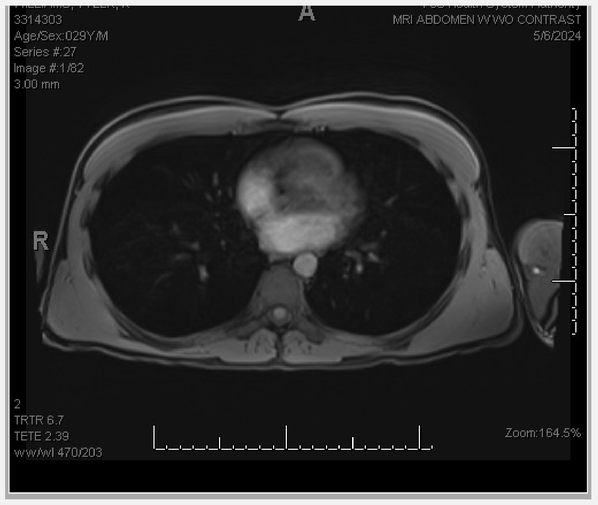
Imaging

1. Abdominal Ultrasound ordered:



- Normal liver shape without hepatomegaly
- Small area of hypoechoic liver was noted in the right hepatic lobe suggestive of focal fatty sparing

2. Abdominal MRI ordered:



- Normal liver size and morphology
- Hepatic steatosis (8.7% fat signal fraction with Q. Dixon technique) without liver lesions

VCTE and Genetic Testing

3. Vibration controlled transient elastography (VCTE) showed liver stiffness measurement (LSM) of 8.3 kPa and controlled attenuation parameter (CAP) of 236 dB/m

4. Genetic testing of 4 genes associated with familial hypercholesterolemia (APOB, LDLR, LDLRAP1, and PCSK9) ordered → **Results revealed that the patient is heterozygous for the APOB gene p. Y3680X pathogenic mutation**

Abdominal ultrasound, MRI and FIBROSCAN led to a final diagnosis of Metabolic Associated Steatotic Liver Disease (MASLD) with moderate fibrosis of the liver without significant fat accumulation

Clinical Course

- Patient was advised to return for another VCTE in a year due to moderately elevated LSM. The patient's lipid levels, liver enzymes and fat-soluble vitamins will continue to be monitored.

Conclusions

- The APOB p.Y3680X variant is typically associated with autosomal recessive hypobetalipoproteinemia. However, this patient, exhibited FHBL with moderate fibrosis despite only one copy of the mutation, highlighting the severity of the p.Y3680X mutation
- Early diagnosis and detection of FHBL are essential for preventing the progression of liver disease
- MASLD has the potential to progress to more severe forms of liver disease, such as cirrhosis, liver carcinoma, and steatohepatitis, in patients with FHBL
- It is important to understand the differences in APOB mutations to guide clinical management

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