Lecithin-Cholesterol Acyltransferase Deficiency from Statin-Induced Autoimmune Hepatitis

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Introduction

A 65yr female presented to the hospital with complaints of severe pruritis, dark urine, pale stools, and jaundice that had been ongoing for two months. She reported that 1 month prior she established care with a PCP and was started on subcutaneous insulin, amlodipine 10mg PO daily and atorvastatin 20mg daily.

Initial labs revealed a transaminitis with AST and ALT at 392 and 400 IU/L respectively along with alkaline phosphate at 2147 IU/L and a total bilirubin of 25.1 mg/dL. Initial imaging with a right upper quadrant ultrasound was normal. Patient continued to have a transaminitis and elevated alkaline phosphate that were not improving. Her initial MELD-Na calculated from Table 1 was 29. All home medications were stopped at admission except insulin. She had no prior history of liver disease and no family history of liver disease. She did not take any supplements and had never consumed alcohol.

An MRCP showed hepatomegaly, mild periportal edema, slightly heterogenous enhancement-conglomerate of findings suggested nonspecific hepatitis. An EUS liver biopsy was performed which revealed subacute liver injury- autoimmune pattern of injury (de novo versus secondary) +/- medication injury (Figures 1-2) Additional laboratory testing revealed positive autoimmune markers; pointing to a drug induced autoimmune hepatitis from atorvastatin as the likely diagnosis.

Test	Value
ANA	+ Specked 1:320
Anti-Smooth Muscle AB *(+ = >31)*	48
AST *(Ref AST 0-37 IU/L)*	486 IU/L
ALT *(REF 0-35 IU/L)*	495 IU/L
INR *(0.8-1.1)*	1.4
ALK-P *(Ref 44-121 IU/L)*	2157 IU/L
T.Bili *(Ref 0-1.2)*	25.1 mg/dL
GGT *(Ref 5-61 U/L)*	1398 U/L
Serum Cr *(Ref 0.38-1.02 MG/Dl)*	0.86 MG/Dl
Serum Na *(Ref 136-145 MMOL/L)*	126 MMOL/L

Table 1

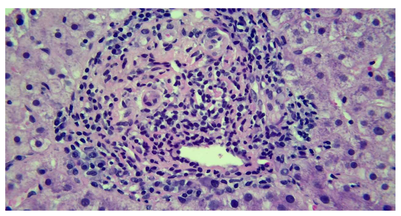
Case

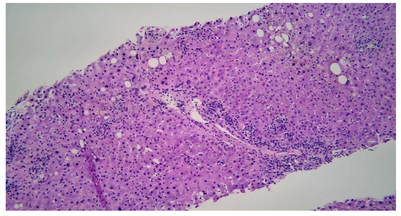
Once biopsy results were obtained the patient was started on steroids for presumed drug induced autoimmune hepatitis. (50mg taper with 5mg taper weekly) with plans to FU in hepatology clinic. Repeat laboratory testing was ordered which revealed new onset lipid derangement (Table 2). Prior lipid testing was grossly normal 2 months prior to admission

Given the patient had not changed her diet in any radical way or started any new medication a consideration to a lipid derangement caused by deficiency in Lecithin-Cholesterol Acyltransferase was considered. The proposed mechanism was drug induced AIH.

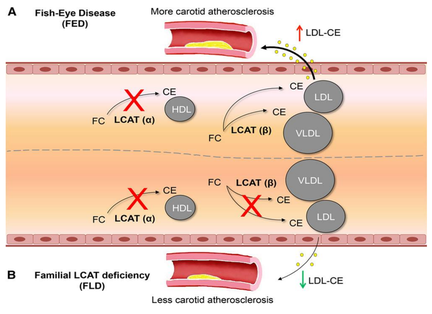
	Baseline Lipid Test	Testing after DILI AIH
Total Cholesterol *Ref Range 170-199 MG/DL*	182 MG/DL	991 MG/DL
HDL *Ref Range Low < 40 :: High => 60MG/DL*	52 MG/DL	7 MG/DL
LDL Calculated *Optimal < 100 :: Very High > 189 MG/DL*	107 MG/DL	907 MG/DL
Non-HDL Cholesterol *Desirable < 139 :: Very High >= 190 MG/DL*	131 MG/DL	984 MG/DL
Triglycerides *Ref Range <= 150 MG/DL*	119 MG/DL	384 MG/DL

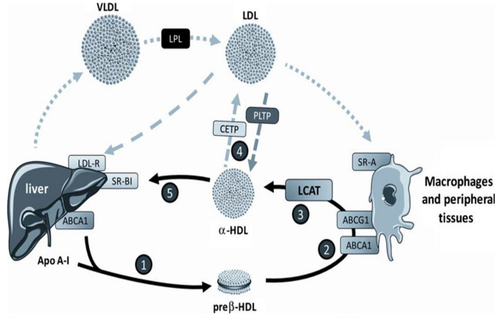
Table 2





Figures 1-2. Left panel shows prominent plasma cells in a portal with chronic inflammation and interface activity (40x, H&E stain). Right panel shows liver with lobular and pericentral inflammation (10x, H&E stain)





Figures 3-4. Left panel shows FED vs. FLD deficiency. Right panel shows LCAT normal physiological role. FLD is absence of LCAT activity towards HDL and LDL. FED is characterized by absences of LCAT activity towards HDL only.

Discussion

LCAT is a 67-kDa sized secretory protein made primarily in the liver. It acts to esterify cholesterol in the plasma (Figures 3 and 4). This acts to form cholesterol esters into lipoproteins. It circulates bound to HDL and LDL. LCAT deficiency is an autosomal recessive disorder. A deficiency of LCAT results in accumulation of unesterified cholesterol in certain body tissues such as cornea, liver (hepatomegaly) and kidney. Most commonly patients die of renal failure due to accumulation of lipoprotein X, an abnormal multivesicular-like protein.

There are two types of hereditary LCAT; the so called Fish-Eye disease (Figure 5) and Familial LCAT deficiency (Figure 3-4). FLD Common lab findings are HDL < 10mg/L, elevated VLDL, elevated triglycerides and high plasma unesterified cholesterol and low plasma cholesterol ester. Patients with FED have very low HDL cholesterol but retain some LCAT activity on LDL and VLDL, thus mainly presenting with corneal opacities (Figure 5). Table 2 illustrates the change in the patient's lipid panel that led to the hypothesis of acquired LCAT deficiency.

Acquired LCAT deficiency is an extremely rare but documented occurrence in the literature. Case reports include a patient with sarcoidosis that developed an LCAT deficiency. Another patient with new onset nephrotic syndrome was found to have an immune mediated cause of LCAT deficiency with autoantibodies detected to LCAT. As of this writing less than 10 cases have been reported in the literature.

Further laboratory testing was ordered; specifically plasma cholesterol ester and plasma unesterified cholesterol. LCAT enzymatic testing was not available at our lab. Unfortunately she contracted pneumonia and passed before being able to complete testing. Despite passing we believe this LCAT deficiency was responsible for the lipid derangements seen after she developed DILI induced AIH.

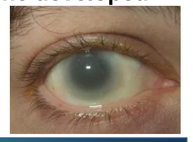


Figure 5 - Corneal opacities in FLD. Cholesterol deposited corneal stroma causes cloudiness or "fish-eye" appearance

Sources

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