SUSPECTED METABOLIC SYNDROME WITH NORMAL FASTING BLOOD GLUCOSE AND BLOOD PRESSURE, AND DYSLIPIDEMIA WITH PERSISTENTLY ELEVATED ALT[1]

CASE REPORT: Female adult patient with Lysosomal Acid Lipase Deficiency (LAL-D)[1]

Based upon a published case report:
Ratziu V, et al. *EMJ Hepatol*. 2015;3:60-7.

YEARS OF AGE

33

INITIAL PRESENTATION TO GENERAL PRACTITIONER:

- Elevated liver enzymes and history of hypercholesterolemia
- Fatigue
- Gastroenteritis
- History of simvastatin use

PATIENT REFERRED TO OUTPATIENT CLINIC—SUSPECTED EBV INFECTION

PHYSICAL EXAMINATION[a]:

- **Normal BP (110/60 mmHg)**
- BMI 27.7 kg/m^2 (waist circumference 94 cm)

LABORATORY RESULTS—LIPID PANEL[a]:

- **HDL-c <1.30 mmol/L**
- TGs 1.77 mmol/L

LABORATORY RESULTS—LIVER FUNCTION TESTS/BLOOD SUGAR[a]:

- **ALT 58 U/L**
- AST 36 U/L
- **Fasting blood sugar 4.8 mmol/L**
- Bilirubin 20.5 µmol/L

DYSLIPIDEMIA WITH PERSISTENTLY ELEVATED ALT

IMAGING FINDINGS:

- Severe steatosis on hepatic ultrasound
- No significant liver fibrosis on FibroScan

INITIAL DIAGNOSTIC CONSIDERATIONS:

METABOLIC SYNDROME—PRESENCE OF LOW HDL-c, CENTRAL OBESITY, AND HIGH TGs

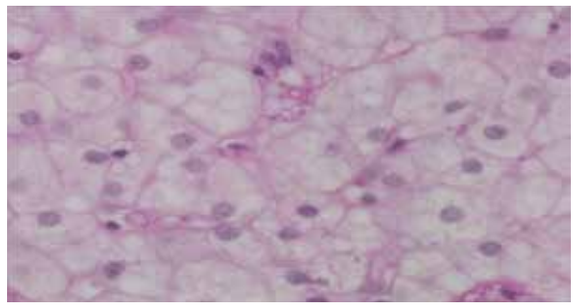
- **NAFLD/NASH**—proposed as likely diagnosis of liver disease
- Wilson disease and other fatty liver diseases—ruled out

INITIAL MANAGEMENT:

- Discontinue statin therapy
- Introduce dietary modifications

3 MONTHS LATER

LIVER BIOPSY RESULTS:



- **Microvesicular steatosis**
- Chronic hepatitis of unknown origin
- Septal fibrosis
- Rare hepatocyte ballooning
- Slight lobular inflammation

DIAGNOSTIC CONSIDERATIONS:

- Autoimmune hepatitis—ruled out
- Borderline **NASH**—based on liver biopsy findings
- Alternative causes of **microvesicular steatosis**—including **LAL-D**

LAL-D DIAGNOSIS

- Low LAL activity in enzyme-based blood test

[a]Normal values: HDL-c >0.9 mmol/L; TGs, 0.38-1.38 mmol/L; ALT ≤35 U/L; AST ≤35 U/L; fasting blood sugar, 3.9-5.8 mmol/L; total bilirubin, 5.1-20.5 µmol/L.[1,2]

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BP, blood pressure; EBV, Epstein-Barr virus; HDL-c, high-density lipoprotein cholesterol; LAL, lysosomal acid lipase; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; TG, triglyceride.

KEY TAKEAWAYS

- Patients with LAL-D are at risk for complications such as **premature atherosclerosis** and **progressive liver failure**[3]
- Suspect LAL-D in patients who have atypical **metabolic syndrome** with **normal fasting glucose and/or blood pressure**; biopsy findings of **microvesicular steatosis** should further raise suspicion of LAL-D[4-6]
- **Dyslipidemia** and **persistently elevated ALT** should elicit immediate testing to **diagnose LAL-D**[3,4,7]

LAL-D and your practice

- How would you have determined the underlying cause of liver disease in this patient?
- How often do you see patients who have atypical metabolic syndrome with a BMI below the 95th percentile or normal fasting glucose and/or blood pressure? When do you start to suspect LAL-D in these patients?
- Are you currently managing any patients with dyslipidemia and persistently elevated ALT?

LAL-D REQUIRES EARLY DIAGNOSIS

- Suspected metabolic syndrome with normal fasting glucose and/or blood pressure should raise suspicion of LAL-D[4-6]
- Biopsy findings of microvesicular steatosis should elicit immediate testing for LAL-D[4-6]
- Dyslipidemia with persistently elevated ALT should prompt immediate testing for LAL-D[3,4,7]
    - » An enzymatic blood test can confirm LAL-D; liver biopsy is not required[4,8]

References: 1. Ratziu V, et al. Would you figure it out? Differential diagnoses: beyond the usual. *EMJ Hepatol*. 2015;3:60-7. **2.** Wians FH Jr. Blood tests: normal values. Merck Manual Professional Version website. http://www.merckmanuals.com/professional/appendixes/normal-laboratory-values/blood-tests-normal-values#v8508814. Accessed October 11, 2016. **3.** Bernstein DL, et al. Cholesteryl ester storage disease: review of the findings in 135 reported patients with an underdiagnosed disease. *J Hepatol*. 2013;58:1230-43. doi:10.1016/j.jhep.2013.02.014. **4.** Reiner Ž, et al. Lysosomal acid lipase deficiency—an under-recognized cause of dyslipidaemia and liver dysfunction. *Atherosclerosis*. 2014;235:21-30. **5.** Grundy SM, et al. Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. *Circulation*. 2004;109:433-8. doi:10.1161/01.CIR.0000111245.75752.C6. **6.** Data on file, Alexion Pharmaceuticals. **7.** Burton BK, et al. *N Engl J Med*. 2015;373:1010-20. doi:10.1056/NEJMoa1501365. **8.** Hamilton J, et al. A new method for the measurement of lysosomal acid lipase in dried blood spots using the inhibitor Lalistat 2. *Clin Chim Acta*. 2012;413:1207-10. doi:10.1016/j.cca.2012.03.019.

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