SUSPECTED NAFLD IN A PATIENT WITH PERSISTENTLY ELEVATED ALT DESPITE WEIGHT LOSS, DYSLIPIDEMIA, AND MIXED STEATOSIS[1]

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

Based upon a published case report:
Himes RW, et al. *Pediatrics*. 2016. doi:10.1542/peds.2016-0214.

YEARS OF AGE

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INITIAL PRESENTATION DURING ROUTINE SCHOOL SCREENING:
- Nuchal acanthosis

PHYSICAL EXAMINATION:
- **BMI 21.1 (94th centile)**

LABORATORY RESULTS—LIVER FUNCTION TESTS[a]:
- **ALT 401 U/L**
- AST 207 U/L

LABORATORY RESULTS—LIPID PANEL[a]:
- **LDL-c 4.3 mmol/L**
- Total cholesterol 6.1 mmol/L

PATIENT REFERRED TO PEDIATRIC GASTROENTEROLOGY CLINIC; GUIDANCE ON WEIGHT REDUCTION

IMAGING RESULTS:
- Normal hepatic echogenicity on ultrasound
- No organomegaly

INITIAL DIAGNOSTIC CONSIDERATION:
- Possible causes of liver disease (including infectious hepatitis A/B/C, alpha-1 antitrypsin PI-type, Wilson disease)—ruled out through additional testing

6 MONTHS LATER

PHYSICAL EXAMINATION:
- **BMI 21.1 (93rd centile)**

LABORATORY RESULTS—LIVER FUNCTION TESTS[a]:
- **ALT 171 U/L**
- AST 131 U/L

LIVER BIOPSY RESULTS:

MIXED STEATOSIS (MICRO- AND MACROVESICULAR)
- **Stage 1 lobular and portal fibrosis**
- Minimal lobular inflammation

DIAGNOSTIC CONSIDERATION:

BIOPSY FINDINGS INTERPRETED AS CONSISTENT WITH NAFLD

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PHYSICAL EXAMINATION:
- **BMI in the 85th centile**

LABORATORY RESULTS—LIVER FUNCTION TESTS[a]:
- **ALT 83 U/L (despite weight loss)**
- AST 61 U/L

LABORATORY RESULTS—LIPID PANEL[a]:
- **LDL-c 3.5 mmol/L**
- Total cholesterol 5.2 mmol/L

REPEAT LIVER BIOPSY FINDINGS:

WIDESPREAD MICROVESICULAR STEATOSIS
- Minimal lobular inflammation, stage 1 lobular fibrosis, and portal fibrosis were unchanged
- Numerous lipid-filled cytoplasmic vesicles in hepatocytes and Kupffer cells

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DIAGNOSTIC CONSIDERATIONS:
- Metabolic diseases, including **LAL-D**, based on predominantly **microvesicular steatosis**

LAL-D DIAGNOSIS
- Low LAL activity in enzyme-based blood test
- Sequencing of *LIPA* revealed homozygous mutation

[a]Normal values: ALT, 7-35 U/L; AST, 15-40 U/L; LDL-c <2.8 mmol/L; total cholesterol <4.4 mmol/L.[1]

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; LAL, lysosomal acid lipase; LDL-c, low-density lipoprotein cholesterol; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis.

KEY TAKEAWAYS

- Patients with LAL-D are at risk for complications such as **progressive liver failure** and **premature atherosclerosis** from a young age[2]
- **Test for LAL-D** in patients with suspected NAFLD who have **persistently elevated ALT** and **dyslipidemia**[2-4]
- If a biopsy is conducted, **microvesicular or mixed steatosis** should elicit immediate testing to **diagnose LAL-D**[3]

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 with suspected NAFLD or NASH who have persistently elevated ALT and dyslipidemia? When do you start to suspect LAL-D in these patients?
- Are you currently managing any patients with NAFLD or NASH who have these atypical symptoms?
- Are you managing any patients with microvesicular or mixed steatosis?

LAL-D REQUIRES EARLY DIAGNOSIS

- Microvesicular or mixed steatosis should prompt immediate testing for LAL-D[3]
- Include LAL-D in the differential diagnosis of patients with suspected NAFLD or NASH who have persistently elevated ALT and dyslipidemia[2-4]
    - » An enzymatic blood test can confirm LAL-D; liver biopsy is not required[3,5]

References: 1. Himes RW, et al. Lysosomal acid lipase deficiency unmasked in two children with nonalcoholic fatty liver disease. *Pediatrics*. 2016;138:e20160214. doi:10.1542/peds.2016-0214. **2.** 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. **3.** Reiner Ž, et al. Lysosomal acid lipase deficiency—an under-recognized cause of dyslipidaemia and liver dysfunction. *Atherosclerosis*. 2014;235:21-30. doi:10.1016/j.atherosclerosis.2014.04.003. **4.** Burton BK, et al. *N Engl J Med*. 2015;373:1010-20. doi:10.1056/NEJMoa1501365. **5.** 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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