UNEXPLAINED HEPATOMEGALY, PROGRESSIVE LIVER DISEASE, AND DYSLIPIDEMIA PRECEDE MULTIORGAN DAMAGE[1]

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

Based upon a published case report:
Santillán-Hernández Y, et al. *World J Gastroenterol*. 2015;21:1001-8. doi:10.3748/wjg.v21.i3.1001.

YEARS OF AGE

2 MONTHS

INITIAL PRESENTATION:
- **Reduced weight and height**
- Alternating episodes of diarrhea and constipation

6 MONTHS

ONGOING PRESENTATION:
- Diarrhea

IMAGING RESULTS:

HEPATOMEGALY ON RADIOGRAPHY

INITIAL DIAGNOSTIC CONSIDERATION:
- Hematologic malignancy—prompted by initial lab workup results

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IMAGING RESULTS:
- **Hepatosplenomegaly** confirmed on ultrasound

LABORATORY RESULTS—LIVER FUNCTION TESTS[a]:
- **ALT 344 U/L**
- Total bilirubin 13.7 µmol/L
- AST 229 U/L

LABORATORY RESULTS—LIPID PANEL[a]:
- **LDL-c 7.2 mmol/L**
- Total cholesterol 8.9 mmol/L
- **HDL-c 0.6 mmol/L**
- TGs 3.6 mmol/L

LABORATORY RESULTS—COAGULATION VALUES[a]:
- Platelet count 330,000
- PTT 30.2 min
- Prothrombin time 13.9 min

DIAGNOSTIC CONSIDERATIONS:
- Chronic EBV infection—based on results of laboratory assessment
- Hepatitis A, B, and C—ruled out based on negative serology

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IMAGING RESULTS:
- **Hepatosplenomegaly** without adrenal calcifications on CT

PATIENT REFERRED TO PEDIATRIC GASTROENTEROLOGY DEPARTMENT—SUSPECTED METABOLIC DISEASE

FURTHER EVALUATION:
- GI bleeding

IMAGING RESULTS:
- Grade 2 esophageal varices on endoscopy

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LIVER BIOPSY RESULTS:
- Multinodular microvesicular steatosis in 10% of hepatocytes
- Foamy cells in portal space and in fibrous tissue
- Gross bands of portoportal fibrosis

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REPEAT LIVER BIOPSY RESULTS:
- Reduced steatosis
- Micronodular cirrhosis

DIAGNOSTIC CONSIDERATION:
- Niemann-Pick disease—based on liver and intestinal biopsy results; ruled out

LAL-D DIAGNOSIS
- Low LAL activity in enzyme-based blood test

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IMAGING RESULTS:
- **Hepatosplenomegaly** and portal hypertension on Doppler ultrasound
- Continued grade 2 esophageal varices on endoscopy

LABORATORY RESULTS—LIVER FUNCTION TESTS[a]:
- **ALT 193 U/L**
- Total bilirubin 7.2 µmol/L
- AST 192 U/L

LABORATORY RESULTS—LIPID PANEL[a]:
- **LDL-c 4.1 mmol/L**
- Total cholesterol 5.5 mmol/L
- **HDL-c 0.8 mmol/L**
- TGs 1.3 mmol/L

LABORATORY RESULTS—COAGULATION VALUES[a]:
- Platelet count 96,000
- PTT 35.1 min
- Prothrombin time 14.8 min

CURRENT MANAGEMENT:
- Propranolol for GI bleeding prophylaxis
- Vitamin K for prolonged bleeding times

[a]Normal values: ALT, 7-45 U/L; AST, 8-50 U/L; total bilirubin, 1.7-15.4 µmol/L; LDL-c <2.6 mmol/L (optimal); HDL-c ≥1.6 mmol/L; total cholesterol <4.4 mmol/L; TGs <1.0 mmol/L; platelet count, 150,000-500,000; prothrombin time, 11-15 min; PTT, 25-33 min.[1]

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CT, computed tomography; EBV, Epstein-Barr virus; GI, gastrointestinal; HDL-c, high-density lipoprotein cholesterol; LAL, lysosomal acid lipase; LDL-c, low-density lipoprotein cholesterol; PTT, partial thromboplastin time; TG, triglyceride.

KEY TAKEAWAYS

- Patients with LAL-D can develop severe morbidities in childhood and are at risk of **progressive liver failure, premature atherosclerosis**, and **multiorgan damage**[2]
- **Test for LAL-D** in patients with **unexplained hepatomegaly**[3]
- **Suspect LAL-D** in patients with **persistently elevated ALT** and **dyslipidemia**[2-4]

LAL-D and your practice

- Do you have any patients in your practice whose liver disease has preceded other multiorgan manifestations?
- Are you currently managing any patients with unexplained hepatomegaly?
- After ruling out the most common causes of hepatomegaly, how do you determine the underlying cause of liver disease in your patients? When do you start to suspect LAL-D?

LAL-D REQUIRES EARLY DIAGNOSIS

- Unexplained hepatomegaly should prompt immediate testing for LAL-D[3]
- Include LAL-D in the differential diagnosis of patients with persistently elevated ALT and dyslipidemia[2-4]
  - » An enzymatic blood test can confirm LAL-D; liver biopsy is not required[3,5]

References: 1. Santillán-Hernández Y, et al. Novel *LIPA* mutations in Mexican siblings with lysosomal acid lipase deficiency. *World J Gastroenterol*. 2015;21:1001-8. doi:10.3748/wjg.v21.i3.1001. **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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