FOLLOWING A MISDIAGNOSIS, PERSISTENT LIVER DISEASE LEADS TO CRYPTOGENIC CIRRHOSIS[1]

CASE REPORT: Female pediatric 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

INITIAL PRESENTATION TO GENERAL PRACTITIONER:
- Fatigue
- Anemia

LABORATORY RESULTS—LIVER FUNCTION TESTS[a]:
- **ALT 166 U/L**
- AST 201 U/L

REFERRAL TO TERTIARY CENTER:

CLINICAL FINDING:
- **Hepatosplenomegaly**

LIVER BIOPSY FINDINGS:
- **Fatty change (steatosis)**
- **Moderate fibrosis**
- Findings suggestive of chronic hepatitis

INITIAL DIAGNOSTIC CONSIDERATIONS :
- Wilson disease—prompted by biopsy finding of steatosis and ruled out
- Celiac disease—prompted by duodenal biopsy findings

INITIAL MANAGEMENT:
- Gluten-free diet—did not result in normalization of liver transaminases

DIAGNOSTIC CONSIDERATION:
- Autoimmune hepatitis—prompted by incomplete response to gluten-free diet along with findings of raised IgG and positive ANA

ADDITIONAL MANAGEMENT:
- Corticosteroids and azathioprine for suspected autoimmune hepatitis

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ONGOING PRESENTATION:
- Persistent lack of response to therapy and finding of neutropenia

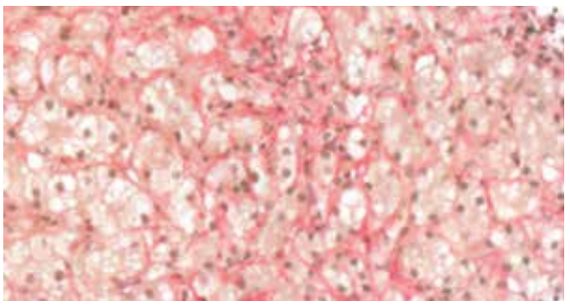
FURTHER EVALUATION:
- **Elevated ALT**, AST, and other liver function measures
- Normal BMI

LABORATORY RESULTS—LIPID PROFILE[a]:
- **HDL-c 0.9 mmol/L**
- TGs 1.84 mmol/L
- Total cholesterol 9.9 mmol/L

IMAGING RESULTS:
- Splenomegaly

LIVER BIOPSY RESULTS:

CIRRHOSIS



Liver biopsy showing ongoing inflammation and periportal fibrosis (hematoxylin/van Gieson stain)

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

[a]Normal values: ALT ≤40 U/L; AST ≤40 U/L; HDL-c >0.9 mmol/L; total cholesterol, 2.8-4.8 mmol/L; TGs, 0.38-1.38 mmol/L.[1,3]

Abbreviations: ALT, alanine aminotransferase; ANA, antinuclear antibody; AST, aspartate aminotransferase; BMI, body mass index; HDL-c, high-density lipoprotein cholesterol; IgG, immunoglobulin G; LAL, lysosomal acid lipase; 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**[4]
- **Test for LAL-D** in patients with **cryptogenic cirrhosis**[5]
- **Persistently elevated ALT** and **low HDL-c** levels should elicit immediate testing to **diagnose LAL-D**[4-6]

LAL-D and your practice

- How would you have determined the underlying cause of liver disease in this patient?
- Are you currently managing any patients with cryptogenic cirrhosis?
- After ruling out the most common causes of fibrosis and cirrhosis in your patients, when do you start to suspect LAL-D?

LAL-D REQUIRES EARLY DIAGNOSIS

- Cryptogenic cirrhosis should prompt immediate testing for LAL-D[5]
- Include LAL-D in the differential diagnosis of patients who have persistently elevated ALT and dyslipidemia[4-6]
    - » An enzymatic blood test can confirm LAL-D; liver biopsy is not required[5,7]

References: 1. Ratziu V, et al. Would you figure it out? Differential diagnoses: beyond the usual. *EMJ Hepatol*. 2013;3:60-70. **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.** Orfanidis NT. Laboratory tests of the liver and gallbladder. https://www.merckmanuals.com/professional/hepatic-and-biliary-disorders/testing-for-hepatic-and-biliary-disorders/laboratory-tests-of-the-liver-and-gallbladder. Accessed October 12, 2016. **4.** 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. **5.** 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. **6.** Burton BK, et al. *N Engl J Med*. 2015;373:1010-20. doi:10.1056/NEJMoa1501365. **7.** 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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