# ELEVATED ALT AND LDL-c IN SIBLINGS WITH A SUSPECTED GENETIC CAUSE OF HYPERCHOLESTEROLEMIA[1]

## CASE REPORT: 3 adult siblings with Lysosomal Acid Lipase Deficiency (LAL-D)[1]

Based upon a published case report:
Stitziel NO, et al. *Arterioscler Thromb Vasc Biol*. 2013;33:2909-14. doi:10.1161/ATVBAHA.

**YEARS OF AGE**

**3 SIBLINGS**
**23-27**

### INITIAL PRESENTATION TO LIPID CLINIC:

**SUSPECTED GENETIC CAUSE OF HYPERCHOLESTEROLEMIA, SUCH AS FCH OR HeFH**

- No identified mutations in various genes known to affect LDL-c on genetic screening
- No family history
- No hepatosplenomegaly noted on physical exam

### INITIAL DIAGNOSTIC CONSIDERATION:

- Autosomal recessive hypercholesterolemia

### LABORATORY RESULTS—LIPID PANEL[a]:

| | Sibling 1 Female, 23 | Sibling 2 Female, 23 | Sibling 3 Male, 27 |
|---|---|---|---|
| **LDL-c (mmol/L)** | **10.6** | **10.0** | **7.8** |
| HDL-c (mmol/L) | 1.8 | 1.5 | 1.9 |
| TGs (mmol/L) | 1.7 | 0.9 | 2.0 |
| Total cholesterol (mmol/L) | 13.1 | 12.5 | 11.9 |

### LABORATORY RESULTS—LIVER FUNCTION TESTS[a]:

| | Sibling 1 Female, 23 | Sibling 2 Female, 23 | Sibling 3 Male, 27 |
|---|---|---|---|
| **ALT** | **56 U/L** | **69 U/L** | N/A |

### LAL-D DIAGNOSIS

- After sequencing of genes known to affect LDL-c, *LIPA* mutations were identified through exome sequencing

### IMAGING RESULTS:

- No hepatomegaly on MRI
- Elevated hepatic cholesterol deposition on MRS
- Recommendation to monitor patients for progression of liver disease

[a]Normal values: LDL-c ≈3.36 mmol/L; HDL-c ≈1.04 mmol/L; TGs <2.82 mmol/L; total cholesterol, 3.9-5.2 mmol/L; ALT, ULN 34 U/L.[1,2]

Abbreviations: ALT, alanine aminotransferase; FCH, familial combined hyperlipidemia; HDL-c, high-density lipoprotein cholesterol; HeFH, heterozygous familial hypercholesterolemia; LDL-c, low-density lipoprotein cholesterol; MRI, magnetic resonance imaging; MRS, magnetic resonance spectroscopy; TG, triglyceride.

## KEY TAKEAWAYS

- Patients with LAL-D are at risk for complications such as **premature atherosclerosis** and **progressive liver failure**[3]
- Patients with **suspected FCH** with **persistently elevated ALT** or **no family history** should elicit immediate testing to **diagnose LAL-D**[4,5]
- Patients with **suspected HeFH** with **no confirmed genetic mutation**, or **persistently elevated ALT**, or **no family history**, should prompt immediate testing for LAL-D[4,5]

## LAL-D and your practice

- How often do you see patients with suspected FCH who have persistently elevated ALT or no family history of the disease?
- Are you currently managing any patients with suspected HeFH who have no confirmed genetic mutation, or persistently elevated ALT, or no family history? When do you start to suspect LAL-D in these patients?
- When considering genetic causes of dyslipidemia, do you consider LAL-D?

## LAL-D REQUIRES EARLY DIAGNOSIS

- Suspected FCH with persistently elevated ALT or no family history should prompt immediate testing for LAL-D[4,5]
- Suspected HeFH with no confirmed genetic mutation, or persistently elevated ALT, or no family history should elicit immediate testing for LAL-D[4,5]
- An enzymatic blood test can confirm LAL-D; genetic screening is not required[4,6]

**References: 1.** Stitziel NO, et al. Exome sequencing and directed clinical phenotyping diagnose cholesterol ester storage disease presenting as autosomal recessive hypercholesterolemia. *Arterioscler Thromb Vasc Biol*. 2013;33:2909-14. doi:10.1161/ATVBAHA.113.302426. **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.** Burton BK, et al. *N Engl J Med*. 2015;373:1010-20. doi:10.1056/NEJMoa1501365. **6.** 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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