ELEVATED ALT AND LDL-c IN SIBLINGS WITH A SUSPECTED GENETIC CAUSE OF HYPERCHOLESTEROLEMIA

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

Based upon a published case report:

YEARS OF AGE

3 SIBLINGS
23-27

KEY TAKEAWAYS

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

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

INITIAL DIAGNOSTIC CONSIDERATION:
- Autosomal recessive hypercholesterolemia

LABORATORY RESULTS—LIPID PANEL:

<table>
<thead>
<tr>
<th></th>
<th>Sibling 1 Female, 23</th>
<th>Sibling 2 Female, 23</th>
<th>Sibling 3 Male, 27</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-c (mmol/L)</td>
<td>10.6</td>
<td>10.0</td>
<td>7.8</td>
</tr>
<tr>
<td>HDL-c (mmol/L)</td>
<td>1.8</td>
<td>1.5</td>
<td>1.9</td>
</tr>
<tr>
<td>TGs (mmol/L)</td>
<td>1.7</td>
<td>0.9</td>
<td>2.0</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>13.1</td>
<td>12.5</td>
<td>11.9</td>
</tr>
</tbody>
</table>

LABORATORY RESULTS—LIVER FUNCTION TESTS:

<table>
<thead>
<tr>
<th></th>
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<th>Sibling 2 Female, 23</th>
<th>Sibling 3 Male, 27</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT (U/L)</td>
<td>56</td>
<td>69</td>
<td>N/A</td>
</tr>
</tbody>
</table>

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

Normal values: LDL-c = 3.36 mmol/L; HDL-c = 1.04 mmol/L; TGs = 1.83 mmol/L; total cholesterol = 3.86-5.2 mmol/L; ALT, ULN 34 U/L.

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.
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\(^4,6\)