Identifying Mixed Phenotype: Evaluating the Presence of Polyneuropathy in Patients with Hereditary Transthyretin-Mediated Amyloidosis with Cardiomyopathy

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Introduction

- Hereditary transthyretin-mediated amyloidosis (hATTR) is a genetic disease with a variable phenotype that includes polyneuropathy as one of the earliest manifestations seen.
- Patients with hATTR amyloidosis are at increased risk of further cardiac complications.
- The finding that polyneuropathy precedes or coincides with cardiomyopathy is generally consistent with results from a previous study comparing 120 patients with hATTR amyloidosis and 91 control subjects with no amyloidosis.

Methods

- Baseline demographics and medical history (MedDRA) collected during screening and the 3-month period before the study.
- Medical history data were linked to the patients' electronic medical record (EMR) and clinical data.
- Clinical data were extracted from the EMR and included information on symptoms and signs related to nervous system disorders, neuromuscular disorders, and mononeuropathies.

Results

Table 1. Baseline Demographics and Disease Characteristics in Patients with hATTR Amyloidosis with Cardiomyopathy

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n=206</th>
<th>n=118</th>
<th>n=35</th>
<th>n=9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) Median (IQR)</td>
<td>69.7 (59.0–77.8)</td>
<td>69.0 (58.4–77.5)</td>
<td>71.0 (61.0–80.0)</td>
<td>70.0 (61.0–80.0)</td>
</tr>
<tr>
<td>Sex (%)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Female</td>
<td>104.6 (217.5)</td>
<td>102.0 (216.0–234.0)</td>
<td>106.0 (195.0–223.0)</td>
<td>106.0 (195.0–223.0)</td>
</tr>
<tr>
<td>Male</td>
<td>95.4 (182.5)</td>
<td>98.0 (186.0–230.0)</td>
<td>94.0 (176.0–207.0)</td>
<td>94.0 (176.0–207.0)</td>
</tr>
</tbody>
</table>

- Objective: To describe presence of polyneuropathy signs and symptoms in patients with hATTR amyloidosis and confirmed cardiomyopathy.
- In this study, 54.4% of all patients and 49.2% of those with the Val122Ile mutation reported terms that coded to nervous system disorders, neuromuscular disorders, and mononeuropathies.
- Conditions captured in this analysis may not be inclusive of all manifestations related to hATTR amyloidosis.

Conclusions

- hATTR amyloidosis is a slowly progressive, multisystem disease with a wide range of phenotypic presentations.
- Recently, there has been increased evidence of a mixed phenotype with both cardiac and neuropathic features in patients across different ethnicities.
- The finding that polyneuropathy precedes or coincides with cardiomyopathy is generally consistent with results from a previous study.
- Further research is needed to explore these findings in larger cohorts and to correlate any changes with the natural history of hATTR amyloidosis.

Limitations

- The study population was limited to medical records/patient reports and not based on a targeted questionnaire or comprehensive interview.
- The study was limited to patients with hATTR amyloidosis and cardiomyopathy (n=206).
- Regulatory approval to use the MedDRA terminology and HLTs based on MedDRA Version 17.1 was obtained.
- The study was not designed to evaluate the natural history of hATTR amyloidosis.