Myelodysplasia and liver disease extend the spectrum of RTEL1 related telomopathies

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<table>
<thead>
<tr>
<th>Family</th>
<th>Individuals</th>
<th>Age at study (years)</th>
<th>Gender</th>
<th>Clinical status</th>
<th>Nucleotide</th>
<th>Amino acid</th>
<th>Variant status</th>
<th>Clinical features/diagnosis</th>
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<td>p.R767Q</td>
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<td>p.R767Q</td>
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<td>c.2992C&gt;T</td>
<td>p.R998*</td>
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<td>p.I572M</td>
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</table>

AA: aplastic anemia; DC: dyskeratosis congenita; HH: Hoyeraal Hreidarsson syndrome; NA: not available; F: female; M: male.
Table S2. Characteristics of index cases with heterozygous VUS and bystander RTEL1 variants

<table>
<thead>
<tr>
<th>Index</th>
<th>Age at study (years)</th>
<th>Gender</th>
<th>Diagnosis</th>
<th>Additional relevant clinical features</th>
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<td>10</td>
<td>23</td>
<td>F</td>
<td>AML</td>
<td>Short stature</td>
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<td>11</td>
<td>20</td>
<td>F</td>
<td>MDS</td>
<td>Skin pigmentation abnormality and squamous cell carcinoma of oesophagus. This patient harbours variants in TERT (heterozygous c.3197G&gt;T; p.P1066L and c.322C&gt;T; p.R108C)</td>
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<tr>
<td>12</td>
<td>10</td>
<td>M</td>
<td>DC</td>
<td>Developmental delay, short stature, dysmorphic facial features, microcephaly, BMF and pulmonary disease</td>
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<tr>
<td>13</td>
<td>24</td>
<td>M</td>
<td>DC</td>
<td>Skin pigmentation abnormality, leukoplakia, thin hair and BMF</td>
</tr>
<tr>
<td>14</td>
<td>24</td>
<td>F</td>
<td>AA</td>
<td>Short stature and oral ulceration with dysphagia. This patient harbours variant in DNAJC21 (homozygous c.793G&gt;T; p.Q265*)</td>
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<tr>
<td>15</td>
<td>6</td>
<td>F</td>
<td>AA</td>
<td>Skin pigmentation abnormality, leukoplakia, thin hair, extensive dental caries and BMF</td>
</tr>
<tr>
<td>16</td>
<td>10</td>
<td>M</td>
<td>AA</td>
<td>Skin pigmentation abnormality, nail dystrophy, leukoplakia, small teeth, sparse scalp hair, epiphora, microcephaly and BMF</td>
</tr>
<tr>
<td>17</td>
<td>8</td>
<td>F</td>
<td>DC</td>
<td>Nail dystrophy and leukoplakia</td>
</tr>
<tr>
<td>18</td>
<td>18</td>
<td>M</td>
<td>DC</td>
<td>Skin pigmentation abnormality, thin hair, extensive dental caries and BMF</td>
</tr>
<tr>
<td>19</td>
<td>28</td>
<td>M</td>
<td>AA</td>
<td>Skin pigmentation abnormality, nail dystrophy, microcephaly, low birthweight, developmental delay and cerebellar atrophy. This patient harbours variants in TERT (heterozygous c.1336_1337insC; p.R446Pfs93* and c.329G&gt;C; p.G110A)</td>
</tr>
<tr>
<td>20</td>
<td>10</td>
<td>F</td>
<td>AA</td>
<td>Skin pigmentation abnormality, nail dystrophy, microcephaly, low birthweight, developmental delay and cerebellar atrophy. This patient harbours variants in TERT (heterozygous c.1336_1337insC; p.R446Pfs93* and c.329G&gt;C; p.G110A)</td>
</tr>
<tr>
<td>21</td>
<td>16</td>
<td>F</td>
<td>DC</td>
<td>Skin pigmentation abnormality, nail dystrophy, leukoplakia, small teeth, sparse scalp hair, epiphora, microcephaly and BMF</td>
</tr>
<tr>
<td>22</td>
<td>18</td>
<td>M</td>
<td>DC</td>
<td>Skin pigmentation abnormality, nail dystrophy, hair loss, extensive dental caries, developmental delay and short stature</td>
</tr>
<tr>
<td>23</td>
<td>37</td>
<td>M</td>
<td>DC</td>
<td>Skin pigmentation abnormality, nail dystrophy, hair loss, frequent otitis, mild hearing loss and extensive caries/ dental loss</td>
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<tr>
<td>24</td>
<td>4</td>
<td>F</td>
<td>AA</td>
<td>Skin pigmentation abnormality, nail dystrophy, microcephaly, low birthweight, developmental delay and cerebellar atrophy. This patient harbours variants in TERT (heterozygous c.1336_1337insC; p.R446Pfs93* and c.329G&gt;C; p.G110A)</td>
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<tr>
<td>25</td>
<td>50</td>
<td>F</td>
<td>DC</td>
<td>Nail dystrophy, cirrhosis, duodenal ulcers, deafness and developmental delay</td>
</tr>
<tr>
<td>26</td>
<td>NA</td>
<td>M</td>
<td>DC</td>
<td>Skin pigmentation abnormality, nail dystrophy, leucoplakia and leukemia</td>
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<td>27</td>
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<td>F</td>
<td>MDS/AML</td>
<td>Skin pigmentation abnormality, nail dystrophy, microcephaly, low birthweight, developmental delay and cerebellar atrophy. This patient harbours variants in TERT (heterozygous c.1336_1337insC; p.R446Pfs93* and c.329G&gt;C; p.G110A)</td>
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<tr>
<td>28</td>
<td>4</td>
<td>M</td>
<td>DC</td>
<td>Skin pigmentation abnormality, nail dystrophy, microcephaly, low birthweight, developmental delay and cerebellar atrophy. This patient harbours variants in TERT (heterozygous c.1336_1337insC; p.R446Pfs93* and c.329G&gt;C; p.G110A)</td>
</tr>
<tr>
<td>29</td>
<td>3</td>
<td>M</td>
<td>DC</td>
<td>Skin pigmentation abnormality, nail dystrophy, abnormal facies, microcephaly, ear abnormality and difficulty in swallowing</td>
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<td>30</td>
<td>0</td>
<td>M</td>
<td>HH</td>
<td>Congenital cytomegalovirus infection, microcephaly, generalized seizures, intracranial calcifications, growth restriction, low birth weight and BMF</td>
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<td>DC</td>
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<td>M</td>
<td>AA</td>
<td>Skin pigmentation abnormality, leukoplakia, epiphora, duodenal ulcers, cirrhosis, hepato-pulmonary syndrome and BMF. This patient harbours variant in TINF2 (heterozygous c.838A&gt;G; p.K280Q)</td>
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<td>M</td>
<td>DC</td>
<td>Skin pigmentation abnormality, nail dystrophy, microcephaly, low birthweight, developmental delay and cerebellar atrophy. This patient harbours variants in TERT (heterozygous c.1336_1337insC; p.R446Pfs93* and c.329G&gt;C; p.G110A)</td>
</tr>
<tr>
<td>34</td>
<td>34</td>
<td>M</td>
<td>AA</td>
<td>Skin pigmentation abnormality, nail dystrophy, leucoplakia, hair loss, microcephaly, premature birth with intrauterine growth restriction, glaucoma, premature aging, malabsorption, developmental delay and BMF. This patient harbours variant in DKC1 (hemizygous c.941A&gt;C; p.K314T)</td>
</tr>
<tr>
<td>35</td>
<td>3</td>
<td>M</td>
<td>DC</td>
<td>Skin pigmentation abnormality, nail dystrophy, leucoplakia, hair loss, microcephaly, premature birth with intrauterine growth restriction, glaucoma, premature aging, malabsorption, developmental delay and BMF. This patient harbours variant in DKC1 (hemizygous c.941A&gt;C; p.K314T)</td>
</tr>
</tbody>
</table>

AML: acute myeloid leukemia; MDS: myelodysplasia; DC: dyskeratosis congenita; AA: aplastic anemia; HH: Hoyeraal Hreidarsson syndrome; BMF: bone marrow failure; NA: not available; F: female; M: male.