NGLY1 deficiency: A rare congenital disorder of deglycosylation

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Introduction

• NGLY1 deficiency is a rare congenital disorder of N-linked deglycosylation
• It represents a severe multisystemic disease which is still poorly known
• To date, only 43 cases have been reported in the literature

Case report

• Siblings born from consanguineous healthy parents
• Originated from Tunisia
• No family history
• Clinical features: Table 1

Table 1: Summary of clinical features

<table>
<thead>
<tr>
<th></th>
<th>Case 1</th>
<th>Case 2</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td>7 years</td>
<td>3 years</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>Male</td>
</tr>
<tr>
<td>Personal history</td>
<td>Prematurity for preeclampsia</td>
<td>-</td>
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<tr>
<td>Symptoms</td>
<td>• Psychomotor delay&lt;br&gt;• Sleep disorders&lt;br&gt;• Hypolacrima&lt;br&gt;• Myoclonic jerks of head and arms at 4 years</td>
<td>• Psychomotor delay&lt;br&gt;• Paroxysmal episodes of brief gaze fixity with unresponsiveness</td>
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<td>Examination</td>
<td>• Mental retardation&lt;br&gt;• Language delay&lt;br&gt;• Autistic features&lt;br&gt;• Palmoplantar sweating&lt;br&gt;• Dysmorphic features (low implanted hair, badly hemmed ears, retrognatism, and short phyllot)</td>
<td>• Mental retardation&lt;br&gt;• Language delay&lt;br&gt;• Autistic features&lt;br&gt;• Generalized choreic movements&lt;br&gt;• Palmoplantar sweating&lt;br&gt;• Dysmorphic features</td>
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Discussion

• We present siblings with NGLY1 deficiency with a homozygous mutation in NGLY1 gene detected by WES
• NGLY1 deficiency is the first recognized autosomal recessive disorder of N-linked deglycosylation (1,2).
• It is very rare. To date, 43 patients harboring mutations in NGLY1 have been reported (1)
• The cardinal signs are developmental delay, hypolacrimia or alacrimia, hypotonia, hyperkinetic movement disorders and elevated transaminases (1)
• Varying lipid abnormalities such as low cholesterol, hypotriglyceridaemia, and high level of lactate, as seen in our patients, were also identified (3)

Conclusions

• NGLY1 deficiency should be evoked in patients with psychomotor delay, hyperkinetic movement disorders, elevation of transaminases, and alacrimia or hypolacrimia
• Genetic diagnosis is necessary to confirm the disease and for genetic counseling

References: