Supplemental materials

Supplemental Table 1. Possible complaints, signs and symptoms associated with vitamin B12 deficiency

Hematologic
Anemia, increased mean corpuscular volume (MCV)
Hypersegmented white blood cells, neutropenia
Thrombocytopenia
Pancytopenia

Neurologic
Peripheral neuropathy
Subacute combined degeneration of the spinal cord
Erectile dysfunction
Ataxia, tinnitus, dizziness
Cognitive disturbances, including difficulties concentrating, focusing on specific task or remembering, thinking, word finding disturbances, mood changes

Neuropsychiatric
Depression, mania, delirium, psychosis

Other
Glossitis, gingivitis
Muscle cramps, fibromyalgia-like symptoms, joint pains
Fatigue
Complaints related to a possible underlying cause, like celiac disease, short bowel syndrome, pancreatic insufficiency
Supplemental Table 2. Overview of relevant laboratory examinations in the patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex / age</td>
<td>F / 55</td>
<td>F / 17</td>
<td>F / 15</td>
<td>F / 33</td>
<td>F / 68</td>
<td>F / 62</td>
</tr>
<tr>
<td>Serum B12 (pmol/l)</td>
<td>51</td>
<td>112</td>
<td>94</td>
<td>190</td>
<td>301</td>
<td>249</td>
</tr>
<tr>
<td>HoloTC (pmol/l)</td>
<td>na</td>
<td>54</td>
<td>44</td>
<td>na</td>
<td>na</td>
<td>na</td>
</tr>
<tr>
<td>MMA (nmol/l)</td>
<td>na</td>
<td>178</td>
<td>218</td>
<td>na</td>
<td>37000</td>
<td>1380</td>
</tr>
<tr>
<td>HCys (µmol/l)</td>
<td>na</td>
<td>11</td>
<td>78.4</td>
<td>na</td>
<td>165</td>
<td>na</td>
</tr>
<tr>
<td>Folate (nmol/l)</td>
<td>9.8</td>
<td>19</td>
<td>6.7</td>
<td>na</td>
<td>&gt;45</td>
<td>na</td>
</tr>
<tr>
<td>cB12 indicator</td>
<td>na</td>
<td>-0.3 (^{a})</td>
<td>-1.4 (^{a})</td>
<td>na</td>
<td>-5.2</td>
<td>-1.3</td>
</tr>
<tr>
<td>Hemoglobin (mmol/l)</td>
<td>7.0</td>
<td>8.3</td>
<td>8.0</td>
<td>7.5</td>
<td>7.5</td>
<td>na</td>
</tr>
<tr>
<td>MCV (fl)</td>
<td>105</td>
<td>88</td>
<td>93</td>
<td>na</td>
<td>110</td>
<td>na</td>
</tr>
<tr>
<td>Parietal cell antibodies</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>na</td>
</tr>
<tr>
<td>Anti-intrinsic factor antibodies</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>na</td>
</tr>
<tr>
<td>Comorbidity</td>
<td>Graves' disease, vitiligo</td>
<td>-</td>
<td>-</td>
<td>Hashimoto's disease</td>
<td>After RYGB</td>
<td></td>
</tr>
</tbody>
</table>

Reference values:
Serum B12 140 - 450 pmol/l; Holotranscobalamin (HoloTC) intermediate 32-70, normal 70-125 pmol/l; MMA, methylmalonic acid: < 300 nmol/l; HCys, homocysteine: < 10 µmol/l
Folate: 10 - 36 nmol/l; Hemoglobin: 7.5 - 9.5 mmol/l; MCV, mean corpuscular volume: 85-98 fl.
cB12, combined indicator of deficiency, -0.5-1.5, adequate; -1.5--0.5, low; -2.5--1.5, possible deficiency; <-2.5, probable deficiency. Ref. 44
na: not available

\(^{a}\) the cB12 in patients B and C should be interpreted with caution as the application of this indicator has not validated in people below the age of 18 years.
Supplemental Table 3. Causes of cobalamin (vitamin B12) deficiency

1. Inadequate intake
   - Vegans or vegetarians
   - Alcohol abuse

2. Disturbed absorption
   - Autoimmune gastritis
   - Gastrectomy or gastric bypass
   - Diseases or resection of the ileum
   - Pancreatic insufficiency
   - Certain medications (metformin, proton pump inhibitors)
   - Bacterial overgrowth

3. Congenital
   - Transcobalamin-II deficiency
   - Absence or dysfunction of intrinsic factor

4. Chemical inactivation
   - Nitrous oxide