The combination of hypercalcaemia, hypercalciuria, and nephrocalcinosis with and without renal impairment is rare in paediatric clinical practice. However, this constellation of findings has been reported in three children with trisomy 21, but the absence of detailed nutritional data has failed to clarify the underlying pathogenesis. This report describes a 4 year old girl with trisomy 21 who was found coincidentally to have hypercalcaemia, hypercalciuria, nephrocalcinosis, and renal impairment in the absence of metabolic alkalosis, following a prolonged period of excessive calcium intake.

A 4 year old girl with trisomy 21 and symptomatic gastrooesophageal reflux was coincidentally found to have hypercalcaemia (3.35 mmol/litre) associated with an increased plasma urea (19.3 mmol/litre) and creatinine (144 µmol/litre) and normal plasma bicarbonate (22 mmol/litre) and phosphate (1.6 mmol/litre).

She was born at 33 weeks gestation, with evidence of intra-partum asphyxia requiring transient ventilatory and inotropic support. Follow up at age 4 months, while she was receiving standard infant milk formula, revealed a normal plasma creatinine (25 µmol/litre), calcium (2.32 mmol/litre), and renal ultrasound. A 99Tecnetium dimercaptosuccinic acid scan at 6 months was also normal.

Medical management comprising cimetidine, cisapride, and Nestergerl to thicken feeds was unsuccessful in controlling her vomiting and because of the persistent confirmed acid reflux, she was referred for fundoplication and gastrostomy insertion.

After the observation of hypercalcaemia, further investigations revealed normal concentrations of alkaline phosphatase (91 U/litre; normal range, 90–850), calcitonin (10 ng/litre; normal value, < 15), and angiotensin converting enzyme (39 U/litre; normal range, 90–850), in addition to normal thyroid function. Her parathyroid hormone (PTH) was suppressed at 0.44 mmol/mmol at baseline to 1.07 mmol/mmol at four hours, with no change in plasma calcium.

The dietary calcium restriction was progressively relaxed and normalised by age 7.6 years. The plasma and urine calcium values have remained normal, with the most recent plasma creatinine being 72 µmol/litre (estimated glomerular filtration rate, 47/ml/min/1.73 m²). At the age of 8.8 years her PTH was 14.9, with normal concentrations of both 25 hydroxycholecalciferol and 1,25 dihydroxycholecalciferol.

Table 1 Nutritional and biochemical data

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Feed</th>
<th>Feed volume ml/kg</th>
<th>Calcium intake (mmol)</th>
<th>Sodium intake (mmol)</th>
<th>Plasma calcium (mmol/l)</th>
<th>Plasma creatinine (mmol/l)</th>
<th>Urinary Ca/Creat (mmol/ mmol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.33</td>
<td>Cows’ milk</td>
<td>110</td>
<td>22.7 [8.8]</td>
<td>15.7 [13–27]</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>1.85</td>
<td>Nutrison Progress</td>
<td>186</td>
<td>24.7 [8.8]</td>
<td>21.7 [14–28]</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>4.4</td>
<td>Nutrison Progress</td>
<td>155</td>
<td>20.6 [8.8]</td>
<td>18.1 [14–28]</td>
<td>3.35</td>
<td>144</td>
<td>2.03</td>
</tr>
<tr>
<td>4.51</td>
<td>Locasol Nutrison</td>
<td>109</td>
<td>8.6 [11.3]</td>
<td>18.7 [17–34]</td>
<td>3.0</td>
<td>108</td>
<td>1.08</td>
</tr>
<tr>
<td>4.7</td>
<td>Locasol</td>
<td>96</td>
<td>2.1 [11.3]</td>
<td>13.9 [21–42]</td>
<td>2.49</td>
<td>94</td>
<td>0.44</td>
</tr>
<tr>
<td>5.5</td>
<td>Locasol Nutrison</td>
<td>85</td>
<td>5.5 [11.3]</td>
<td>18.2 [21–42]</td>
<td>2.63</td>
<td>88</td>
<td>0.22</td>
</tr>
<tr>
<td>6.0</td>
<td>Locasol</td>
<td>96</td>
<td>10.1 [11.3]</td>
<td>13.9 [21–42]</td>
<td>2.59</td>
<td>92</td>
<td>0.05</td>
</tr>
<tr>
<td>7.8</td>
<td>Mixed diet</td>
<td>14.6</td>
<td>13.8</td>
<td>22.3 [21–42]</td>
<td>2.54</td>
<td>72</td>
<td>&lt;0.03</td>
</tr>
</tbody>
</table>

Figures in parenthesis for calcium and sodium intake indicate recommended daily nutritional intakes (RDI). Ca/Creat, calcium/creatinine ratio; N/A, not available.
Intestinal calcium absorption occurs through both a passive and an active vitamin D dependent mechanism. Increased calcium ingestion results in a compensatory decrease in vitamin D mediated absorption and an increase in faecal calcium excretion. In our patient, there was evidence of suppression of 1,25 vitamin D3 and increased urinary calcium excretion following an oral calcium load. In healthy children, calcium restriction before a calcium loading test resulted in a slightly higher urinary calcium to creatinine ratio compared with those not restricted beforehand, but not to the extent seen in our patient. These findings, along with the biochemical and clinical improvement following dietary calcium restriction, suggest a possible genetic predisposition to enhanced calcium absorption via the passive route in trisomy 21, despite the presence of hypercalcaemia, and suggest that this is an example of “milk drinker’s” hypercalcaemia.

**REFERENCES**

Hypercalcaemia in association with trisomy 21 (Down's syndrome)

I J Ramage, A Durkan, K Walker and T J Beattie

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