Early and severe manifestation of McCune-Albright syndrome with GNAS mutation in the liver tissue

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BACKGROUND
McCune-albright syndrome is classically defined by the clinical triad of fibroblast dysplasia of bone (FD), café-au-lait spots and precocious puberty. It is a rare disease with variable presentation caused by somatic gain of function mutation in GNAS gene. It can affect both endocrine and non-endocrine tissue. In addition to precocious puberty, other hyperfunctioning endocrinopathies may be involved including hyperthyroidism, growth excess, cushing syndrome and renal phosphate wasting. Skin and skeletal manifestation is the most non-endocrine pathology, but other systems like gastrointestinal and hepatobiliary systems has been also reported.

OBJECTIVES
To report a case with early and severe manifestation of McCune-Albright syndrome where diagnosis was not a straightforward.

CASE DESCRIPTION
We report a 2 years old girl who was presented to medical attention at the age of 16 days with cholestasis jaundice and multiple hyperpigmented skin lesions involving right sided of the face, back, buttocks and thigh. She was found to have hyperthyroidism caused by hyperfunctioning nodule in the the left lobe of the thyroid gland (Figure 1), it was uncontrolled with medical treatment. At 4 months of age, she developed vaginal bleeding with high estradiol level and found to have large left ovarian cyst (Figure 2). It was recurrent and difficult to control. At 6 months of age, she developed lesions involving right lobe of the liver (Figure 3), these lesions were progressively worsening and required right lobectomy and lesion was confirmed histopathologically to be hepatic adenoma. She had multiple skelatal fracture involving right femur and clavicle which was a results of diffuse polyostotic fibroblast dysplasia. Lastly, she shows an evidence of growth acceleration with advanced bone age which was a result of growth hormone excess (Table 1) with normal pituitary MRI

RESULTS

<table>
<thead>
<tr>
<th>Time</th>
<th>Glucose Level Mmol/L</th>
<th>GH LEVEL ug/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>3.8</td>
<td>4.45</td>
</tr>
<tr>
<td>30 min</td>
<td>12.6</td>
<td>&gt;80</td>
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<tr>
<td>60 min</td>
<td>11.6</td>
<td>&gt;80</td>
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<tr>
<td>90 min</td>
<td>9.2</td>
<td>49.20</td>
</tr>
<tr>
<td>120 min</td>
<td>7.2</td>
<td>36.50</td>
</tr>
</tbody>
</table>

GNAs mutation was negative in both peripheral blood and skin tissue samples. Heterozygous GNAS mutation with a change from Arginine (CGT) at codon 201 to Histidine (CAT) was identified in liver tissue sample.

CONCLUSION
To our knowledge, such a severe neonatal form of McCune-Albright syndrome is rarely reported in the literature. GNAS mutation should be evaluated in the tissue affected if the blood and skin tests are negative.

REFERENCES

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