Idiopathic Hypercalcemia of Infancy

By

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The disease called "Idiopathic hypercalcemia of infancy" is clinically characterized by growth failure, anorexia, constipation, vomiting and a peculiar face. Laboratory studies disclose hypercalcemia and elevating of blood urea. Butler\(^1\) and Fanconi\(^2,3\) reported the first two cases in 1951. In 1952, the syndrome was clearly delineated by Lightwood and Payne\(^4\) for the first time. Idiopathic hypercalcemia of infancy has thus far been discussed mainly in Great Britain,\(^1,4-17\) but recently in United States\(^18-20\) several cases have been reported. In the present paper we shall describe the first report of this disease in Japan.

Report of Cases

Case 1. The boy weighed 3.75 kilograms at birth, April 24, 1956. His first visit to our Clinic was at the age of 3 months because of obstinate vomiting and constipation. At the age of 4 months, he was admitted to our Hospital as a suspected case of invagination because of frequent vomiting, but he improved with transfusion and was discharged. But thereafter vomiting and constipation persisted in spite of various treatment, and he was often attacked with fever. At the age of 1 year and 9 months, he was readmitted to the Hospital because of measles. Though the course was severe, he recovered from the disease at length. But by this time, he had already had a peculiar face (Fig. 1). He was malnourished, hypotonic and his mental development was delayed. Heart sounds were clear. From the time of readmission to his full age of 2 years biochemical examinations of serum were performed. As is given in Table I, serum calcium level was elevated. Serum nonprotein nitrogen was slightly elevated, but serum phosphorus level, alkaline phosphatase activity and cholesterol level were within normal ranges. Roentgenogram of the bones showed dense lines at the end of the long bones and a slight osteosclerosis. Calcification was not found in the kidneys. He had been fed on cow's milk from his birth, but he had not vitamin D intake specially. At the age of 2 years
Fig. 1. Case 1. Elfin appearance with a big mouth and thickened upper lip.

### Table I

Biochemical Findings of Serum of Our Own Cases of Idiopathic Hypercalcemia of Infancy

<table>
<thead>
<tr>
<th></th>
<th>Calcium (mg/dl)</th>
<th>Phosphorus (mg/dl)</th>
<th>Alkaline phosphatase activity (S. J. R. unit)</th>
<th>Nonprotein nitrogen (mg/dl)</th>
<th>Cholesterol (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>11.6–14.5</td>
<td>5.5</td>
<td>4.1–4.8</td>
<td>27.0–40.8</td>
<td>176</td>
</tr>
<tr>
<td>Case 2</td>
<td>9.7–13.6</td>
<td>2.5–8.2</td>
<td>2.5–12.7</td>
<td>21.0–49.0</td>
<td>204</td>
</tr>
<tr>
<td>Case 3</td>
<td>10.1–14.0</td>
<td>5.0–6.0</td>
<td>4.7–16.8</td>
<td>28.0</td>
<td>—</td>
</tr>
</tbody>
</table>

and 1 month, he could not yet stand still.

Case 2. The girl weighed 3 kilograms at birth September 24, 1947. She suffered from persistent vomiting and constipation from the age of about 5 months. She was admitted to the Hospital on March 3 and remained to stay until April 4, 1958, because of bronchopneumonia. On the examination at this time, slight systolic murmurs were heard on the apex. Strabismus was noticed. From then on systolic murmurs became louder and louder and strabismus was more definite. Constipation and vomiting were very obstinate. She was readmitted to the Hospital on July 3 and stayed in it until September 12, 1958, because of moniliasis of the lungs due to candida albicans. During her admission and even later, she was often attacked with fever. Biochemical examinations of serum were performed repeatedly from January to August, 1958. As is given in Table I, serum calcium level and nonprotein nitrogen were elevated. Blood picture was normal except for a slight anemia. Sulkowitch
test and protein reaction of the urine were positive on July 4, 1958. Roentgenogram showed a slightly increased density of the bones and dense lines at the end of the long bones, but no calcification of the kidneys was found. She had been fed on cow's milk and in addition received 0.5 cc. multivitamins solution containing 500 units of vitamin D₂ per cc. daily. But since her first admission, the multivitamins solution intake had been suspended. On the examination at the age of 2 years, September 20, 1959, heart sounds were clear and serum calcium level was reduced to normal, but she could not walk yet. Strabismus was still noticed.

Case 3. The boy weighed 3.8 kilograms at birth, June 5, 1957. He was admitted to the Hospital on July 12, 1957, because of persistent fever. After admission, he was treated as a suspected case of sepsis. Blood cultures were repeatedly performed, but the results were negative. The unexplained fever persisted. He began to vomit from the age of about 2 months on, and vomiting became more and more frequent. Constipation also was very obstinate. His face presented a peculiar appearance (Fig. 2), which became gradually striking. Serum calcium level was 14.0 mg./dl. on the 12th day of his admission. Dehydration and thirst were noticed. He was hypotonic. He was discharged with no remarkable improvement on October 10, 1957. During his admission, the increase of his body weight was very slow and he gained only about 1 kilogram during the time of 3 months. Blood picture was normal except for a slight anemia. Red sedimentation rate was not accelerated. Roentgenogram showed an increased density of the bones and dense lines at the end of the long bones. Slight calcification was found in the kidneys. He had been fed on both mother's and cow's milk since his birth, but he had

![Fig. 2. Case 2. Elfin appearance with a big mouth and hypertelorism.](image)
not vitamin D intake specially. Nonprotein nitrogen level at his discharge was within normal range.

Comment

Our own cases belong to the severe form of idiopathic hypercalcemia of infancy such as has been described by Lightwood and Stapleton. They presented each the classic "elfin appearance" with a big mouth and a thickened upper lip. Anorexia, constipation, vomiting, very slow gain or standstill of weight, growth failure and mental impairment were typical. In Case 2, systolic murmurs were heard over her heart. Serum calcium levels in all the three cases were elevated. This is, as is well known, the most important finding for the diagnosis of this syndrome: "Idiopathic hypercalcemia of infancy." Nonprotein nitrogen level was also elevated except in Case 3, but in this case the estimation was performed at the time of his discharge, the possibility that his nonprotein nitrogen level might, if examined much more early during his stay, have been found to be elevated, is not excluded. Roentgenograms of the bones in all the cases showed dense lines at the end of the long bones. In Case 3, slight calcification was found in the kidneys. As to the etiology of this syndrome, nothing certain is known. Individual hypersensitivity to vitamin D has been suggested as a possible etiology by many authors. Case 1 and Case 3 did not receive any additional vitamin D intake. In Case 2, 250 units of vitamin D were indeed daily given, but this dosis is by no means an excessive one.

SUMMARY

Three cases of idiopathic hypercalcemia of infancy were presented. The present paper is the first report of this syndrome in Japan. In all the cases the typical clinical features such as anorexia, constipation, vomiting, growth failure and mental impairment were noticed. Serum calcium levels were elevated in all the cases. Nonprotein nitrogen level was elevated except in one case.

References

2) Fanconi, Schweiz. med. Wschr., 1951, 81, 908.
6) Lightwood and Stapleton, ibid., 1953, 2, 255.


12) Morgan, Mitchell, Stowers and Thompson, *ibid.*, 1956, 1, 925.

13) Stapleton, McDonald and Lightwood, *ibid.*, 1956, 1, 932.


16) Stapleton and Evans, Helvet paediat. acta, 1955, 10, 149.

17) Schlesinger, Butler and Black, *ibid.*, 1952, 7, 335.


21) Fanconi and Spar, Helvet. paediat. acta, 1955, 10, 156.
