Changes in Somatomedin Activity in Anorexia Nervosa

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Abstract

Somatomedin (SM) activity, GH, T3 and T4 were investigated in 6 girls with anorexia nervosa during hospitalization and at outpatient clinic. On admission, serum T3 (27-62 ng/dl) and SM activity (0.24-0.55 U/ml) were low in all cases, while basal GH was extremely high in 2 cases. A significant negative correlation was found between SM activity and basal GH during the course of treatment (r = -0.61, p<0.02). The change in SM activity was related to that of the serum T3 level and a significant positive correlation was found between SM activity and serum T3 (r = 0.80, p<0.001).

These data suggest that decreased SM activity may suppress the inhibitory effect of SM on GH release and may raise the basal GH level. SM activity is one of the indicators of the nutritional condition in anorexia nervosa as well as the serum T3 concentration.

Somatomedin (SM) is known to mediate the peripheral action of growth hormone on cartilage and other tissues (Daughaday et al., 1972; Van Wyk et al., 1974). It has also become apparent that SM levels can be dependent upon the nutritional status. This was shown in fasted rats (Philips and Younge, 1976) and also in children with malnutrition (Grant et al., 1975; Hintz et al., 1978). Anorexia nervosa during childhood may be considered a form of chronic malnutrition and depressed SM levels have been reported (Rappaport et al., 1980).

We studied the change in SM activity in relation to triiodothyronine (T3), thyroxine (T4), growth hormone (GH) and weight changes in patients with anorexia nervosa.

Subjects and Methods

Subjects

The characteristics of the subjects are presented in Table 1. The group consists of 6 girls, aged 14 years to 16 years at the time of admission to Toranomon Hospital. The diagnosis of anorexia nervosa was made on the basis of criteria of a typical case by Suematsu et al., (1983), although case 3 had not yet developed menarche. Their body weight ranged from 27.0 to 36.9 kg (−27.5 to −45% of the ideal weight for height). All patients were treated with behavior therapy.
Table 1. The characteristics of the subjects on admission

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>% Ideal Weight</th>
<th>Pubertal Stage (Tanner)</th>
<th>Duration of Amenorrhea (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14 y 3 m</td>
<td>146.0</td>
<td>30.0</td>
<td>-27.5</td>
<td>B3 P3</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>14 y 11 m</td>
<td>167.4</td>
<td>36.9</td>
<td>-40</td>
<td>B4 P4</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td>15 y 3 m</td>
<td>154.0</td>
<td>33.7</td>
<td>-30</td>
<td>B3 P3</td>
<td>11</td>
</tr>
<tr>
<td>4</td>
<td>15 y 5 m</td>
<td>155.8</td>
<td>31.5</td>
<td>-37</td>
<td>B3 P3</td>
<td>(—)</td>
</tr>
<tr>
<td>5</td>
<td>15 y 9 m</td>
<td>155.2</td>
<td>27.0</td>
<td>-45</td>
<td>B3 P3</td>
<td>22</td>
</tr>
<tr>
<td>6</td>
<td>16 y 6 m</td>
<td>148.8</td>
<td>28.5</td>
<td>-34</td>
<td>B4 P4</td>
<td>2</td>
</tr>
</tbody>
</table>

during their hospitalization, and their weight increased to almost -20% of their ideal weight in 2 to 4 months. Ideal body weight was calculated as follows: (height-100)×0.9. After discharge, they have been followed up by a psychotherapist and a pediatrician at the outpatient clinic.

Methods

Serum T₄, T₃ and GH were determined by radioimmunoassay and the normal basal value was 5.5-14.0 ng/dl, 90-210 ng/dl, and less than 5 ng/ml, respectively.

Somatomedin (SM) activity was estimated by the increase in labelled sulphate uptake into chick embryo chondrocytes (Maesaka et al., 1982). The index of precision for assays (n=20) was 0.1±0.04. All values were compared to a normal adult serum pool, one ml of which defined a unit of SM activity. Normal values for pubertal girls ranged from 0.86 to 2.02 U/ml.

Statistical analysis was performed using Student's t-test.

Results

The laboratory findings on admission are summarized in Table 2 except those in parentheses, which were taken one week after admission. Serum SM activity was low in all patients, while basal GH was extremely high in two patients. Serum T₃ was low in five patients and T₄ in three.

When patients gained weight up to -9.4% to -28% of their ideal weight for their height, all patients achieved a SM activity in the normal range (0.86-1.5 U/ml). The relationship between body weight as a percentage of ideal weight and SM activity is shown in Fig. 1. SM activity in three patients (Case 1, 4, and 5) increased in proportion to the increase in their weight, but these values in the other three (Case 2, 3 and 6) patients did not show such a correlation. There was no significant correlation between SM activity and the percentage of ideal body weight.

Increased basal GH levels in case 2 and in case 6 on admission decreased to normal levels when the patients began to gain weight.

The correlation between SM activity and serum GH is shown in Fig. 2a. A significant negative correlation (N=15, r=-0.61, p<0.02) was observed. A positive correlation (r=0.44) between SM activity and T₄ was observed as shown in Fig. 2b, but it was not significant. The correlation between SM activity and serum T₃ is shown in Fig. 2c. A significant positive correlation was found between them (N=22, r=0.80, p<0.001).

Fig. 3 shows the changes in SM activity, T₃ and body weight in cases 5 and 6 during...
treatment. In case 5 (Fig. 3a) serum SM activity and T3 level increased in proportion to the increase in body weight, but in case 6 (Fig. 3b), SM activity increased initially, but decreased later despite the increase in body weight. The change in T3 levels followed that of SM activity.

Discussion

On admission, a pattern of hormonal changes was characteristic of malnutrition: decreased serum T3, T4 and decreased SM activity. Basal GH secretion and stimulated secretion was reported to be normal or elevated in malnutrition and in anorexia nervosa (Maeda et al., 1976; Vigersky et al., 1977; Hintz et al., 1978; Rappaport et al., 1980). In our study, two patients had a markedly increased basal GH level, while their SM activity was markedly decreased. Bioactivity of GH in their serum was estimated by Nb2 lymphoma cell bioassay (Tanaka et al., 1980) and their GH proved to be bioactive (data not shown). Also it has been reported that administration of hGH or T3 to a patient with anorexia nervosa did not stimulate the generation of SM activity (Rappaport et al., 1980). Therefore, it might be concluded that endogeneous and exogeneous GH could not stimulate SM activity in anorexia nervosa. On the other hand, it is likely that decreased SM activity stimulate the secretion of GH. It is reported that SM has an inhibitory effect on GH release from cultured pituitary cells in the rat (Berelowitz et al., 1981; Tannenbaum et
Fig. 2a. The correlation between basal GH and SM activity (N=15, r=−0.61, p<0.02).

Fig. 2b. The correlation between T4 and SM activity (N=17, r=0.44, p>0.05).

Fig. 2c. The correlation between T3 and SM activity (N=22, r=0.80, p<0.001).
(●: during hospitalization, ○: at out-patient clinic.)
al., 1983) and in the human (Ceda et al., 1985). Therefore, in anorexia nervosa, a decrease in SM production in the liver due to malnutrition may suppress the inhibitory effect of SM on GH release and may increase the basal GH level in the serum. The negative correlation between GH and SM activity supports this hypothesis.

The low concentration of serum $T_3$ has been shown not only in anorexia nervosa
but also in starvation, protein caloric malnutrition and acute illness (Miyai et al., 1975; Moshang, Jr., et al., 1975; Croxson and Ibbertson, 1977). Moreover, in extreme illness, serum T₄ may also be depressed. In these undernourished states, impaired peripheral conversion of T₄ to T₃ by an inhibitor in the serum (Chopra et al., 1985) with increased conversion of T₄ to reverse T₃ (Chopra et al., 1975) is responsible for a low serum T₃ concentration. Although the exact mechanisms remains unclear, it is speculated that this phenomenon is part of an adaptive mechanism to conserve calories during such adverse circumstances.

The correlation between the serum T₃ level and SM activity suggests several possible mechanism by which T₃ may affect SM activity: 1) a direct effect on chondrocyte metabolism, 2) a direct effect on SM generation in liver, 3) an effect on other serum factors affecting chondrocytes. The first mechanism is unlikely. Although T₃ significantly increased the sulphation uptake in our SM bioassay, a T₃ concentration of μg/ml is necessary in increase the SM activity from the levels of anorexia nervosa to that of a normal subject. The second mechanism is possible since Marek et al., (1981) has shown increased SM activity in thyrotoxic patients and decreased activity in patients with hypothyroidism. The presence of SM inhibitor in starved rat serum (Salmon Jr., 1975; Price et al., 1979) supports the last mechanism. The second mechanism is possible since Marek et al., (1981) has shown increased SM activity in thyrotoxic patients and decreased activity in patients with hypothyroidism. The production of SM inhibitor and inhibitor of extrathyroidal conversion of T₄ to T₃ may be closely related to an undernourished condition, although the moiety of these inhibitors is different. The reason why SM activity and the serum T₃ concentration decreased in case 2 and 6 is unclear, even though the body weight was increasing. There may be another mechanism except nutritional intake between the production of these inhibitors and body weight gain.

In conclusion, SM activity was markedly low in 6 girls with anorexia nervosa and increased with body weight gain. Decreased SM may suppress the inhibitory effect of SM on GH release and may raise the basal GH level. SM activity is one of the indicators of the nutritional condition in anorexia nervosa as well as the serum T₃ concentration.

References


