BRIEF COMMUNICATION

Number and Percentage of NK-Cells Are Decreased in Growth Hormone-Deficient Adults


Department of Medicine, Divisions of Endocrinology and *Internal Medicine, University Hospital Nijmegen, 6500 HB Nijmegen, The Netherlands

Snell–Bagg mice and Ames dwarf mice repeatedly show severe immunodeficiencies, affecting mostly the thymus-dependent lymphocyte system, probably caused by growth hormone deficiency. In growth hormone-deficient children contradictory data on the immune status have been reported. We investigated indices of cellular immunity in 22 adult patients with proven growth hormone deficiency in comparison to those in 100 healthy volunteers. Cellular immunity was assessed using total leukocyte count, percentage lymphocytes, and percentage and absolute numbers of CD3, CD4, CD8, CD19, and CD3–CD56+ (NK)-cells. Comparison revealed statistically significantly lower percentage and absolute number of NK-cells (P < 0.001). Except for a trend toward an increased CD4/CD8 ratio, no statistically significant differences for B- and T-lymphocytes could be observed. No correlation between the percentage and absolute number of NK-cells, on one hand, and the duration of growth hormone deficiency or prolactin level, on the other hand, could be demonstrated. In all these respects men did not differ from women. So, in growth hormone-deficient adults the percentage and absolute number of NK-cells are decreased.

PATIENTS AND METHODS

Twenty-two patients (15 female and 7 male; mean age, 42 years; range, 27–59 years) with growth hormone deficiency were included in this study. The diagnosis of growth hormone deficiency was based on an arginine provocation test with a growth hormone peak concentration ≤10 mU/liter and an IGF-I concentration below the normal value corrected for age and sex. Most patients (n = 17) had multiple pituitary deficiencies and received adequate, hormonal replacement therapy, except for growth hormone for the last 2 years. The control group consisted of 100 healthy volunteers (48 male and 52 female; mean age, 43 years; range, 18–70 years).

In all patients the following parameters were studied; hemoglobin, white blood count (WBC), red blood count (RBC), thrombocytes, the percentage and absolute number of lymphocytes, CD3+ (total T-lymphocytes), CD4+ (T-helper cells), CD8+ (T-suppressor cells), CD19+ (B-lymphocytes), and CD14+ cells (monocytes) and CD3–CD56+ cells (NK-cells). Hematologic indices were measured using a Technicon H1 electronic cell counter. The percentages of CD3-, CD4-, CD8-, CD14-, and CD19-positive cells and the NK-cells were measured using flow cytometry and direct immunofluorescence.

The unpaired Student t test was used to compare data of patients and controls, and the Spearman rank correlation test was used for the within population comparisons.

All patients signed informed consent to the protocol...
which was approved by the University Hospital Ethical Committee.

RESULTS

Growth hormone deficiency was mostly due to hypophysectomy for the treatment of a pituitary adenoma. Other causes included M. Sheehan, trauma, craniopharyngeoma, and hypothalamic insufficiency (see Table 1).

Standard hematological analysis revealed no statistically significant differences when the patients' data were compared with the controls.

Comparison of indices of the cellular immunity of growth hormone-deficient patients with those of the control group revealed a statistically significant lower percentage and absolute number of NK-cells ($P < 0.001$) (Table 2). No statistically significant differences for B- and T-lymphocytes could be demonstrated between patients with growth hormone deficiency and the normal population, except for a trend to an increased CD4/CD8 ratio ($P = 0.053$).

No statistical significant correlation between the number or percentage of NK-cells and the estimated duration of growth hormone deficiency or prolactin levels could be demonstrated. In all these respects men did not differ from women.

DISCUSSION

This study revealed no differences in thymic-derived cells between the adults with growth hormone defi-

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Demographic Data</th>
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<tbody>
<tr>
<td>Patient</td>
<td>Birth date</td>
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<td>1</td>
<td>10 Sept. 1948</td>
</tr>
<tr>
<td>2</td>
<td>21 Oct. 1963</td>
</tr>
<tr>
<td>3</td>
<td>4 July 1962</td>
</tr>
<tr>
<td>4</td>
<td>2 March 1968</td>
</tr>
<tr>
<td>5</td>
<td>9 July 1943</td>
</tr>
<tr>
<td>6</td>
<td>29 Nov. 1952</td>
</tr>
<tr>
<td>7</td>
<td>11 Nov. 1945</td>
</tr>
<tr>
<td>8</td>
<td>15 Feb. 1940</td>
</tr>
<tr>
<td>9</td>
<td>20 May 1956</td>
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<td>10</td>
<td>20 Sept. 1950</td>
</tr>
<tr>
<td>11</td>
<td>23 Feb. 1968</td>
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<td>12</td>
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<td>13</td>
<td>2 May 1965</td>
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<tr>
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<td>17 June 1954</td>
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<td>6 March 1961</td>
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TABLE 2

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<tr>
<th></th>
<th>Lymphocytes, $\times 10^9$/liter</th>
<th>CD-3 positive cells $\times 10^9$/liter</th>
<th>CD4-positive cells $\times 10^9$/liter</th>
<th>CD8-positive cells $\times 10^9$/liter</th>
<th>CD4/CD8 ratio</th>
</tr>
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<tbody>
<tr>
<td>GHD Mean</td>
<td>2.4</td>
<td>1.75</td>
<td>1.14</td>
<td>0.66</td>
<td>28.5</td>
</tr>
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<td>25–75%</td>
<td>1.7–3.1</td>
<td>1.14–2.39</td>
<td>0.74–1.55</td>
<td>0.43–0.86</td>
<td>1.34–2.58</td>
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<tr>
<td>Normal Mean</td>
<td>2.1</td>
<td>1.4</td>
<td>0.8</td>
<td>0.7</td>
<td>35</td>
</tr>
<tr>
<td>25–75%</td>
<td>1.6–2.4</td>
<td>1.1–1.7</td>
<td>0.7–1.1</td>
<td>0.5–0.9</td>
<td>31–40</td>
</tr>
</tbody>
</table>

CD19-positive cells $\times 10^9$/liter

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<tr>
<th></th>
<th>CD14-positive cells $\times 10^9$/liter</th>
<th>CD3<del>CD56</del> cells $\times 10^9$/liter</th>
<th>CD4/CD8 ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>GHD Mean</td>
<td>0.3</td>
<td>0.14**</td>
<td>6.2**</td>
</tr>
<tr>
<td>25–75%</td>
<td>0.2–0.4</td>
<td>0.09–0.18</td>
<td>4.0–9.0</td>
</tr>
<tr>
<td>Normal Mean</td>
<td>0.3</td>
<td>0.3**</td>
<td>14**</td>
</tr>
<tr>
<td>25–75%</td>
<td>0.2–0.4</td>
<td>0.2–0.4</td>
<td>10–19</td>
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</tbody>
</table>

* Statistically significant difference, $P < 0.001$ (Student $t$ test).
** Statistically significant difference, $P < 0.001$ growth hormone deficient patients vs controls (Student $t$ test).

ciency and the normal population. The number and percentage of B-cells are also comparable with the values found in the normal population. Remarkably the number and percentage of NK-cells were significantly lower in the patient group than in the normal population.

Hyperprolactinemia has been shown to inhibit immune function (3); moreover, in hyperprolactinemic men, a reduced NK-cell activity was demonstrated compared to hyperprolactinemic patients treated with bromocriptine (7), but these findings could not be reproduced (8). In our study we could not demonstrate a correlation between the absolute number of NK-cells and the prolactin concentration. Therefore, we consider growth hormone deficiency as a possible cause for the decrease found in number and percentage NK-cells.

REFERENCES


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