Beneficial Effects of Herbal Medicine on Susceptibility to Infection in a Patient with Immunoglobulin Deficiency

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Abstract: A case of immunoglobulin deficiency suffered from recurrent enterocolitis and otitis media was treated by Shoukenchuto, one of the Japanese herbal medicines (Kampo), and his susceptibility to infection markedly improved. The increase in the T cell percentage and in the lymphocyte proliferation in our patient suggests the importance of regulatory function of T cells for clinical improvement. The findings in our case and the previously reported cases suggest the usefulness of Japanese herbal medicine or Chinese medicine as an alternative or a supportive therapy for patients with immunological abnormalities.

Keywords: Herbal medicine, Shoukenchuto, immunoglobulin deficiency, CD4, CD8, lymphocyte proliferation.

We present a case of immunoglobulin deficiency with recurrent enterocolitis and otitis media whose clinical symptoms improved after treatment with Japanese herbal medicine (Kampo).

CASE REPORT

A 6-year-old boy developed complex partial seizures and EEG showed sporadic spikes in the central and parietal lobes. He was diagnosed as having partial epilepsy. Initially, valproate was administered, but carbamazepine was required for control of his seizures. After one year of medication with carbamazepine, he frequently suffered from enterocolitis or otitis media requiring many hospital visits almost every weeks and four times of hospital admission during the 2 years. Everytime, he required to be treated with continuous drip infusion and antibiotics repeatedly (Fig. 1). His laboratory tests showed...
Table 1. Immunological Evaluation of the Patient

<table>
<thead>
<tr>
<th>Age</th>
<th>Drug Dosage (mg/day)</th>
<th>Immunoglobulin (mg/dl)</th>
<th>B Cell Count (%)</th>
<th>Cell Surface Marker</th>
<th>Lymphocyte Proliferation (Stimulation Index)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>VPA CBZ ZNS SKCT</td>
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<td>VPA CBZ ZNS SKCT</td>
<td>VPA CBZ ZNS SKCT</td>
<td>VPA CBZ ZNS SKCT</td>
</tr>
<tr>
<td>6yr 8m</td>
<td>600 0 0 0 0</td>
<td>788 70 282</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7yr 0m</td>
<td>600 0 0 0 0</td>
<td>883 85 285</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7yr 4m</td>
<td>600 300 0 0 0</td>
<td>765 37 185</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>8yr 0m</td>
<td>600 300 0 0 0</td>
<td>587 36 124</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>8yr 10m</td>
<td>600 300 0 0 0</td>
<td>617 11 133</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>9yr 1m</td>
<td>600 500 0 0 0</td>
<td>693 15 172</td>
<td>634 o 23 &lt;0.45</td>
<td>0 0 15 14</td>
<td>-</td>
</tr>
<tr>
<td>9yr 8m</td>
<td>600 200 50 0</td>
<td>584 10 99</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>9yr 10m</td>
<td>600 0 350 0</td>
<td>616 9 89</td>
<td>367 9.5 24 &lt;3.0</td>
<td>-</td>
<td>22.9 63.0 28.4 36.6 0.8 121.2 91.0 17.8</td>
</tr>
<tr>
<td>10yr 10m</td>
<td>600 0 350 0</td>
<td>680 7 92</td>
<td>443 &lt;8.0 38 &lt;3.0</td>
<td>1 0 11 11</td>
<td>-</td>
</tr>
<tr>
<td>11yr 4m</td>
<td>600 0 350 5000</td>
<td>849 5 115</td>
<td>471 &lt;8.0 38 &lt;3.0</td>
<td>1 1 14 13</td>
<td>15.1 68.7 36.0 42.0 0.9 220.9 199.7 47.7</td>
</tr>
</tbody>
</table>

Normal Ranges

(6yr) 630-1490 45-258 72-305 (8-10yr) 390-1235 61-430 10-98 1.1-95 (adults) 1-3% 1-3% 3-12% 1-10% (adults) 5-24% 58-84% 25-56% 17-44% 0.6-2.9
(7yr) 660-1540 51-279 73-310 (10-12yr) 380-1420 73-455 16-194 1.4-153
(8yr) 690-1570 56-298 74-313
(9yr) 700-1600 60-313 74-312
(10yr) 720-1020 66-332 74-311
(11yr) 740-1640 69-343 73-310

a significantly decreased IgA level and slightly decreased IgG level (Table 1). Further immunological examinations revealed that he was deficient in IgA, IgG2, and IgG4. The levels of IgG2 against both *Hemophilus influenzae* and *Streptococcus pneumoniae* were also markedly decreased. The levels of his serum IgA were within the normal range during valproate medication, but the levels decreased below the normal range after 7 months of carbamazepine medication (Fig. 1). He was diagnosed as having carbamazepine-related immunoglobulin deficiency as we previously described in detail [1]. Carbamazepine was replaced with zonisamide, but he still experienced recurrent enterocolitis and otitis media and his immunoglobulin levels did not normalize (Fig. 1, Table 1).

In addition to susceptibility to infections, he always complained of general fatigue and loss of appetite, although he had sufficient rest and sleep. Physical examination revealed that his lower eyelids were dark colored and his abdominal tension was weak. He was found to have general asthenia according to the conventional Chinese medicine diagnosis as compatible with the indication of Shoukenchuto (SKCT) (delicate constitution in childhood, fatigue, nervousness, and chronic gastroenteritis). We prescribed SKCT extract granules (TJ-99, TSUMURA & Co, Japan) as 5.0 g/day (0.15g/kg/day), expecting an improvement of his general asthenia itself, not the infections. SKCT (TJ-99) contains a dried extract of the mixed crude drugs (peony root, cinnamon bark, jujube, glycyrrhiza, and ginger) and maltose.

As we expected, he no longer complained of general fatigue and loss of appetite, and the dark color of his lower eyelids almost disappeared. In addition to these improvements, surprisingly, he did not suffer from enterocolitis or otitis for 6 months after medication with SKCT, not requiring any other treatment such as antibiotics (Fig. 1). Immunological examinations after the treatment revealed that his serum IgG2, IgG4 and IgA levels still remained very low, but the total IgG level, and the number of circulating IgA-, IgM-, and IgD-positive B cells increased. In addition, the numbers of CD3-, CD4-, and CD8-positive cells increased, while that of CD19-positive cells decreased (Table 1). Lymphocyte proliferation assays by mitogens remarkably increased compared with the values before SKCT medication.

**DISCUSSION**

*In vitro* and *in vivo* experiments showed that Japanese herbal medicine (Kampo) has many kinds of effects on the immune system [2], but the effect of SKCT has not been elucidated well. In a child with recurrent bronchitis, pneumonia, and enterocolitis, SKCT decreased the incidence of these diseases. Immunological examinations showed a low CD8-positive cells before treatment (CD3: 60.5%, CD4: 47.9%, CD8: 10.0%, CD4/CD8: 4.8), and the percentage normalized after the treatment (CD3: 68.1%, CD4: 47.9%, CD8: 19.2%, CD4/CD8: 2.5) [3].

Miyakawa *et al.* [4] also reported the effects of Kampo medicine on a T cell subset in 11 children with general asthenia, which was represented by susceptibility to respiratory infection or enterocolitis. Shou-sai-ko-to (0.2g/kg) was administered to six children with a low percentage of CD4-positive cells, while SKCT (0.4g/kg) was given to five patients with a low percentage of CD8-positive cells. All the patients showed clinical improvement and the percentages of their T cell subsets normalized. The results suggested the usefulness of T cell subset measurement for drug selection in addition to the conventional diagnostic classification for Chinese medicine.

Our patient was treated with SKCT for his general asthenia, not for immunological abnormalities, but his susceptibility to infection markedly improved. The increase in the T cell percentage, not of the B cell percentage, in our patient suggests the importance of regulatory function of T cells for clinical improvement. The findings in our case and the previously reported cases suggest the usefulness of Japanese herbal medicine or Chinese medicine as an alternative or a supportive therapy for patients with immunological abnormalities. However, further clinical and experimental studies should be performed to clarify the mechanisms.

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**REFERENCES**


