LETTER TO THE EDITOR

Treatment of patients with polyarthritis and anti-HTLV-I antibodies with interferon-alpha

Human T cell lymphotropic virus type I (HTLV-I), the aetiologic agent of adult T cell leukemia/lymphoma (ATLL), is associated with the chronic neurodegenerative syndrome termed HTLV-I-associated myelopathy (HAM) or tropical spastic paraparesis (TSP). The proliferative synovitis have been reported to be in patients with ATLL and HAM/TSP. Patients with chronic inflammatory arthropathy are shown to be sero-positive for anti-HTLV-I antibodies (Ab) with a high frequency in the southwest of Japan, which is one of the endemic areas for HTLV-I. HTLV-I proviral DNA and viral gene expression have been detected in the synovial cells of polyarthritic patients with anti-HTLV-I. Transgenic mice that carry the HTLV-I genome develop chronic arthritis which resembles rheumatoid arthritis. It is known that IFN-α possesses a potent antiviral effect in treating viral diseases such as the chronic type C hepatitis and HAM. The present study was carried out to determine the efficacy and safety of IFN-α in treating patients with polyarthritis and anti-HTLV-I Ab.

Seven patients with polyarthritides were administered natural IFN-α (Otsuka Pharmaceutical, Tokushima, Japan) 2.5 to 4 x 10^6 IU daily for four weeks, reduced to three times a week for the following four weeks. Patients who responded favourably to this agent were administered for an additional four weeks. Four of the seven serum samples (cases 1–4) were positive for anti-HTLV-I Ab by particle agglutination assay (Serodia-ATL kit, Fujirebio, Japan), and confirmed by Western blotting (Eiitset ATL-WB kit, Eisai, Japan), while three of the seven samples (cases 5–7) were negative for anti-HTLV-I Ab. The clinical and laboratory features of these patients are shown in the table.

After eight weeks of IFN-α treatment, all four seropositive patients exhibited significant improvement in most of the clinical parameters for disease activity (figure). The number of tender and swollen joints decreased significantly from baseline. Swollen joints disappeared in all four seropositive patients after eight weeks of treatment. The three seronegative patients showed no improvement in most of the clinical parameters of disease activity. The number of tender joints was increased in case 5 and 6, and the number of swollen joints, in case 6. The erythrocyte sedimentation rate (ESR) and C reactive protein (CRP), each decreased in the four seropositive patients. In case 1 and 4, CRP values improved within the range of normal after eight and 12 weeks of treatment. However, the three seronegative patients showed no improvement in either the ESR or CRP. Patients with anti-HTLV-I Ab had an increased spontaneous proliferation of peripheral blood mononuclear cells (PB-MNC). Three of four seropositive patients (cases 1, 2 and 4) showed an increased

<table>
<thead>
<tr>
<th>Patient</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age/sex</td>
<td>71/F</td>
<td>36/M</td>
<td>60/F</td>
<td>64/F</td>
<td>58/M</td>
<td>78/F</td>
<td>45/F</td>
</tr>
<tr>
<td>Duration of disease (years)</td>
<td>2</td>
<td>5</td>
<td>3</td>
<td>6</td>
<td>4</td>
<td>6</td>
<td>11</td>
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<tr>
<td>Diagnosis of RA</td>
<td>Probable</td>
<td>Definite</td>
<td>Classic</td>
<td>Classic</td>
<td>Classic</td>
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</tr>
<tr>
<td>Class/stage</td>
<td>2/I</td>
<td>2/II</td>
<td>2/I</td>
<td>2/II</td>
<td>2/II</td>
<td>2/III</td>
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</tr>
<tr>
<td>Previous therapy</td>
<td>NSAIDs</td>
<td>PSL</td>
<td>GST</td>
<td>GST</td>
<td>PSL</td>
<td>GST</td>
<td>MTX</td>
</tr>
<tr>
<td>(prednisolone and/or SAARDs)</td>
<td>GST</td>
<td>D-Pc</td>
<td>MTX</td>
<td>D-Pc</td>
<td>MTX</td>
<td>Bucillamine</td>
<td>MTX</td>
</tr>
<tr>
<td>Lymphnode swelling</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>Skin erosion</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>Titer of anti-HTLV-I antibodies (PA method)</td>
<td>512</td>
<td>512</td>
<td>512</td>
<td>512</td>
<td>16</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Leucocyte counts ((mm^3)</td>
<td>6400</td>
<td>6000</td>
<td>6440</td>
<td>4850</td>
<td>9400</td>
<td>10500</td>
<td>4900</td>
</tr>
<tr>
<td>CRP level (mg/dl)</td>
<td>4.0</td>
<td>3.9</td>
<td>9.0</td>
<td>9.0</td>
<td>5.7</td>
<td>5.7</td>
<td>5.7</td>
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<tr>
<td>Rheumatoid factor (RAH) titre (IU)</td>
<td>&lt;40</td>
<td>320</td>
<td>80</td>
<td>320</td>
<td>5120</td>
<td>2560</td>
<td>5120</td>
</tr>
<tr>
<td>ESR (mm/1h)</td>
<td>104</td>
<td>114</td>
<td>92</td>
<td>50</td>
<td>68</td>
<td>140</td>
<td>64</td>
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<td>Shadow</td>
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</tr>
</tbody>
</table>

PSL = prednisolone; GST = gold sodium thiomolate; D-Pc = D-penicillamine; CCA = lornzetar disodium; MTX = methotrexate; PA method = particle agglutination method; SAARDs = slow-acting anti-rheumatic drugs.

Clinical and laboratory features of patients

Clinical and laboratory findings before and after IFN-α treatment. (A) Change in number of tender joints from pretreatment baseline value; (B) Change in number of swollen joints; (C) Change in ESR (%); (D) Change in CRP (%). Open circles (○) depict four patients with anti-HTLV-I Ab, closed circles (●) three patients without anti-HTLV-I Ab. Bars show mean (SD). *p < 0.05, vs pretreatment baseline value. (E) Spontaneous proliferation of peripheral blood mononuclear cells from patients with anti-HTLV-I Ab. (F) Spontaneous proliferation of peripheral blood mononuclear cells from patients without anti-HTLV-I Ab. Vertical axis shows (3H)-thymidine incorporation (cpm). Number depicts case. Shadow indicates the normal range.
spontaneous proliferation of PB-MNC at entry. The elevated spontaneous proliferation was considerably decreased in all three patients. In the three seronegative patients, the spontaneous proliferation of PB-MNC was within the normal range at entry, and they exhibited no significant difference in this parameter as a result of treatment. Although fever, epigastralgia, leukocytopenia and increases in transaminase were found, these adverse effects were not serious.

This appears to be the first report to show that IFN-α is effective clinically in treating polyarthritis patients who are seropositive for anti-HTLV-I Ab. Our present data strongly support the hypothesis that HTLV-I infection may be involved in the development of chronic inflammatory arthropathy in a subset of patients with polyarthritis.

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