PREDNISOLONE AS A NEW APPROACH FOR TREATMENT OF HTLV-1 ASSOCIATED POLYNEUROPATHY

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ABSTRACT
Objective: We have previously shown the implication of HTLV-1 in polyneuropathy in a HTLV-1 endemic area in Mashhad. Treatment with corticosteroids (prednisolone and methylprednisolone) have been recommended for HTLV-1 associated diseases. In the current study we attempted to evaluate the efficiency of prednisolone in HTLV-1 associated polyneuropathy

Methodology: All recognized cases of HTLV-1 polyneuropathy admitted to Imam Reza Hospital (between 1999-2004) were selected for the study. The other common causes of polyneuropathy were excluded using biochemical, hematological, and neurologic examination. Anti-HTLV-1 IgG assays were carried out and positive anti-HTLV-1 results were then confirmed by Western Blot Analyzing. All of the HTLV-1 associated polyneuropathy patients were given prednisolone, 1mg/kg and tapering 5mg/ per week, for three month.

Results: Muscle force and paresthesia of all cases were returned to normal pattern. This therapeutic regimen led to reduction of disease severity. Muscle force increased to V/V and paresthesia of all cases were severely decreased.

Conclusion: The results of present study suggest that immunosuppressive treatment is very effective for HTLV-1 associated polyneuropathy patients.

KEYWORDS: HTLV-1, Polyneuropathy, Prednisolone, Immunosuppressive.

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fatigue, multiple sclerosis like syndrome, cerebellar syndrome, spinocerebellar syndrome and motor neuron disease.\textsuperscript{3,7} Mashhad city is an endemic area for HTLV-1 infection.\textsuperscript{8} Therefore, we have suggested that one of the causes of polyneuropathy in this area is HTLV-1 infection.

Polyneuropathy is a term that describes the syndromes resulting from diffuse lesions of peripheral nerves.\textsuperscript{9} We have previously shown the implication of HTLV-1 in polyneuropathy in a HTLV-1 endemic area in Mashhad.\textsuperscript{10} Although, the efficiency of immunosuppressive treatment in different type of polyneuropathy has been controversial, treatment with corticosteroids (prednisolone and methylprednisolone) have been recommended for HTLV-1 associated diseases.\textsuperscript{11,12} Therefore, it is more likely that prednisolone could be an effective treatment for HTLV-1 associated polyneuropathy and thus in the current study we attempted to evaluate the efficiency of prednisolone in HTLV-1 associated polyneuropathy.

**METHODOLOGY**

All recognized cases of HTLV-1 polyneuropathy admitted to Imam Reza Hospital (between 1999-2004) were selected for the study. For exclusion of the other common causes of polyneuropathy such as diabetes, uraemia, hypothyroidism, collagen vascular disease, B12 deficiency, paraproteinemia, paraneoplastic syndrome,\textsuperscript{13} the tests and procedures used included glucose, urea, CBC, ESR, immunoglobulin electrophoresis tests, chest X ray, abdomen and pelvic sonography, complete systemic and neurologic examination, nerve conduction velocity (NCV) and electromyography (EMG) (Reporter, Italy). Moreover, history for alcohol consumption, occupational, accidental and suicidal poisoning were obtained.

Sera for this study were collected after obtaining patients informed consent. Serum samples were then stored at -20°C until anti-HTLV-1 IgG assays were carried out with commercial enzyme linked immunosorbant assay (ELISA) (Diapro, Italy) according to the manufacturer’s instruction. Positive anti-HTLV-1 results were then confirmed by Western Blot Analyzing (WBA).

**RESULTS**

The first case was a 30 years old female, which suffered from paresthesia and weakness in four limbs for 22 days before admission to hospital. In physical examination, proximal muscle force of four limbs was IV/V and distal in four limbs was II/V. All limbs had areflexia but objective sensation of the limbs was normal. Although HTLV-1 infection was not reported in her family history, her ELISA and WB tests for anti-HTLV-1 were positive. The axonal and demylinated sensorimotor polyneuropathy was confirmed by NCV and EMG. Cerebrospinal fluid (CSF) protein was 55mg/dl and anti-HTLV-1 in CSF was positive.

The second patient was a 49 years old man with distal paresthesia of four limbs for two years duration that progressed to muscle weakness before referring to neurology department. Physical examination showed distal hypoesthesia and areflexia of four limbs. The muscle force of four limbs was IV/V. ELISA and WB tests for HTLV-1 were positive. As the previous subject, NCV and EMG confirmed the axonal and demylinated sensorimotor polyneuropathy. CSF protein was 40mg/dl and anti-HTLV-1 in CSF was positive.

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age (year)</th>
<th>Onset of disease</th>
<th>Paresthesia</th>
<th>Pain</th>
<th>Muscle weakness</th>
<th>Transfusion history</th>
<th>Familial infection</th>
<th>Addiction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>30</td>
<td>22days</td>
<td>+</td>
<td>_</td>
<td>+</td>
<td>_</td>
<td>_</td>
<td>_</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>49</td>
<td>2years</td>
<td>+</td>
<td>_</td>
<td>+</td>
<td>_</td>
<td>_</td>
<td>_</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>70</td>
<td>1month</td>
<td>+</td>
<td>_</td>
<td>+</td>
<td>_</td>
<td>_</td>
<td>_</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>48</td>
<td>9years</td>
<td>+</td>
<td>+</td>
<td>_</td>
<td>_</td>
<td>+</td>
<td>_</td>
</tr>
</tbody>
</table>
The third case was a 70 years old female who was admitted to hospital with uncertain paraneoplastic syndrome. In physical examination, muscle force of distal and proximal of four limbs was II/V and all limbs had areflexia but objective sensation of the limbs was normal. Anti-HTLV-1 was positive using ELISA and WBA. The axonal and demyelinated sensorimotor polyneuropathy was confirmed by NCV and EMG. CSF protein was 45mg/dl and anti-HTLV-1 in CSF was positive.

The fourth case was a 48 years HTLV-1 positive old man with distal paresthesia of four limbs for nine years duration which led to muscle weakness before referring to neurology department. In her family history, her mother was HTLV-1 positive suffered from acute T cell leukemia (ATL). Physical examination showed distal hypesthesia and areflexia of four limbs. The muscle force of four limbs was IV/V. the axonal sensorimotor polyneuropathy was confirmed by NCV and EMG. CSF protein was 40mg/dl and anti-HTLV-1 in CSF was positive.

All of the HTLV-1 associated polyneuropathy patients were given prednisolone, 1mg/kg and tapering 5mg/ per week, for three month. This therapeutic regimen led to reduction of disease severity. Muscle force increased to V/V and paresthesia of all cases were severely decreased. The clinical data for the subjects are summarized in Table I,II & III.

**DISCUSSION**

It has been suggested that some neurological disorders are associated with HTLV-1 including: HAM/TSP, peripheral neuropathy, radiculoneuropathy, myopathy, peripheral facial nerve palsy. In HAM/TSP, peripheral nerve and muscles could be also affected.

Polyneuropathy is a term that describes the syndromes resulting from diffuse lesions of

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**Table-II: Experimental findings in HTLV\textsubscript{1} polyneuropathy cases**

<table>
<thead>
<tr>
<th>Case</th>
<th>Muscle force</th>
<th>Sensation disorders</th>
<th>Serum protein</th>
<th>NCV</th>
<th>CSF proten</th>
<th>Anti HTLV\textsubscript{1}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>IV/V</td>
<td>Areflexia</td>
<td>_</td>
<td>+</td>
<td>55</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>V/V</td>
<td>Areflexia</td>
<td>Hyposthesia</td>
<td>+</td>
<td>40</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>II/V</td>
<td>Areflexia</td>
<td>Hyposthesia</td>
<td>+</td>
<td>45</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>V/V</td>
<td>Areflexia</td>
<td>Hyposthesia</td>
<td>+</td>
<td>40</td>
<td>+</td>
</tr>
</tbody>
</table>

Prox: proximal, Dist : distal

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**Table-III: Clinical status and experimental findings of HTLV\textsubscript{1} associated polyneuropathy cases after treatment with prednisolone**

<table>
<thead>
<tr>
<th>Case</th>
<th>Pain</th>
<th>Paresthesia</th>
<th>Sensation disorders</th>
<th>Muscle force</th>
<th>Tendon reflexes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>_</td>
<td>_</td>
<td>Normal</td>
<td>V/V</td>
<td>IV/V</td>
</tr>
<tr>
<td>2</td>
<td>_</td>
<td>_</td>
<td>Normal</td>
<td>V/V</td>
<td>V/V</td>
</tr>
<tr>
<td>3</td>
<td>_</td>
<td>_</td>
<td>Normal</td>
<td>V/V</td>
<td>V/V</td>
</tr>
<tr>
<td>4</td>
<td>_</td>
<td>_</td>
<td>Normal</td>
<td>V/V</td>
<td>V/V</td>
</tr>
</tbody>
</table>

Prox: proximal, Dist : distal
Treatment of HTLV-1 associated polyneuropathy with Prednisolone

All studied cases in our report were HTLV-1 positive and the disease started with paresthesia progressing to muscle weakness except in subject four, which did not have muscle weakness. Studied subjects had globing and stoking except patient one. All patients had axonal sensorimotor polyneuropathy and patient one had demyelination too. However, in one case we found a family history of HTLV-1 infection and ATL, there was no confirmed history of addiction, transfusion and family history of HTLV-1 infection in other cases.

The implication of HTLV-1 in polyneuropathy in Mashhad (Iran) has been previously reported. However, the benefit of prednisolone therapy in different type of polyneuropathy has been controversial, for treatment of HTLV-1 associated diseases; corticosteroids (prednisolone and methylprednisolone) have been suggested. Therefore, it is more likely that prednisolone could be an effective treatment for HTLV-1 associated polyneuropathy. Our results shown that in all of the HTLV-1 associated polyneuropathy cases, prednisolone, 1 mg/kg and tapering 5 mg/ per week for three month, led to reduction of disease severity. Muscle force and paresthesia of all cases returned to normal suggesting that prednisolone was effective in the treatment of HTLV-1 associated polyneuropathy.

REFERENCES