Acute Human T-Lymphotrophic Virus Type 1–Associated Myelopathy

A Clinicopathologic Study

Naoki Kasahata, MD; Junichi Shiota, MD, PhD; Yumi Miyazawa, MD; Imaharu Nakano, MD, PhD; Shigeo Murayama, MD, PhD

Background: Recently, acute human T-lymphotropic virus type 1–associated myelopathy (HAM) was reported clinically without pathologic information. We report an autopsy case of acute HAM.

Objective: To report the case of a 52-year-old man with acute-onset gait disturbance followed by rapidly progressive paraplegia, who died 9 months later.

Results: The postmortem study showed swelling of the thoracic spinal cord. Histologically, there was inflammation and vacuolation in the white matter.

Conclusion: We propose that these pathologic findings, mimicking tropical spastic paraparesis, may represent the characteristic pathologic features of acute HAM.

Arch Neurol. 2003;60:873-876

Human T-lymphotropic virus type 1 (HTLV-1)–associated myelopathy (HAM) has a gradual onset and a slowly progressive course.1-3 Recently, a patient with rapidly progressive HAM was described,4 but no histologic study had been performed. To our knowledge, this is the first report of an autopsy case of rapidly progressive HAM. Histologically, there was characteristic vacuolation in the white matter of the spinal cord. In cases of tropical spastic paraparesis (TSP), a similar pathologic characteristic, status spongiosus, was stressed by Roman et al.3 Until HTLV-1 was confirmed to be an etiologic factor in TSP,3,5 most TSP cases were not treated with steroids, as in ours. Thus, the close similarity of the present case to TSP may indicate that the difference in pathologic characteristics between HAM and TSP may be influenced by medical intervention.

REPORT OF A CASE

A 52-year-old man had rapidly progressive paraparesis, urinary disturbance due to neurogenic bladder, and a high titer of HTLV-1 in the cerebrospinal fluid. He was admitted to the hospital. He had no family history of leukemia or paraplegia. He had alcoholism and a history of stimulant drug abuse without an apparent history of using narcotics. He also had diabetes mellitus and positive antihepatitis C virus antibody but no history of blood transfusion.

On neurologic examination, he had psychiatric symptoms of amnesia and aggressiveness, flaccid paraplegia, and hyperreflexia of the bilateral biceps and bilateral patellar tendons. Neither Babinski sign nor sensory disturbance was apparent.

Serum analysis revealed a white blood cell count of 9.4×10^3/µL (stab neutrophil, 1%; segmented neutrophil, 77%; lymphocytes, 18%; monocytes, 3%; basophils, 1%); red blood cell count, 4.18×10^6/µL; hemoglobin, 14.0 g/dL; hematocrit, 39.3% (0.39/1.00); mean corpuscular volume, 94 fl; mean corpuscular hemoglobin, 33.5 pg; mean corpuscular hemoglobin concentration, 35.6% (2.2 fmol); platelet count, 235×10^3/µL; T cells, 85.3%; B cells, 6.9%; CD4, 63.3/µL; CD8, 22.6/µL; and CD4/CD8, 2.80. A serum test for syphilis, Treponema pallidum hemagglutination, and anti–human immunodeficiency virus antibody test were negative. The titer of anti–HTLV-1 antibody was 1:4096 in serum by the particle agglutination method. His cerebrospinal fluid chemistry demonstrated 9.3 white blood cells/mm³, mononuclear cell–polymorphonuclear cell ratio, 26.2; pH, 7.5; total protein, 57 mg/dL;
glucose, 138 mg/dL (7.7 mmol/L); chloride, 113 mEq/L; IgG, 9 mg/dL; IgA, 1 mg/dL; IgM, <1 mg/dL; and anti-HTLV-1 antibody titer, 1:1024. Swelling of the thoracic cord was suspected on computed tomographic scan after myelography. He progressed to complete paraplegia in 2 months. Administration of 750 mg of cyanocobalamin per day did not alter the course of progression. Diabetes mellitus and psychiatric symptoms hindered steroid treatment; instead, interferon alfa at 3 million units per week was administered between September 14, 1993, and January 30, 1994, without clinical improvement. Parenteral supplementation with multivitamins, including vitamin cyanocobalamin, did not modify the clinical course. He had recurrent urinary tract infections and decubitus and died of sepsis on May 11, 1994. The total clinical course was 11 months.

The autopsy was carried out with a postmortem interval of 9 hours 20 minutes. There was pneumonia and old tuberculosis of the subcarinal lymph nodes, but no apparent visceral complications of diabetes mellitus. The brain weighed 1410 g. On gross examination, the brain was unremarkable. The spinal cord appeared pale and showed swelling from T4 to T10 (Figure 1).

Cross-sections showed rostrally accentuated degeneration of Goll columns and caudally pronounced degeneration of the pyramidal tracts. Histologic examination showed myelin pallor accentuated in the lateral columns and the deep posterior columns and vacuolation in the circumferential white matter in the middle to lower thoracic segments (Figure 2A) associated with perivascular infiltration of lymphocytes in the lateral columns (Figure 2B). There was moderate thickening of the leptomeninges. Caudally, there was pyramidal tract degeneration and mild white matter vacuolation in the lumbar cord (Figure 2C). Rostrally, myelin pallor of the gracile fascicles and anterior and posterior spinocerebellar tracts was observed. There was occasional perivascular and parenchymal lymphocyte infiltration at the anterior horn of the lumbar spinal cord. The periventricular myelin was pale, and occasional neuronophagia was noted in the precentral gyrus. The left sural nerve showed a mild decrease in myelinated fibers with interfascicular variability, clusters of small myelinated fibers, and macrophages.

An ultrastructural study showed vacuolation of the myelin sheaths, abundant macrophages in and around them, and isomorphic gliosis (Figure 2D and E). These findings suggested chronic progressive axonal degeneration. An ultrastructural study of the sural nerve showed relatively well-preserved unmyelinated fibers.

Acute-onset and rapid progression constituted the unique clinical features of this case (Table). Swelling of the spinal cord was suspected radiologically and confirmed pathologically. In typical HAM, there is chronic progressive inflammation resulting in severe degeneration of the white matter.6-11 The most characteristic site of involvement is the lower thoracic spinal cord. The lateral columns are always the most severely involved. These features were observed in this patient, although there was a more extensive response of inflammatory cells. The involvement of the peripheral nerves, often reported in association with HAM,12 was confirmed pathologically and may have been responsible for the hypotonicity of the lower limbs observed in this case, as is suggested by another case report.13 This case also had a brain lesion, which often accompanies HAM,14 although neuronophagia of Betz cells has not been described.

In addition, vacuolation of the spinal white matter was conspicuous in this case. The extension of severe spongiosis to the ventrolateral column is atypical for subacute combined degeneration. Moreover, supplementation with cyanocobalamin did not improve the patient’s symptoms. There were no pathologic findings of pellagra encephalopathy. Thus, it was suggested that this finding could be attributed to the acute phase of HAM. Vacuolation of spinal white matter was reported in a patient with HAM of 2 years’ duration.8 Vacuolation is sometimes reported as a finding in TSP and is described as status spongiosis.3 This vacuolation of spinal white matter may correspond to radiologic and
macroscopic evidence of swelling of the thoracic spinal cord, and may be a characteristic pathologic finding of acute HAM.

Accepted for publication October 28, 2002.

Author contributions: Study concept and design (Drs Kasahata and Murayama); acquisition of data (Drs Kasahata, Shiota, Miyazawa, Nakano, and Murayama); analysis and interpretation of data (Drs Kasahata, Nakano, and Murayama); drafting of the manuscript (Drs Kasahata and Murayama); critical revision of the manuscript for important intellectual content (Drs Shiota, Miyazawa, Nakano, and Murayama); obtained funding (Dr Murayama); administrative, technical, and material support (Drs Nakano and Murayama); study supervision (Dr Murayama).

This study was funded by Support in Aid from the Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan.

This case was presented at the XIVth International Congress of Neuropathology, Birmingham, England, September 6, 2000.

We thank Ms Sugiura for technical support in the ultrastructural study.

Corresponding author and reprints: Shigeo Murayama, MD, PhD, Department of Neuropathology, Tokyo Metropolitan Institute of Gerontology, 33-2, Sakae-chou, Itabashi-ku, Tokyo 173-0015, Japan (e-mail: smurayama@tmig.or.jp).

**REFERENCES**

5. Roman GC, Roman LN. Tropical spastic paraparesis: a clinical study of 50 patients from Tumaco (Colombia) and review of the worldwide features of the syndrome. J Neurol Sci. 1988;87:121-138.

---

**Clinical and Pathologic Differences Between Typical HAM and the Present Case (Acute Variant)**

<table>
<thead>
<tr>
<th>Clinical course</th>
<th>Typical HAM</th>
<th>Present Case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tonus</td>
<td>Spastic</td>
<td>Flaccid</td>
</tr>
<tr>
<td>Thoracic cord</td>
<td>Atrophic</td>
<td>Swelling</td>
</tr>
<tr>
<td>Vacuolation</td>
<td>Sometimes seen in shorter clinical course</td>
<td>Prominent</td>
</tr>
</tbody>
</table>


