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Clinical Report

Quantitative assessment of spasticity in human T-cell lymphotropic virus type I–associated myelopathy/tropical spastic paraparesis

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People with human T-cell lymphotropic virus type I–associated myelopathy/tropical spastic paraparesis (HAM/TSP) develop spasticity. The authors examined 34 patients with HAM/TSP in Perú using a device that measures tone in the gastroc-soleus-Achilles tendon unit and provides a quantitative spasticity assessment (QSA). Tone in the 34 patients was more than double that of women with asymptomatic HTLV-I infection. The device may help to track progression in HTLV-I infection. *Journal of NeuroVirology* (2005) **11,** 70–73.

Keywords: HTLV-I; myelopathy; spasticity

Background

Human T-cell lymphotropic virus type I (HTLV-I) causes HTLV-I–associated myelopathy/tropical spastic paraparesis (HAM/TSP). Of 10 to 20 million HTLV-I–infected people in the world, approximately 3000 have HAM/TSP (de The and Bomford, 1993; Leon *et al*, 1997; Osame, 1999). The estimated lifetime incidence of HAM/TSP in HTLV-I–seropositive people is between 0.025% and 2.4% (Maloney *et al*, 1998; Murphy *et al*, 1997). We are attempting to define the neurologic spectrum of HTLV-I infection using a sensitive and quantitative measure of muscle tone. At one end of the spectrum, we have detected increased muscle tone in women with asymptomatic HTLV-I infection, as compared to women without HTLV-I infection (Zunt *et al*, 1999). We now examine the other end of the spectrum to determine if quantitative assessment of spasticity is feasible in patients with HAM/TSP, if results are comparable to those of people with spastic paraparesis caused by other diseases, and if clinical examination can predict the results of the quantitative assessment.

Symptoms of HAM/TSP usually develop during the fifth decade of life and typically include leg weakness, back pain, and bladder dysfunction. All affected individuals eventually demonstrate signs of spasticity in the lower limbs (Roman and Roman, 1988). Spasticity is a state of increased muscle tone that results in a velocity-dependent resistance to muscle stretch. Measurement of spasticity involves stretching a muscle and then measuring the response to this stretch. The difficulty of applying a consistent stretch and accurately measuring the response to this stretch may compromise the reliability and accuracy of such measurements performed during the routine neurologic examination. A device developed at the University of Washington solves this problem by providing a quantitative spasticity assessment (QSA). Mean QSA value is 24 Newton-meters/radian (N-m/r) for adults without neurologic disease and 98 N-m/r for adults with spasticity due to noninfectious causes (Lehmann *et al*, 1989; Price *et al*, 1991). In our prior study of women in Perú with asymptomatic HTLV-I infection, the mean QSA score

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was 27.1 N-m/r, significantly higher than in a comparison group without HTLV-I infection (Zunt *et al*, 1999).

In view of the high prevalence of spasticity in people with HAM/TSP and the potential benefit of quantitative measurement of spasticity for better understanding the pathogenesis of HAM/TSP and monitoring response to therapy, we decided to quantitate spasticity in people with HAM/TSP. We performed standard neurologic examinations and QSA in a group of study subjects with clinical signs of HAM/TSP identified in Lima, Perú.

Results

Signs and symptoms of the 34 patients with confirmed HAM/TSP are described in Tables 1 and 2. The nine patients who could not be scheduled to undergo QSA testing did not differ significantly from the 34 who did on any of the variables listed in Table 1 or 2. Mean and median QSA values were 62.5 N-m/r (SD 54.5) and 39.9 (range 14.1 to 234.3), respectively. Also listed in Tables 1 and 2 are the relations between the results of QSA and the variables listed. Values on QSA were significantly correlated only with increased tone on examination. Fifteen of the 34 (44%) subjects were taking medications to relieve spasticity. There was no statistically significant difference in mean QSA value between subjects taking or not taking medications. Figure 1 shows boxplots of QSA values for patients with HAM/TSP, and for asymptomatic Peruvian women with and without HTLV-I infection. Mean QSA score was significantly different between groups ($P < .001$), and remained significant when only females from each group were compared ($P < .001$). Mean age of patients with HAM/TSP (44.3 years) was significantly higher than women with asymptomatic infection (34.8 years; $P < .001$).

Table 1 Neurologic symptoms in people with clinical evidence of human T-lymphotropic virus type 1–associated myelopathy/tropical spastic paraparesis (HAM/TSP)

Variable[a]	*HTLV-I seropositive n = 34*	*Association with QSA P value*[b] *n = 34*
Age in years (±SD)	44.7 (13)	.1
Female (%)	27 (79)	.3
Symptoms		
Difficulty walking	34 (100)	—
Duration in years (±SD)	9.8 (6.0)	.7
Pain in legs	21 (62)	.6
Duration in years (±SD)	7.0 (5.4)	.3
Pain in back	24 (71)	.6
Duration in years (±SD)	6.0 (7.0)	.9
Pain in joints	21 (61)	.2
Pain in arms	9 (27)	.7
Abnormal sensation in arms	19 (56)	.7
Duration in years (±SD)	3.4 (3.1)	.6
Bladder dysfunction	29 (85)	.1
Constipation	25 (74)	.1
Number of symptoms	4.4 (1.7)	.5

[a]For continuous variables mean (±standard deviation); for discrete variables counts (%).
[b]*P* value based on Spearman's correlation for continuous variables and Mann-Whitney *U* for discrete variables.

Table 2 Neurologic dysfunction in people with human T-lymphotropic virus type 1–associated myelopathy/tropical spastic paraparesis (HAM/TSP)

Dysfunction[a]	*HTLV-I seropositive n = 34*	*Association with QSA P value*[b] *n = 34*
Mental status	10 (29)	.2
Cranial nerve	1 (3)	.6
Strength	23 (68)	.4
Deep tendon reflexes	30 (88)	.5
Muscle tone[c]	30 (88) (mean score = 2)	.006
Sensation	2 (6)	.3
Coordination	2 (6)	.2
Gait	33 (88)	.6
QSA	62.5 (55.6)	—

[a]For continuous variables mean (±standard deviation); for discrete variables counts (%).
[b]*P* value based on Pearson's correlation for continuous variables and Mann-Whitney *U* for discrete variables.
[c]Increased tone defined as score of 1 or higher on the Ashworth scale.

Discussion

Spasticity eventually develops in patients with HAM/TSP. This study enrolled 51 people with symptoms and signs of HAM/TSP, 43 of whom had serologic evidence of HTLV-I infection.

We used a QSA device to quantitatively measure muscle tone in the study subjects. We know of no previous studies that attempted to quantitate muscle tone in people with HAM/TSP. QSA values in patients with HAM/TSP were more than

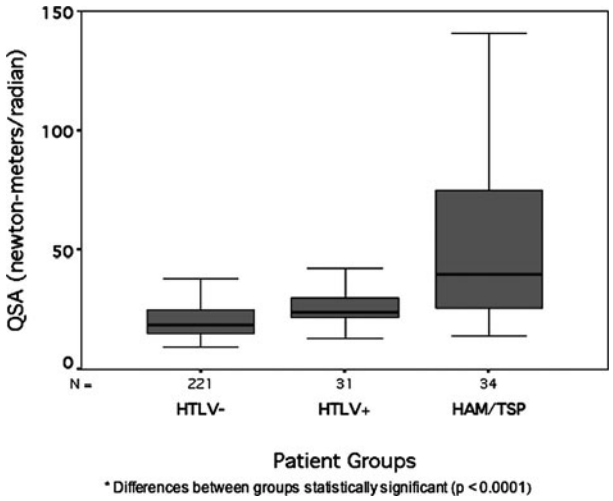

Figure 1 Median QSA values. Difference between groups statistically significant ($P < .0001$).

twice those measured in women with asymptomatic HTLV-I infection (mean, 62.5 versus 27.1 N-m/r), but less than those measured in patients with spasticity due to noninfectious causes (mean, 62.5 versus 98 N-m/r).

One limitation of this study is the limited experience with QSA in adults. Although QSA has demonstrated differences in muscle tone between women with asymptomatic HTLV-I infection and people with HAM/TSP, it has not been evaluated longitudinally in either group. In addition, variations in QSA values occur over time in children, presumably due to maturation, and day-to-day variation in adults may be larger.

Long-term follow-up of these patients will determine the reproducibility of the QSA for measuring muscle tone in adults with HAM/TSP and whether values will correlate with other clinical evidence of progression of disease. Should the QSA prove reproducible and reliable for quantitating spasticity, it could also be used to monitor quantitatively the effect of therapy upon the spasticity of HAM/TSP. In addition, QSA may prove more sensitive than the neurologic examination for detecting spasticity.

Subjects and Methods

Study design
A study neurologist invited all study subjects with clinical evidence of HAM/TSP registered at the Instituto de Ciencias Neurológicas (ICN) in Lima, Perú, to participate in the study. Informed consent was obtained from all study subjects. The study protocol was approved by the human subjects committees of the University of Washington and the Universidad Nacional Mayor de San Marcos in Lima. Between March and November 1997, 51 consenting patients with spastic paraparesis were screened for HTLV-I infection. Their sera were tested by commercially available enzyme-linked immunosorbent assay (ELISA) for HTLV-I antibody (Cambridge Bioscience, Worcester, MA), and those positive on ELISA were confirmed using an rp21e enhanced Western blot assay (Cambridge Bioscience, Worcester, MA). ELISA-positive specimens were considered HTLV-I seropositive if the Western blot revealed bands at p24, and gp46 or rp21env. If only other viral-specific bands were present, such as p53 or p19, the patient was considered indeterminate. Of the 51 patients tested, 43 (84%) were HTLV-I positive and were diagnosed with HAM/TSP, and 34 patients completed all parts of the study.

Neurologist's assessment
One of the study neurologists (SM, JZ) administered a questionnaire and performed a standard examination. The questionnaire included questions about demographics and about pain or sensory dysfunction in the arms or legs, weakness of the limbs, stiffness, and impotence or incontinence of bladder or bowel. The neurologic examination entailed a detailed and standardized assessment of cranial nerve function, muscle strength, deep tendon reflexes, sensory function (light touch, pinprick, and vibration), coordination, and gait. In addition, tone in the lower limbs was assessed using the modified Ashworth scale (Bohannon and Smith, 1987).

Quantitative spasticity assessment
The QSA device developed at the University of Washington measures the variation in elastic and viscous stiffness of the gastroc-soleus-Achilles tendon unit by oscillating the foot over precise sinusoidal displacements at various frequencies, and measuring the resulting torque response of the tendon unit (Lehmann *et al*, 1989). Assessment involved placing the subject supine on an examining table with the foot attached to the machine by means of a footplate. The computer randomly varied the frequency of sinusoidal oscillation. Displacement and torque were measured simultaneously during the testing, and using Fourier analysis, the torsional stiffness was measured in Newtonmeters/radian (N-m/r). The variation of stiffness over the range of applied frequencies formed the basis of a single QSA summary variable, the stiffness path length. Higher QSA values denote greater variations in torsional stiffness over the range of applied frequencies. The QSA value was derived for the left ankle, unless there was a previous injury or surgery to that ankle, in which case the right ankle was used. In a previous study, this system has shown significant and reproducible differences between people with and without spasticity resulting from cerebral palsy (Price *et al*, 1991).

Statistical analysis
We used Mann-Whitney *U* tests for correlation of QSA with neurologic symptoms and signs that were discrete variables, Spearman's test for those that were continuous variables, such as age and duration of symptoms, and Kruskal-Wallis test for comparison of QSA between patients in this study and patients enrolled in our prior study (Zunt *et al*, 1999). Descriptive analyses provided percents, means, medians, and standard deviations. Statistical analyses used SPSS for Macintosh, version 10 (SPSS Inc., Chicago).

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