



Relationship Between Clinical and Urodynamic Findings in HTLV-1-Infected Patients with HAM/TSP

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Abstract

Background: Human T-lymphocyte virus type-1 (HTLV-1) infection and HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP) are endemic in the northeastern population of Iran. Urologic manifestations of the syndrome are different in various stages of HAM and should be evaluated via urodynamic study. The northeastern region of Iran is among the endemic areas; therefore, a comprehensive study is needed to investigate the clinical symptoms and urodynamic findings of these patients.

Methods: In this study, we examined the clinical features and urodynamic findings of 50 HAM/TSP patients who referred to the urology clinic of Imam Reza Hospital in Mashhad. Data were collected using checklists and analyzed by SPSS software. The significance level of 0.05 was used in all statistical tests.

Results: Among 50 patients, 27 (54%) were female. The mean age was 57.56 ± 11 years. The most common clinical findings in patients were urinary frequency (88%), followed by urgency (86%). In addition, the most common urodynamic finding was detrusor overactivity (DO; 78%). Among the studied patients, 62% had pain in the low back or lower extremities, 10% had detrusor sphincter dyssynergia (DSD), 66% had a kind of sensory abnormality, 46% had urinary incontinence, 4% had retention, and 34% had no clinical signs. Regarding neurological symptoms, 36% had rigidity and 28% had an abnormal gait. There was a significant relationship between abnormal gait and DO, DSD, urodynamic incontinence, and decreased urinary compliance ($P = 0.01, 0.02, 0.009, \text{ and } 0.002$, respectively).

Conclusions: We found that neurologic symptoms and lower urinary tract symptoms (LUTS) do not always synchronize and LUTS may be related to neurologic symptoms. Therefore, urinary and urodynamic evaluations must be performed in the first step for HAM/TSP patients. Among LUTS, only was urinary urgency related to urodynamic findings. Neurologic symptoms were significantly associated with DSD and thus, they can alarm for upper urinary tract damage.

Keywords: HTLV-1, Urodynamic Findings, Lower Urinary Tract Symptoms

1. Background

Human T-cell lymphotropic virus type 1 (HTLV-1) infection with over 20 million affected patients worldwide is an endemic disease in Northeastern Iran. This virus can spread through blood-borne transmission and breastfeeding. The HTLV-1 infection can lead to serious complications including adult T-cell leukemia and neurological disorders such as HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP) (1-3).

Neurological symptoms of HAM/TSP present after a latent phase, usually starting with gait abnormalities and continuing with motor and sensory impairments, particularly in the low back and lower extremities (4-7). Moreover,

disorders of the urogenital system are of utmost importance in these patients and can greatly impair their quality of life (8-10). The majority of patients with HAM/TSP present with upper and lower urinary tract symptoms (LUTS) including urinary frequency, urgency, and incontinence. The LUTS have been reported to be associated with neurological disorders in these patients (2, 8, 11, 12).

The complete functional assessment of detrusor and external urinary sphincter through urodynamic study can greatly contribute to the detection of the defective neurologic focus, help tremendously in diagnosis and management of HTLV-1-infected patients, and allow for early therapeutic interventions (2, 8).

2. Objectives

We performed this descriptive study to investigate the urodynamic abnormalities in HAM/TSP patients who referred to an outpatient clinic and evaluate the possible linkage with their neurological impairments.

3. Methods

In this cross-sectional study, we selected 50 patients with HAM/TSP who referred to the Urology Clinic of Imam Reza Hospital, Mashhad, during 2017 - 2018 using a non-random goal-directed sampling method. All participants consented before they took part in the study. The Ethics Committee of Mashhad University of Medical Sciences approved the performance of this study.

The inclusion criteria were having LUTS or neurologic findings of HTLV-1 and giving informed written consent. All patients were cases of HTLV-1 whose HAM diagnosis was confirmed by laboratory and clinical findings. Patients with any of the following were excluded from the study: pregnancy and a documented history of neurologic (e.g. spinal trauma, multiple sclerosis, etc.) or urologic diseases (e.g. active urinary infection, urethral stricture, benign prostatic hyperplasia, etc.) that interfered with assessed findings.

After obtaining informed consent from all patients, a thorough medical history was taken with an emphasis on stimulatory (dysuria, frequency, urgency, and nocturia) and obstructive urinary symptoms (dribbling, hesitancy, poor stream, retention, etc.). Then, a complete physical examination, especially neurologic examination, was performed. After the prescription of prophylactic antibiotics, all patients underwent urodynamic studies under standard settings by a single expert operator. Data were collected using checklists for further extraction and analysis.

Urodynamic studies were performed in three phases of uroflowmetry, cystometry, and pressure-flow study (PFS). During uroflowmetry, maximal urinary flow (Q_{max}), mean urinary flow (Q_{ave}), and the shape of the urinary diagram were recorded and assessed. The inner pressure of the bladder (P_{ves}), abdomen (P_{abd}), and detrusor (P_{det}), as well as capacity, compliance, involuntary contractions of detrusor, and urinary leak, were assessed and recorded by cystometry. PFS was performed to investigate the urination of patients in terms of urinary obstruction and detrusor contraction force, based on Abraham-Griffith nomogram. Moreover, urodynamic urinary incontinence (UD) was recorded during urodynamic studies.

The collected data were analyzed using SPSS software (version 22 for Windows, IBM Statistics, Chicago, USA). The Kolmogorov-Smirnov test was used to assess the normal distribution of the data. The independent samples *t*-test, Mann-Whitney test, and chi-square test were used to compare data between groups. Descriptive statistics were used to present data.

4. Results

Of 50 HAM/TSP patients studied, 27 (54%) were female and 23 (46%) were male. The mean age was 57.56 ± 11 years, ranging from 30 to 72 years. Seen in 33 patients (66%), sensory abnormality was the most common observed neurological finding, followed by pain in the low back or lower extremities ($n=31$; 62%), rigidity ($n=18$; 36%), abnormal gait ($n=14$; 28%), increased DTR ($n=12$; 24%), spastic paraplegia ($n=10$; 20%), and impaired balance ($n=5$; 10%). Seventeen patients (34%) had no clinical signs.

Among LUTS, urinary frequency (88%) was the most prevalent symptom, followed by urgency (86%), urinary incontinence (46%), and retention (4%). The most common findings in urodynamic study were detrusor overactivity (DO; 78%), UD incontinence (40%), fast flow (36%), low compliance (34%), obstruction (12%), detrusor sphincter dyssynergia (DSD; 10%) and detrusor underactivity (8%).

Gait disorder was significantly associated with DO ($P=0.01$), DSD ($P=0.009$), UD incontinence ($P=0.02$), and low compliance ($P=0.002$). Spastic paraplegia was significantly associated with DO ($P=0.03$), DSD ($P=0.02$), UD incontinence ($P=0.01$), and low compliance ($P=0.001$), but had no significant association with obstruction ($P=0.12$).

Among LUTS, only had urgency a significant association with urodynamic findings including DO ($P=0.01$), DSD ($P=0.04$), and UD incontinence ($P=0.005$). Dysuria and frequency were not significantly associated with urodynamic findings ($P=0.42$ and 0.12 , respectively).

Urinary incontinence had no significant relationship with obstruction ($P=0.32$) and underactivity ($P=0.12$). However, retention was significantly related to obstruction ($P=0.01$) and underactivity ($P=0.02$).

5. Discussion

The HTLV-1 infection is endemic in the northeastern population of Iran and a large number of population is suffering from its complications such as HAM/TSP. Patients with this disorder often complain of neurological and urinary symptoms that impair their quality of life. Therefore,

it is of cardinal importance to know more about this viral infection and its urological complications that are the consequences of HAM/TSP. Reports claim that the majority of these patients have urinary dysfunction, which is a common complaint of the HAM/TSP patients (8, 13-15).

In this study, we found a relatively high prevalence of neurological symptoms including pain in low back and lower limbs, sensory abnormalities, rigidity, gait disorder, increased DTR, spastic paraplegia, and impaired balance. Among LUTS, the urinary frequency was the most prevalent symptom, followed by urgency. The most common finding in the urodynamic study was DO, followed by UD incontinence.

Our results indicated that gait abnormality and paraplegia were significantly associated with DO, DSD, UD incontinence, and low compliance. We also found that among LUTS, only had urgency a significant association with urodynamic findings. Urinary retention was significantly associated with obstruction and underactivity in our study.

Castro et al. indicated that urodynamic disorders in HTLV-I-infected patients show the effect of the virus on the urinary system in the early stages. In contrast, the virus affects the upper urinary tract in the HAM/TSP patients, leading to DSD. Consistent with our study, they indicated that DO was the most prevalent urodynamic finding and most probably the cause of urinary symptoms (11). Rocha et al. also indicated 90.5% of patients had abnormal urodynamic findings, among whom the most important ones were bladder hyperreflexia and DSD (16). This is also in line with the findings of Lima et al. who reported bladder hyperreflexia in 80.76% of HAM/TSP patients. Their results were also similar to ours in terms of underactivity rate (3.84% vs. 8%). However, they reported the prevalence of DSD to be 34.16%, which is much higher than that found in our study. They also reported that 34% of patients had flow disorders, which is consistent with our results (17).

Contrary to the abovementioned studies and our results, Mori et al. found that detrusor hypoactivity was the most substantial finding in HTLV-I-infected patients (18). This was inconsistent with the results of another study by Sakiyama et al. who found DO in 66% of patients, while 15% had no or decreased detrusor contractions along with sensory impairment of the bladder. They also reported DSD as a common finding in these patients (14).

A limitation of the current study was the small sample size, which can be imputed to the social stigma of the disease, leading to underreporting of the disease by patients and their resistance against referring to treatment centers.

Another limitation was the low availability of diagnostic tools in small cities and villages in the region.

5.1. Conclusions

Based on the results, we can say that the most common LUTS in the population of the study were urinary frequency, followed by urgency. Although the most common urodynamic finding in the patients was DO, the most important one can be DSD because it was significantly associated with serious neurologic impairments and thus, it can be a prognostic factor in evaluating disorders of the upper urinary tract.

Among LUTS, only was urinary urgency markedly associated with urodynamic findings. Since the neurologic findings of the patients do not always coincide with the LUTS and LUTS might present earlier, urologic and urodynamic assessments should be performed in early stages of the disease.

Footnotes

Authors' Contribution: Study concept and design: Mahmoud Tavakkoli and Maliheh Keshvari Shirvan. Analysis and interpretation of data: Maryam Salehi and Salman Soltani. Drafting of the manuscript: Alireza Ghoreifi Nezhadian. Critical revision of the manuscript for important intellectual content: Mahmoud Tavakkoli, Maliheh Keshvari Shirvan, Alireza Ghoreifi Nezhadian, Amin Mirsani, and Salman Soltani. Statistical analysis: Maryam Salehi. Acquisition of data: Hossein Keramati.

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