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URODYNAMIC ALTERATIONS IN PATIENTS WITH HTLV-1 INFECTION

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ABSTRACT

Objectives: The HTLV-1 is a retrovirus that causes several diseases, including tropical spastic paraparesis or HTLV-1 associated myelopathy (or TSP/HAM, as designated by the World Health Organization - WHO) described in 1985. In Brazil, the first cases were reported in 1989. In order to evaluate the urodynamic alterations of infected patients, 48 cases were studied: 26 TSP/HAM and 22 non-TSP/HAM.

Material and Method: Evaluation was performed by testing, cystometry, abdominal pressure, differential pressure, detrusor leak point pressure, maximum flow pressure, and electromyography.

Results: 80.76% TSP/HAM patients showed hyperreflexic bladder, and 34.16% had detrusor-sphincter dyssinergia; 82.6% of this group had abnormal uroflow tests. Non-TSP/HAM patients had hyperreflexic bladders in 22.72% of the cases, and detrusor-sphincter dyssinergia was not assessed. For these patients, uroflow rate was normal in 70% of the cases.

Conclusions: Patients infected by the HTLV-1, with or without myelopathy, present significant urodynamic abnormalities and must have a complete urologic and urodynamic evaluation.

Key words: human T-lymphotrofic virus 1; paraparesis, tropical spastic; spinal cord diseases; urodynamics

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INTRODUCTION

Human T-lymphotrophic virus 1 (HTLV-1) is a retrovirus belonging to the subfamily of oncornavirus, related remotely to acquired immunodeficiency syndrome virus (HIV) (1). HTLV-1 is responsible for several diseases, including tropical spastic paraparesis and HTLV-1 associated myelopathy, reported almost simultaneously in 1985 (2,3). Later it was concluded that it was the same disease (4), and the presence of demyelinating myelopathy in individuals infected by HTLV-1 was designated of TSP/ HAM by the World Heath Organization (WHO) (5). The major endemic region is Japan (6). In Brazil, the first cases were reported in patients from Ceará and São Paulo, in 1989 (7). In Rio Grande do Sul (RS), a prevalence of 0.39% was observed among blood donators repeatedly positive (8). Among Japanese individuals living in RS, prevalence is 2.39%, i.e., higher than among non-Japanese individuals and Europeans, the latter with a prevalence of 0.003% (9). In Brazil, since 1944 HTLV-1 testing is mandatory before blood donation (10). Transmission occurs through contact with the blood of individuals infected by HTLV-1, blood transfusions, sharing of contaminated needles, sexual intercourse, and even through breastfeeding (11-15).

TSP/HAM is a chronic condition, progressive and demyelinating, affecting preferentially the medulla spinalis, where it may involve lower thoracic and upper lumbar segments. The disease is mainly of upper neuron, with mild sensitive disturbs and consequent urinary dysfunction (16). Laboratory diagnosis is made through screening tests, as ELISA, and confirmatory studies, as Western blot. From the urological point of view, and, primarily, considering urodynamic findings, few authors described the alterations observed in infected patients. Generally, TSP/HAM patients are evaluated, but those who do not present myelopathy are not described. In this paper, patients with HTLV-1 infection, TSP/HAM or not, are assessed.

MATERIALS AND METHODS

Forty-eight patients infected by HTLV-1, without treatment, were evaluated; 17 were male and 31 female, and age ranged from 13 to 69 years (mean=44.66 years; SD=9.91; median=45 years). All patients were positive by AP (Serodia, Fujerebio, Japan) or ELISA screening tests, and by confirmatory serum and CSF Western blot 2.4. Twenty-six patients developed TSP/HAM and 22 presented varied neurological conditions, without corresponding, however, to WHO inclusion criteria (15) for TSP/HAM, and they were urologically asymptomatic or oligosymptomatic. TSP/HAM patients presented urologic symptoms as urgency, frequency, urge-incontinence, alterations of urinary stream and, some cases, urinary retention, as well as gait disturbs. All patients were evaluated by a multidisciplinary team including a neurologist, an urologist and a physical therapist. Laboratory and imaging exams were demanded to all patients, as well as urodynamic assessment. Patients with distinct urological conditions or with HIV co-infection were excluded. Patients were educated about the objectives of the evaluation, and a signed an informed consent was obtained.

Urodynamic evaluation consisted in uroflow testing, cystometry, abdominal pressure, differential pressure, electromyography and measure of leak point pressure. In uroflow analysis, normograms of Liverpool (17) were used. For pressure measurements, we used 2 plastic catheters 4F and 6F (pressure and infusion, respectively). At electromyography electrodes in plates were positioned at perineal muscles or in the anal sphincter. The evaluation criteria followed the rules of the International Society of Urinary Continence (18). All patients received prophylactic antibiotics two hours before the evaluation. Urodynamic exams were made in a DS-5600, Polimed, Viotti and associates, device.

For statistical analysis we used Pearson's Chisquare test or the exact Fisher test. An analysis of logistic regression was also performed to establish associations among the variables. Level of minimum significance adopted was α =0.05.

RESULTS

TSP/HAM was observed in 26 (54.2%) patients. Twenty-two (45.8%) patients were infected by HTLV-1, without presenting all the criteria necessary to be declared TSP/HAM. 68.18% were asymptomatic or oligosymptomatic, and 31.82% presented void urgency or urgency with incontinence. Among TSP/ HAM patients, 100% presented urinary symptoms; 4 (15.38%) presented normal cystometry, 21 (80.76%) had hyperreflexy, and 1 (3.84%) patient had hyporreflexy (Table-1). We observed that 34.61% of TSP/HAM patients presented hyperreflexy associated with detrusor-sphincter dyssinergia. Among non-TSP/ HAM patients, 14 (63.63%) had normal cystometry, 5 (22.72%) hyperreflexy and 3 (13.63%) hyporreflexy. Detrusor-sphincter dyssinergia was not assessed in these patients (Table-2). Presence of hyperreflexy in TSP/HAM patients was significantly greater than in patients without myelopathy (p=0.0001). Detrusor-sphincter dyssinergia observed in TSP/HAM patients was not detected in non-TSP/ HAM patients, and this difference was significative (p=0.0022).

Uroflow testing in TSP/HAM patients was considered normal by Liverpool normograms in 4

 Table 1 - Results of cystometry in TSP/HAM patients.

	No.	%
Hiperreflexic bladder	21	80.76
Hiporreflexic bladder	01	3.84
Normal	04	15.38
Total	26	100

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Table 2 - Results of cystometry in non-TSP/HAM patients.

	No.	%
Hiperreflexic bladder	05	22.72
Hiporreflexic bladder	03	13.63
Normal	14	63.63
Total	22	100

(17.4%) patients, and abnormal in 19 (82.6%) patients. We excluded 3 (12%) patients for which assessment was not possible (Table-3). In cases non-TSP/HAM, 14 (70%) patients had normal uroflow rates and for 2 cases the assessment was not possible (Table-4). There was a statistically significant difference among these patients (p=0.0005).

Reduction in proprioceptive sensitivity was observed in 4 (8.39%) patients with vesical hyporreflexy. An analysis of logistic regression was made regarding TSP/HAM presence as for age, gender, cystometry findings, electromyography, and uroflow testing. Uroflow testing related to gender and age showed an exposition of 8.04 (p=0.0498), constituting the major variable, followed by cystometry with exposition of 2.85 (p=0.3182). Although uroflow testing and cystometry are highly correlated (r=0.76; p<0.00001), analysis of logistical regression suggests uroflow testing is significant in relation to myopathy. Power of the present study for the tests used was greater than 0.85.

DISCUSSION

HTLV-1 infection in this sample affected patients at adult age, with a predominance of women. Other series of patients confirm those findings. Bruschini et al. report on their series of 4 patients and mean of 49 years, all females (19). Imamura et al report the condition in 25 patients (9 men and 16 women), with mean age of 58.2 years (20).

Patients infected with HTLV-1, primarily TSP/HAM patients, present neurological lesions affecting medullary centers and its corresponding pathways, mainly lower thoracic and upper lumbar segments (16), i.e., between pontine-mesencephalic formation and sacral medulla. Alterations as vesical hyperreflexia and detrusor-sphincter dyssinergia are, thus, expected. The presence of vesical hyperreflexia was significant in TSP/HAM patients, compared to those without myelopathy (p=0.0001). Presence of detrusor-sphincter dyssinergia occurred only in TSP/ HAM patients. All presented abnormal flow rates and significant urinary residue. Whalton & Kaplan (21) reported presence of dyssinergia in 4 patients of a series of 5 patients (80%). A more significative number of patients is evaluated by Yamashita & Kumazawa. Among 26 cases, all with TSP/HAM, they found 96% of hyperreflexy and 68% of detrusor-sphincter dyssinergia (21).

Micturition and urodynamic alterations precede neurological alterations in 26% of the cases (20), and hyperreflexic bladder is the most frequent finding in reviewed series, varying from 50% to100% of all cases. Saito et al. (23) observed hyperreflexy in 3 patients out of 4 evaluated. Bruschini et al. reported the presence of hyperreflexy in 50% of studied patients (19).

A variable penetrance of the disease is demonstrated by 15.38% of normal cystometry in TSP/ HAM patients, i.e., patients with great neurological impairment due to the disease, and gait disturbances, may present a normal pattern of vesical behavior.

Table 3 - Uroflow test in TSP/HAM patients.

Table 4 - Uroflow	test in non-TSP	HAM patients.
	No.	%

	No.	%		No.	%	
Normal	04	17.4	Normal	14	70	
Abnormal	19	82.6	Abnormal	06	30	
Total	23	100	Total	20	100	

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In 3.84% of TSP/HAM patients and 13.63% of non-TSP/HAM patients, vesical hyporreflexy was observed. This kind of finding is generally associated with lesions to the peripheral innervation of the bladder (24). In TSP/HAM, there are pathological evidences of ventral and dorsal roots involvement by inflammatory exudates. In addition, it is clinically known that a small proportion of patients have evidences of lower limb denervation (24).

Uroflow testing results are in accordance to the neurological conditions, and to cystometry and electromyographic findings: 82.6% of TSP/HAM patients presented abnormal uroflow testing, while 70% of non-TSP/HAM patients had normal uroflow testing. Four patients were observed with TSP/HAM and normal flow rates (17.4%): 2 presented hyperreflexic bladder and were women. The other two had normorreflexy. Patients with hyperreflexy may have normal flow, including "superflows" (25), especially if they are female, in which case obstructive uropathy is not frequent. Non-TSP/HAM patients with abnormal uroflow rates were found associated with hyporreflexy (2 cases) and hyperreflexy (4 cases). Both patients with hyporreflexy were female and presented detrusor-sphincter dyssinergia. Eardley et al reported 50% of normorreflexy and 50% of hyperreflexy in TSP/HAM patients infected by HTLV-1 (24).

Patients with completely normal urodynamic evaluation totalized 14 individuals without myelopathy and 1 with myelopathy, i.e., 31.25% of the sample.

The present work shows that individuals infected by HTLV-1, both TSP/HAM and non-TSP/ HAM, present hyperreflexic bladder as the major urodynamic finding. However, other types of vesical behavior were observed, indicating that this is a complex disease, deserving attention of neurologists and urologists regarding possible consequences for the upper urinary tract.

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EDITORIAL COMMENTS

The authors of this study deserve congratulations for the excellent investigation on this population of patients, and for the relevance of the information offered. A non-negligible population of patients sent to urodynamic exam present urinary symptoms of dubious or unknown origin. In many cases, urodynamic alterations are important, and require urological treatment to protect upper urinary tract, to the treatment of urinary incontinence, and to reduce the episodes of urinary infection. In this context, every urologist must raise hypothesis of an etiologic diagnosis, to give the patient a prognostic orientation and treatment for his/her disease, in addition to urological treatment. Nevertheless, several urodynamic alterations remain unexplained, or are incorrectly classified. Knowledge of different medullary diseases of inflammatory origin producing urinary alterations many times help and protect the patient, as it happen to the transversal myelitis of LES and that of multiple sclerosis. Infection by HTLV-1 virus, promoting chronic and progressive demyelization lesion, is a diagnosis barely known by urologist. As the authors state, its urinary symptoms, as in other demyelinizing diseases may precede neurological alterations. In this case, the urologist should talk to the patient about the possibility of a neurological disease. The authors showed clearly that patients with established diagnosis of HTLV-1 infection, even without spastic paraparesis, may present major urodynamic alterations, probably requiring treatment. Nevertheless, new studies are necessary to answer some questions. Which are the urinary symptoms presented by individuals with this infection? How many patients with detrusor-sphincter dyssinergia have high post-void residual and impairment of upper urinary tract? With this high rate of hiperreflexy, which is the bladder functional capacity, and how many patients will need bladder augmentation? These and other questions will probably be answered through careful clinical observations and increasing the knowledge about this neurological pathology.

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