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Ichino M[1], Igawa Y[1], Ogawa T[1], Seki S[2], Ishizuka O[1], Nishizawa O[1]
1. *Department of urology Shinshu-university school of medicine,* ***2.*** *Seki Urological clinic*

LOWER URINARY TRACT DYSFUNCTION IN PATIENTS WITH FAMILIAL AMYLOIDOTIC POLYNEUROPATHY: CHARACTERISTICS AND THERAPEUTIC EFFECTS OF LIVER TRANSPLANTATION

Hypothesis / aims of study

Familial amyloidotic polyneuropathy (FAP) is characterized by a progressive sensitive-motor and autonomic polyneuropathy caused by extracellular deposition of fibrillar amyroid protein which contains a mutant transthyretin (TTR) molecule. Because more than 95% of TTR is produced by the liver, liver transplantation (LT) is the preferred treatment of FAP (1). It is known that FAP patients frequently show lower urinary tract dysfunction (LUTD) induced by autonomic dysfunction (2, 3) but few investigations have been performed. The aim of this study was to determine characteristics of LUTD of FAP patients and effect of LT on LUTD.

Study design, materials and methods

We retrospectively reviewed the medical records of 18 (10male, 8female) type1 FAP patients with an average age of 37.4 (26-6) years old. Lower urinary tract symptoms, ultrasonography and video-urodynamic studies (V-UDSs) were evaluated. Fourteen of 18 patients underwent LT. Five of them referred after LT(less than 1 year in 5, after 5 years in 1). Three patients underwent spinal cord surgery before their diagnosis of FAP because the cause of their symptoms had been suspected of spinal cord abnormality.

Results

Lower urinary tract symptoms were evaluated in 17 patients except 1 with severe diarrhea; 8 patients showed difficulty on urination, 8 complained of reduced bladder sensation and 11 showed urinary incontinence. Eight of the 11 incontinent patients had urinary incontinence unconsciously and the others had stress incontinence. Three patients suffered from urinary retention after LT. Three patients had a history of UTI. By ultrasonography, bladder deformity and hydronephrosis were observed in 8 and 1 patients, respectively. The mean value of post−void residual urine (PVR) was 76(0-300)ml and PVR was less than 50 ml in 7 of 16 patients. V-UDS were performed in 13 (6 after LT) patients (Table 1). The remaining 5 could not undergo V-UDS because of severe gastrointestinal dysfunction or mental disorder. During the filling phase, 1 patient showed detrusor overactivity. Six patients showed low compliant bladder, 2 and 7 patients showed absent and reduced bladder sensation, respectively. The patient, whose hydronephrosis was detected, had markedly low bladder compliance (2.9 ml/cmH_2O). Abdominal leak point pressure (ALPP) was low in 6 (2 male and 4 female) patients. Pressure flow studies were evaluated in 12 patients who could void. Eleven of the 12 patients showed intermittent flow due to both acontractile detrusor and relaxation failure of the bladder neck or external sphincter. VUR was observed in one with low compliance. Ten patients started clean intermittent catheterization (CIC) after V-UDS. Urinary incontinence improved in all of them and hydronephrosis improved, too. We followed 4 patients who underwent V-UDS before or immediately after LT. None of them had episodes of UTI. Three patients performed CIC and did not have deterioration of incontinence. The remaining one continued straining voiding, and V-UDS at 1 year after LT showed that her low bladder compliance and acontractile detrusor did not change, but ALPP decreased and bladder deformity progressed. In 3 patients without LT, 2 had repeated UTI and hypokinesis, and thus were managed with a transurethral catheter. Another 1 underwent repeated V-UDS 1 year after her first V-UDS and showed reduced bladder compliance.There was only one patient, who had normal detrusor and urethral function during voiding before LT, and the patient has kept normal flow rate with continuous urine flow for 10 years after LT.

Table 1. The result of V-UDS and urinary management after V-UDS

	With LT	Without LT	5 years after LT
no. of patients	9	3	1
reduced sensation	5/9	3/3	1/1
low compliance	4/9	2/3	0/1
low ALPP	3/9	2/2	1/1
acontractile detrusor	8/9	3/3	1/1
urinary management after V-UDS	CIC ;7/9	CIC ;3/3 (indwelling catheterization;2)	

Interpretation of results

LUTD was commonly observed in patients with FAP. The LUTD observed in the early stage in FAP patients is characterized as reduced bladder sensation, acontractile detrusor and non-relaxing urethra, and in association with disease progression, bladder compliance decreased. The types of urinary incontinence commonly observed in FAP patients, are overflow incontinence attended by reduced sensation and stress incontinence. Liver transplantation may prevent the progression of LUTD in FAP patients.

Concluding message

LUTD is commonly observed and progressive in FAP patients. Liver transplantation may prevent the progression of LUTD in FAP patients although it does not cure the disease.

References

1 Liver Transpl (2000) 6; 263-276
2 Int J Urol (2006) 13; 1475-1478.
3 Neurourol Urodyn (1997)16; 55-61.

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Is this a clinical trial?	**No**

What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**No**
This study did not require eithics committee approval because	**this is a part of our routine clinical practice.**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**