NEUROGENIC BLADDER CAUSES MARKED BLADDER REMODELING IN MICE WITH EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS

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Introduction

- Neurogenic bladder (NGB) causes severe dysfunction of the lower urinary tract and leads to severe deterioration of quality of life and marked morbidity and mortality in ~60% of patients with multiple sclerosis (MS)
- NGB causes marked remodeling of the bladder with wall thickening, trabeculation, and cellule formation (Figure 1)
- Experimental autoimmune encephalomyelitis (EAE) is a widely used animal model to study MS
  - 2-3 weeks after immunization mice develop acute EAE
  - EAE mice exhibit a pattern of relapse/remission (Figure 2) neuroparalytic cycles similar to patients with MS
- The objective of our study was to examine the elements of bladder remodeling in EAE mice as a robust model of NGB

Fig. 1. Cystoscopic Image From Patient with NGB.

Fig. 2. Time Course of EAE Progression.

Methods

Animals
- Female SJL/J mice were immunized via subcutaneous injection to initiate EAE as described previously (Yu et al, 1996)

Evaluations
- Clinical scores (CS) were evaluated 15-30 days after induction of EAE based on 5 levels of neurological disability
  - 0: no disease
  - 1: decreased tail tone or slightly clumsy gait
  - 2: tail atony and/or moderately clumsy gait and/or poor righting ability
  - 3: limb weakness
  - 4: limb paralysis
  - 5: moribund state
- Mice were euthanized at day 70 and bladders harvested for histological studies

Fig. 3. Bladder Weight:Body Weight Ratio Was Significantly Increased in EAE Mice Compared with CFA Controls (P < 0.05).

Fig. 4. Morphological Evidence of Bladder Remodeling with Increasing Clinical Score in EAE Mice.

Fig. 5 Bladder Remodeling in EAE Mice: Total Wall and Lumen Areas Increase With Increasing Clinical Score.

Fig. 6 Bladder Remodeling in Smooth Muscle, Collagen, and Urothelium of EAE Mice.

Results

Conclusions & Future Directions

- In EAE mice higher CS were associated with
  - Increased cross sectional area of smooth muscle, collagen, and urothelium
  - Increased proportion of collagen
- EAE mice represent a valid animal model to investigate the pathophysiology and potential treatments for patients with MS and NGB
- In future studies, EAE mice may be used to further investigate the morphological changes associated with NGB-induced bladder remodeling

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