

Infections/Inflammation of the GU Tract: Interstitial Cystitis
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ANTI-TNF THERAPY PRESERVES BLADDER BARRIER FUNCTION IN A MOUSE MODEL OF NEUROGENIC CYSTITIS

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Introduction and Objective: Interstitial cystitis (IC) is often regarded as a neurogenic cystitis. Mast cells have been suggested to play a role in the pathogenesis of IC, and mast cells are redistributed in bladders of ulcerative IC patients. We recently adapted the rat model of pseudorabies virus (PRV)-induced neurogenic cystitis to the mouse. Our murine model of neurogenic cystitis exhibits mast cell activation and recruitment to the lamina propria. Furthermore, mast cells exhibited a TNF-dependent migration to the lamina propria associated with urothelial apoptosis and loss of barrier function. To further characterize the role of TNF in the development of bladder pathology in neurogenic cystitis, we tested the hypothesis that anti-TNF antibodies protect against PRV-induced loss of barrier function. Methods: Anti-TNF or isotype control antibodies were administered via i.p. injection. Mice were subsequently infected with Bartha strain of PRV in the tail-base muscle to induce neurogenic cystitis, and bladders were harvested and processed at 3-5 days after infection. Bladders were dissected, mounted within an Ussing chamber, and trans-epithelial resistance (TER) was determined as a measurement of bladder barrier function using a voltohmmeter. Bladder mast cells were visualized in tissue sections by acidified toluidine blue staining. Results: The number of lamina propria mast cells in C57BL/6J mice treated with anti-TNF antibodies was reduced by 62.5% relative to mice receiving isotype control antibodies ($p=0.011$). Consistent with this finding, TER values in the anti-TNF group were significantly higher than isotype controls ($124.0 \Omega \text{ cm}^2 \pm 13.5$ vs. $93.2 \Omega \text{ cm}^2 \pm 18.9$, respectively; $p=0.012$). These data indicate that anti-TNF therapy stabilizes TER. Conclusions: Anti-TNF therapy abrogates mast cell trafficking to the lamina propria and preserves bladder barrier function during neurogenic cystitis.

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