Acceleration of Aortopathy in the Setting of Neurogenic Hypertension

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Introduction: Neurogenic hypertension is defined as uncontrolled blood pressure while on more than 5 different anti-hypertensives. It's estimated that 50% of patients with essential hypertension have neurogenic hypertension. The direct effects of neurogenic hypertension on aortopathy have yet to be elucidated.

Methods: BPH/2J (neurogenic hypertensive) and BPN/3J (normotensive) mice underwent noninvasive blood pressure measurement. Thoracic aortae were assessed for changes in compliance by parallel-wire myography and alterations in aortic wall structure via histology. Thoracic aortic aneurysms were induced through periadventitial application of a 0.5M $CaCl_2$ solution to the descending thoracic aorta. Thoracic aortic diameter was measured 4-weeks post-surgery by digital microscopy. Allopregnanolone, a novel therapeutic, was administered to BPH/2J mice (5mg/kg/day) via osmotic pump for 6-weeks starting 2-weeks prior to thoracic aortic aneurysm surgery. Thoracic aortic diameter was measured 4-weeks post-surgery.

Results: BPH/2J mice had increased systolic blood pressures (n=9-12, BPH/2J 172±5mmHg; BPN/3J 129±10mmHg, $p<0.05$). Total medial collagen was elevated in the thoracic aorta of BPH/2J mice (n=6, collagen volume fraction, BPH/2J 18±5.2%, BPN/3J 10.5±2.4%, $p<0.05$) that correlated with a decrease in thoracic aortic compliance (n=6, BPH/2J -0.2±0.14 slope of stress/relaxation curve, BPN/3J -0.72±0.15, $p<0.05$). BPH/2J mice had larger thoracic aortic aneurysms 4-weeks post-surgery (n=10, BPH/2J 61.3±10% increase from baseline diameter; BPN/3J 23.9±3.4%, $p<0.05$). In a pilot study, allopregnanolone suppressed thoracic aortic aneurysm acceleration (n=4 BPH/2J, allopregnanolone 42.9±6.8%, vehicle 61.7±14.1%, $p<0.05$).

Conclusion: Neurogenic hypertension can trigger extracellular matrix remodeling resulting in compensatory stiffening of the thoracic aorta. In the presence of aortopathy, neurogenic hypertension can accelerate disease progression which may be suppressed by allopregnanolone.