The Utility of BNP to Predict Acute Rejection in Pediatric Heart Transplant Recipients

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Introduction: Biopsy remains the gold-standard for assessment of cellular rejection after pediatric heart transplant (htx). Non-invasive biomarkers of acute rejection may help limit the need for invasive procedures, especially in small children. Brain-type natriuretic peptide (BNP) has been proposed to correlate with acute rejection in pediatric htx patients.We sought to assess the predictive value of BNP for any episodes of significant rejection and whether BNP differentiates grade of rejection following pediatric htx.

Methods: Retrospective single-center review of BNP samples obtained at the time of endomyocardial biopsy ≥ 90 days after htx between 9/05 and 9/12. Biopsies were graded according to 2005 ISHLT guidelines. Rejection with hemodynamic compromise (RHC) was defined as a clinical event with low cardiac output that warranted inotropic support regardless of rejection grade. Rejection was defined as any clinical event/biopsy resulting in enhanced immunosuppression. Subsequent BNP samples during an episode of rejection were excluded.

Results: One hundred seventeen patients underwent 623 endomyocardial biopsies. Forty three patients (37%) had 80 episodes of cellular rejection (1R=60, 2R=12, 3R=3, RHC=5). Mean BNP for the cellular rejection group was 293 ± 522 pg/mL vs. 111 ± 130 pg/mL for the non-rejection group (p<0.0001). By ROC analysis, the AUC was 0.622 for all episodes of rejection. When comparing grades 2R/3R/RHC (moderate/severe cellular rejection, n=22) to grades 0R/1R (no/mild cellular rejection, n=602), the mean BNP was 668 ± 845 pg/mL vs. 113 ± 135 pg/mL, respectively (p<0.0001). The AUC was 0.755 (SE 0.074, p<0.001) for the moderate/severe rejection group with an ideal cutoff of 188 pg/mL (sensitivity 0.68, specificity 0.87).

Conclusions: Elevated BNP levels are associated with significant cellular rejection and RHC in pediatric heart transplant recipients. Future studies will determine whether BNP may be a useful diagnostic adjunct in this patient population.