T-bet：a New Marker for antibody-mediated rejection?

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The transcription factors T-bet and GATA3 determine the differentiation of helper T cells into Th1 or Th2 cells, respectively. An altered ratio of their relative expression promotes the pathogenesis of certain immunological diseases, but whether this may also contribute to the pathogenesis of antibody-mediated rejection (ABMR) versus T cell-mediated rejection (TCMR) is unknown. Here, we characterized the intragraft expression of T-bet and GATA3 and determined the correlation of their levels with the presence of typical lesions of ABMR and TCMR. We found a predominant intraglomerular expression of T-bet in patients with ABMR, which was distinct from that in patients with TCMR. In ABMR, interstitial T-bet expression was typically located in peritubular capillaries, although the overall quantity of interstitial T-bet was less than that observed in TCMR. The expression of intraglomerular T-bet correlated with infiltration of CD4+ and CD8+ lymphocytes, which express T-bet, as well as intraglomerular CD68+ monocyte/macrophages, which do not express T-bet. The predominance of intraglomerular T-bet expression relative to GATA3 expression associated with poor response to treatment with bolus steroid. In summary, predominance of intraglomerular T-bet expression correlates with antibody-mediated rejection and resistance to steroid treatment. For chronic AMR, transplant Glomerulopathy, there was also a significant increase in T-bet expression in both glomerular and peritubular capillaries. This expression was strongly correlated with $CD4_t$, $CD8_t$, and $CD68_t$ cell infiltration within glomerular and peritubular capillaries. The expressionof GATA3, a Th2 regulator, was rarely found in the transplant glomerulopathy group. Transplant glomerulopathy was associated with diffuse peritubular capillary dilation without reduced capillary density. Moreover, the degree of capillary dilation was significantly correlated with the number of infiltrating $CD68_t$ cells. Since endothelial injury is a typical lesion that follows alloantibody reactivity, our results suggest that T-bet is involved in the pathogenesis of this glomerulopathy.