vs 3A–3B) and a lower number of infiltrating leucocytes (p=0.15) in anti-TNF-treated recipients compared to controls. In contrast with the alloantibody data, TNF blockade did not affect the Th1/Th2 balance, TLR expression and the expression of the regulatory molecules TGFβ, IDO, HO-1 and FoxP3. Clinically, graft survival was prolonged from 6 days to 13 days by a single intraperitoneal injection with anti-TNF (8 mg/kg) at day 0. Upon multiple injections (days 0, 3 and 6), the mean graft survival was further prolonged to 23 days. A higher dosage of anti-TNF (15 mg/kg) or concomitant treatment with suboptimal doses of ciclosporin did not have a significant additional effect.

Conclusions TNF blockade completely blocks the induction of alloantibodies, which results in a significant prolongation of graft survival in this allotransplantation model. TNF blockade may have a similar effect on humoral responses in other situations, including clinical treatment of patients with immune-mediated inflammatory disorders.

A147 MODULATION OF HUMORAL IMMUNE RESPONSES AS A NOVEL MECHANISM OF ACTION OF TUMOUR NECROSIS FACTOR BLOCKADE

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Objectives Based on our observations of IgM but not IgG anti-dsDNA antibody induction in patients treated with tumour necrosis factor (TNF) blockers, we proposed the hypothesis that TNF blockade interferes with the induction of T cell-dependent humoral responses. This study aimed to assess this hypothesis by assessing the induction of alloantibodies in a rat cardiac allograft model.

Materials and Methods LEW.1W hearts were ectopically transplanted in LEW.1A rats which were treated with anti-rat TNF or control antibody (3G8). Graft rejection was monitored clinically and serum was obtained every 5 days until day 25. Transplanted hearts were obtained 5 days after transplantation and were assessed by histology, immunohistochemistry and quantitative RT-PCR for cytokines (Th1/Th2), TLRs and regulatory molecules.

Results ELISA analysis of serum in the LEW.1W to LEW.1A rat allotransplantation model showed a clear induction of alloantibodies in the control-treated rats from day 5. This induction was significantly impaired by single anti-TNF treatment and completely blocked by triple anti-TNF injection. Accordingly, IgG deposition in the grafts at day 5 was significantly lower in anti-TNFα-treated animals than in control animals (p=001), without significant differences for IgM deposition. This was histologically associated with a better conserved histological architecture (Banff grade 2–3A