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Monoclonal Antibody Therapy with Ciclosporin and Steroids in Nonmatched Cadaveric Renal Transplants[1]

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Abstract. Thirty-six ciclosporin-prednisone-treated recipients of nonmatched cadaver renal allografts were given a course of Orthoclone OKT3 monoclonal antibody for steroid-resistant cell-mediated rejection. Although side effects were common, only 2 patients had to be withdrawn from therapy and there were no deaths related to therapy. Twenty-three (63.9%) allografts were rescued with OKT3 therapy and 21 (58.3%) of the grafts have continued to function well. We conclude that OKT3 is an effective agent for the treatment of steroid-resistant cell-mediated rejection and that rebound rejection can be prevented in most patients if adequate therapy with ciclosporin-prednisone is maintained.

Introduction

Antilymphocyte globulin for the treatment of steroid-resistant rejection was introduced into clinical practice by Starzl et al. [1] and its value has been proved in the treatment of steroid-resistant allograft rejection. The limitations of therapy with this heterologous polyclonal agent are summarized by Fung et al. [2] elsewhere in this symposium. Orthoclone OKT3 is a monoclonal reagent directed against a specific T-cell antigen receptor complex known to be important in both antigen recognition and T-cell activation [3, 4]. The development of such a refined biologic product offers an attractive alternative to the treatment of acute cellular allograft rejection with conventional antilymphocyte preparations.

The first successful clinical trials with OKT3, which were conducted by Cosimi et al. [5, 6] at the Massachusetts General Hospital, provided convincing evidence of the increased effectiveness of this agent compared with traditional treatment with high-dose steroids. However, there was a significant incidence of recurrent rejection after resumption of maintenance therapy with azathioprine and prednisone.

Since 1981, ciclosporin low-dose prednisone therapy has been the standard form of immunosuppression for cadaveric renal transplants at the University of Pittsburgh. In August 1985, we began a pilot trial of OKT3 therapy for the treatment of steroid-resistant rejection in cadaveric renal and hepatic allografts under ciclosporin-steroid therapy. We report here our results for the first 36 consecutive renal allograft recipients treated in this trial.

Materials and Methods

Case Material

Between August 15, 1984, and December 15, 1985, 40 recipients of cadaveric renal allografts were treated with OKT3 monoclonal antibody. Four of the patients also received a simultaneous pancreas transplant, and they are excluded from this report. Thirty-six recipients of a renal allograft alone have been followed for 2–20 months since transplantation.

The 36 patients included in this series ranged in age from 9 to 63 years (mean 36.9 ± 13.5 SD). There were 22 males and 14 females. Twenty-three patients received a primary graft and 13 patients received a second graft. The causes of renal failure were known in all but 7 patients and are summarized in table I. There were 7 diabetics in the series.

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