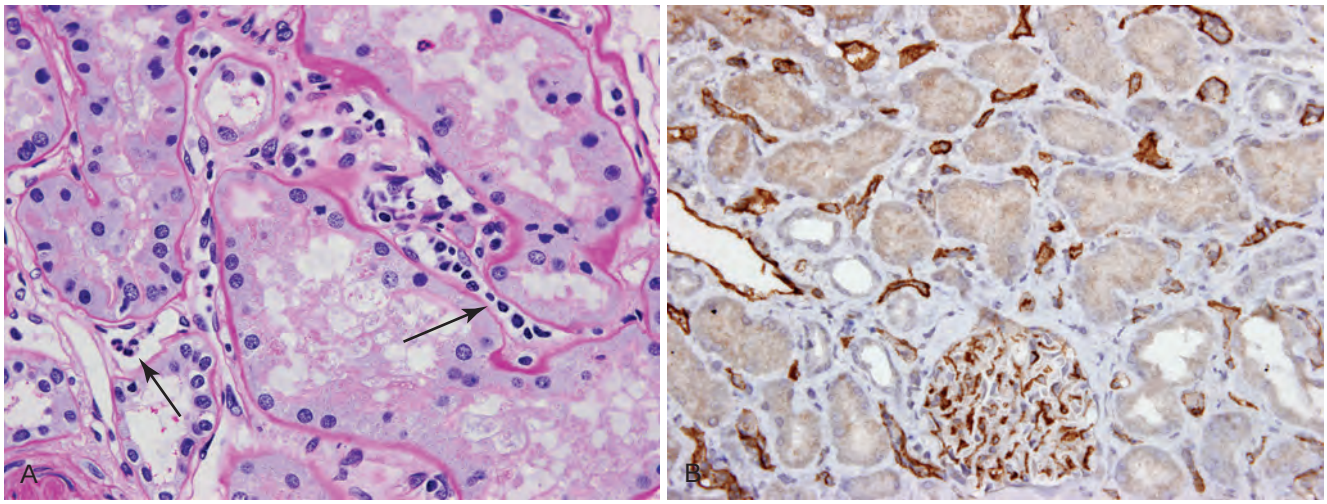

Figure 6-35 Acute antibody-mediated (humoral) rejection. **A,** Light micrograph showing inflammation (capillaritis) in peritubular capillaries (*arrows*). **B,** Immunoperoxidase stain shows C4d deposition in peritubular capillaries and a glomerulus. (Courtesy Dr. Zoltan Laszik, Department of Pathology, University of California San Francisco, Calif.)

combinations. Immunosuppressive drugs in current use include steroids (which reduce inflammation), mycophenolate mofetil (which inhibits lymphocyte proliferation), and tacrolimus (FK506). Tacrolimus, like its predecessor cyclosporine, is an inhibitor of the phosphatase calcineurin, which is required for activation of a transcription factor called nuclear factor of activated T cells (NFAT). NFAT stimulates transcription of cytokine genes, in particular, the gene that encodes IL-2. Thus, Tacrolimus inhibits T cell functions. Additional drugs that are used to treat rejection include T cell- and B cell-depleting antibodies, and pooled intravenous IgG (IVIG), which suppresses inflammation by unknown mechanisms. Plasmapheresis is used in cases of severe antibody-mediated rejection. Another, more recent, strategy for reducing antigraft immune responses is to prevent host T cells from receiving costimulatory signals from dendritic cells during the initial phase of sensitization. This can be accomplished by interrupting the interaction between the B7 molecules on the dendritic cells of the graft donor with the CD28 receptors on host T cells, for example, by administration of proteins that bind to B7 costimulators.

Although immunosuppression prolongs graft survival, it carries its own risks. The price paid in the form of increased susceptibility to opportunistic infections is not small. One of the most frequent infectious complications is reactivation of *polyoma virus*. The virus establishes latent infection of epithelial cells in the lower genitourinary tract of healthy individuals, and upon immunosuppression, it is reactivated, infects renal tubules, and may even cause graft

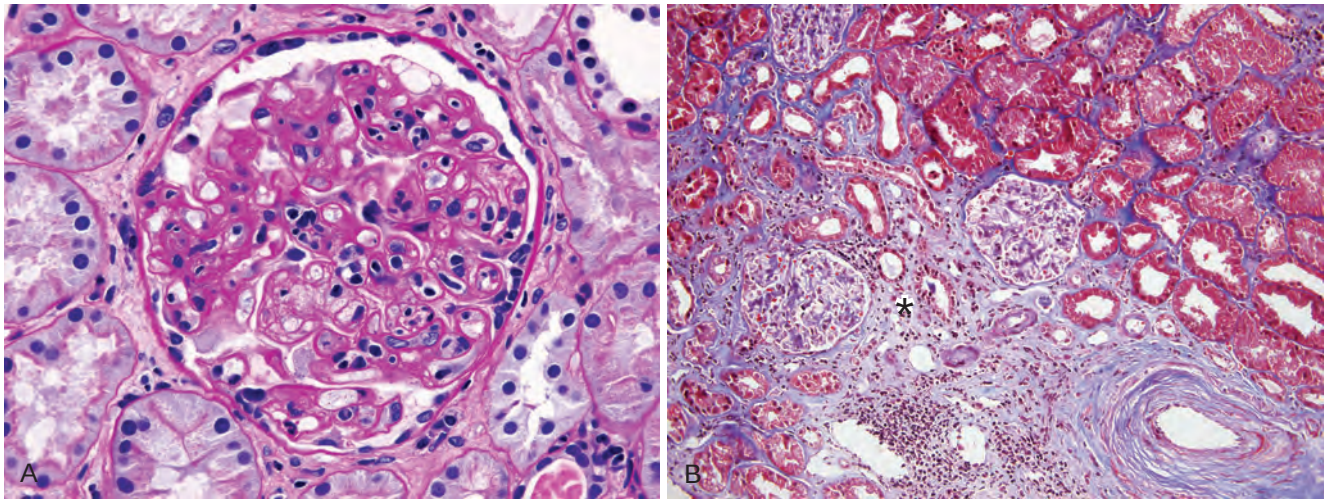

Figure 6-36 Chronic rejection of a kidney allograft. **A,** Transplant glomerulopathy, the characteristic manifestation of chronic antibody-mediated rejection. The glomerulus shows inflammatory cells within the capillary loops (glomeruliitis), accumulation of mesangial matrix, and duplication of the capillary basement membrane. **B,** Interstitial fibrosis and tubular atrophy. In this trichrome stain, the blue area (*asterisk*) shows fibrosis, contrasted with the normal kidney on the top right. At the bottom right is an artery showing prominent arteriosclerosis. (Courtesy Dr. Zoltan Laszik, Department of Pathology, University of California San Francisco, Calif.)