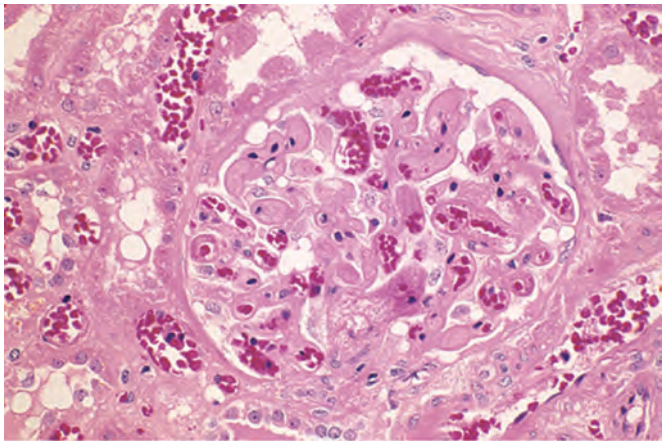

Figure 6-33 Hyperacute rejection. Hyperacute rejection of a kidney allograft showing platelet and fibrin thrombi, early neutrophil infiltration, and severe ischemic injury in a glomerulus.

one patient, cellular or humoral immune mechanisms may predominate.

- **Acute cellular (T cell-mediated) rejection.** Histologically, acute T cell–mediated rejection may be seen as two patterns.
  - In the **tubulointerstitial pattern** (sometimes called type I), there is extensive interstitial inflammation with infiltration of tubules, referred to as **tubulitis**, associated with focal tubular injury (Fig. 6-34*A*). As might be expected, immunohistochemical staining reveals both CD4+ and CD8+ T lymphocytes, which express markers of activated T cells, such as the α chain of the IL-2 receptor.
  - The **vascular pattern** shows inflammation of vessels (**endotheliitis**, type II) (Fig. 6-34*B*), sometimes with necrosis of vascular walls (type III). The affected vessels have swollen endothelial cells, and at places the lymphocytes can be seen between the endothelium and the vessel wall. The recognition of cellular rejection is important because, in the absence of an accompanying humoral rejection, patients respond well to immunosuppressive therapy.
- **Acute antibody-mediated rejection** is manifested mainly by damage to glomeruli and small blood vessels. Typically, the lesions consist of inflammation of glomeruli and peritubular capillaries, associated with deposition of the complement breakdown product C4d, which is produced during activation of the complement system by the antibody-dependent classical pathway (Fig. 6-35). Small vessels may also show focal thrombosis.

Cyclosporine, an immunosuppressive drug, is also nephrotoxic, and hence the histologic changes resulting from cyclosporine therapy (e.g., arteriolar hyaline deposits) may be superimposed.

Chronic Rejection

In recent years acute rejection has been largely controlled by immunosuppressive therapy, and chronic rejection has emerged as an increasingly frequent cause of graft failure. Patients with chronic rejection present clinically with progressive renal failure manifested by a rise in serum creatinine over a period of 4 to 6 months. Chronic rejection is dominated by vascular changes, which include (1) intimal thickening with inflammation, (2) glomerulopathy, with duplication of the basement membrane, likely secondary to chronic endothelial injury, and (3) peritubular capillaritis with multilayering of peritubular capillary basement membranes (Fig. 6-36). Interstitial fibrosis and tubular atrophy with loss of renal parenchyma may occur secondary to the vascular lesions. Chronically rejecting kidneys usually have interstitial mononuclear cell infiltrates, including NK cells and plasma cells.

Methods of Increasing Graft Survival

The value of HLA matching between donor and recipient varies in different solid-organ transplants. In kidney transplants, there is substantial benefit if all the polymorphic HLA alleles are matched (both inherited alleles of *HLA-A, -B,* and *DR*). However, HLA matching is usually not even done for transplants of liver, heart, and lungs, because other considerations, such as anatomic compatibility, severity of the underlying illness, and the need to minimize the time of organ storage, override the potential benefits of HLA matching.

Except for identical twins, who obviously express the same histocompatibility antigens, *immunosuppressive therapy* is a practical necessity in all other donor-recipient

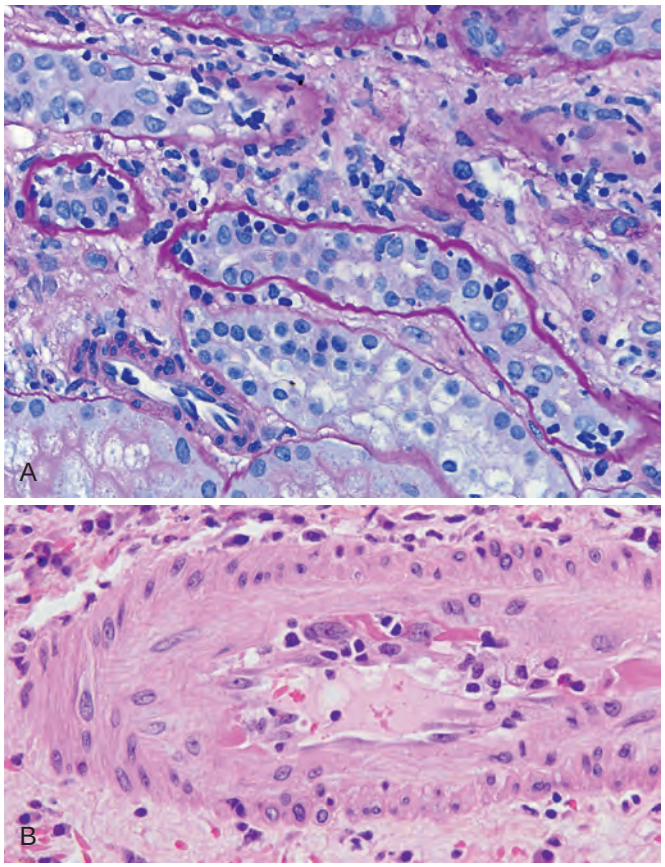

Figure 6-34 Acute T cell–mediated (cellular) rejection of a kidney allograft. **A,** Inflammatory cells in the interstitium and between epithelial cells of the tubules (tubulitis). **B,** Rejection vasculitis, with inflammatory cells attacking and undermining the endothelium (endotheliitis). (Courtesy Drs. Zoltan Laszik and Kuang-Yu Jen, Department of Pathology, University of California San Francisco.)