

# Acute Renal Failure in the Transplanted Kidney

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**A**cute renal failure (ARF) in the transplanted kidney represents a high-stakes area of nephrology and of transplantation practice. A correct diagnosis can lead to rapid return of renal function; an incorrect diagnosis can lead to loss of the graft and severe sequelae for the patient. The diagnostic possibilities are many (Fig. 10-1) and treatments quite different, although the clinical presentations of new-onset functional renal impairment and of persistent nonfunctioning after transplant may be identical.

In transplant-related ARF percutaneous kidney allograft biopsy is crucial in differentiating such diverse entities as acute rejection (Figs. 10-2 to 10-9), acute tubular necrosis (Figs. 10-10 to 10-14), cyclosporine toxicity (Figs. 10-15 and 10-16), posttransplant lymphoproliferative disorder (Fig. 10-17), and other, rarer, conditions.

In the case of acute rejection, standardization of transplant biopsy interpretation and reporting is necessary to guide therapy and to establish an objective endpoint for clinical trials of new immunosuppressive agents. The Banff Classification of Renal Allograft Pathology [1] is an internationally accepted standard for the assessment of renal allograft biopsies sponsored by the International Society of Nephrology Commission of Acute Renal Failure. The classification had its origins in a meeting held in Banff, Alberta, in the Canadian Rockies, in August, 1991, where subsequent meetings have been held every 2 years. Hot topics likely to influence the Banff Classification of Renal Allograft Pathology in 1999 and beyond are shown in Figs. 10-17 to 10-19.

CHAPTER

10

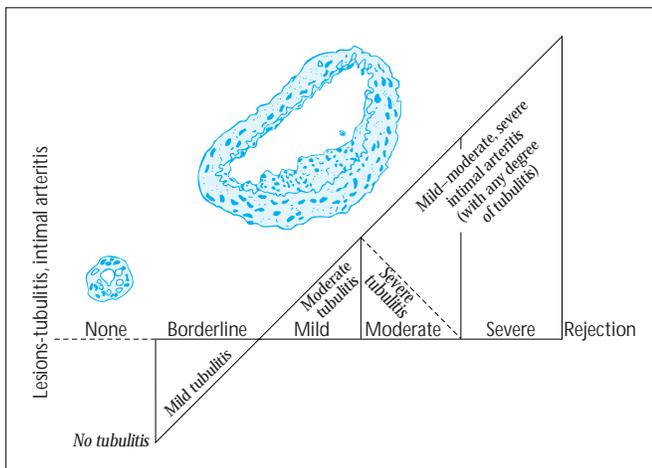
## Acute Rejection

### DIAGNOSTIC POSSIBILITIES IN TRANSPLANT-RELATED ACUTE RENAL FAILURE

1. Acute (cell-mediated) rejection
2. Delayed-appearing antibody-mediated rejection
3. Acute tubular necrosis
4. Cyclosporine or FK506 toxicity
5. Urine leak
6. Obstruction
7. Viral infection
8. Post-transplant lymphoproliferative disorder
9. Vascular thrombosis
10. Prerenal azotemia

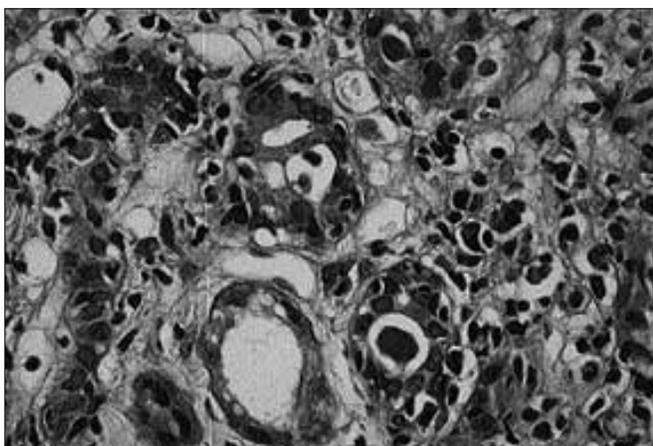
**FIGURE 10-1**

Diagnostic possibilities in transplant-related acute renal failure.



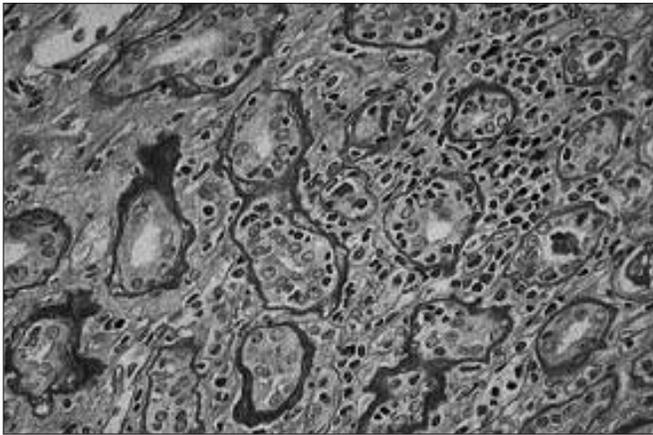
**FIGURE 10-2**

Diagnosis of rejection in the Banff classification makes use of two basic lesions, tubulitis and intimal arteritis. The 1993–1995 Banff classification depicted in this figure is the standard in use in virtually all current clinical trials and in many individual transplant units. In this construct, rejection is regarded as a continuum of mild, moderate, and severe forms. The 1997 Banff classification is similar, having the same threshold for rejection diagnosis, but it recognizes three different histologic types of acute rejection: tubulointerstitial, vascular, and transmural. The quotation marks emphasize the possible overlap of features of the various types (eg, the finding of tubulitis should not dissuade the pathologist from conducting a thorough search for intimal arteritis).



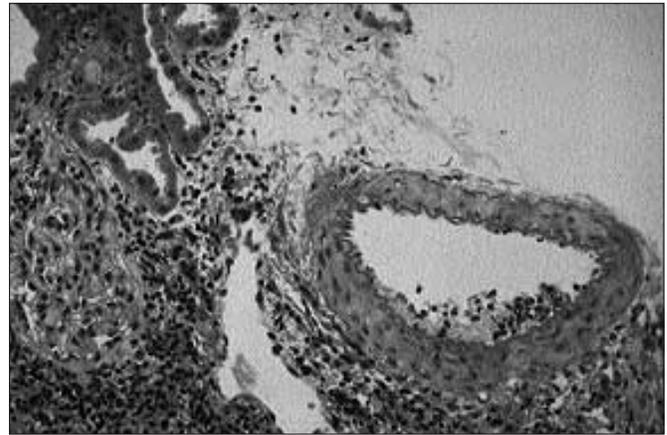
**FIGURE 10-3**

Tubulitis is not absolutely specific for acute rejection. It can be found in mild forms in acute tubular necrosis, normally functioning kidneys, and in cyclosporine toxicity and in conditions not related to rejection. Therefore, quantitation is necessary. The number of lymphocytes situated between and beneath tubular epithelial cells is compared with the number of tubular cells to determine the severity of tubulitis. Four lymphocytes per most inflamed tubule cross section or per ten tubular cells is required to reach the threshold for diagnosing rejection. In this figure, the two tubule cross sections in the center have eight mononuclear cells each. Rejection with intimal arteritis or transmural arteritis can occur without any tubulitis whatsoever, although usually in well-established rejection both tubulitis and intimal arteritis are observed.



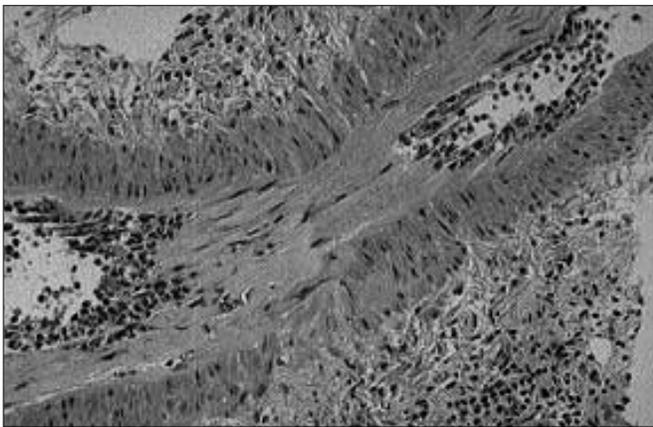
**FIGURE 10-4** (see Color Plate)

In this figure the tubules with lymphocytic invasion are atrophic with thickened tubular basement membranes. There are 13 or 14 lymphocytes per tubular cross section. This is an example of how a properly performed periodic acid-Schiff (PAS) stain should look. The Banff classification is critically dependent on proper performance of PAS staining. The invading lymphocytes are readily apparent and countable in the tubules. In the Banff 1997 classification one avoids counting lymphocytes in atrophic tubules, as tubulitis there is more “nonspecific” than in nonatrophied tubules. (From Solez *et al.* [1]; with permission.)



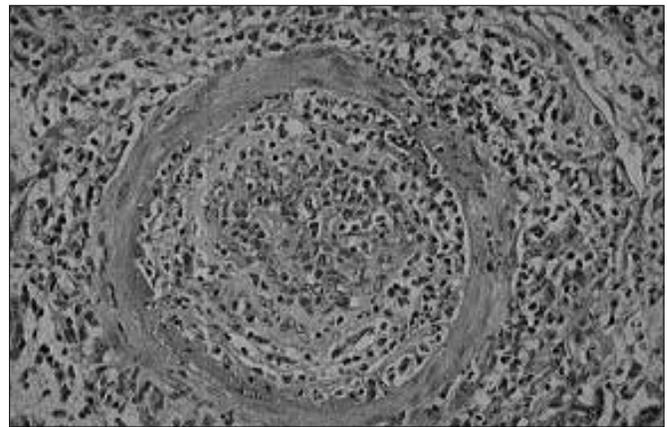
**FIGURE 10-5**

Intimal arteritis in a case of acute rejection. Note that more than 20 lymphocytes are present in the thickened intima. With this lesion, however, even a single lymphocyte in this site is sufficient to make the diagnosis. Thus, the pathologist must search for subtle intimal arteritis lesions, which are highly reliable and specific for rejection. (From Solez *et al.* [1]; with permission.)



**FIGURE 10-6**

Artery in longitudinal section shows a more florid intimal arteritis than that in Figure 10-5. Aggregation of lymphocytes is also seen in the lumen, but this is a nonspecific change. The reporting for some clinical trials has involved counting lymphocytes in the most inflamed artery, but this has not been shown to correlate with clinical severity or outcome, whereas the presence or absence of the lesion has been shown to have such a correlation. (From Solez *et al.* [1]; with permission.)



**FIGURE 10-7**

Transmural arteritis with fibrinoid change. In addition to the influx of inflammatory cells there has been proliferation of modified smooth muscle cells migrated from the media to the greatly thickened intima. Note the fibrinoid change at lower left and the penetration of the media by inflammatory cells at the upper right. Patients with these types of lesions have a less favorable prognosis, greater graft loss, and poorer long-term function as compared with patients with intimal arteritis alone. These sorts of lesions are also common in antibody-mediated rejection (see Fig. 10-9).