Renal Pathology Series: Kidney Transplant

www.pjkd.com.pk

Renal Transplant Pathology Series-III (B)

Dr. Muhammed Mubarak

Professor of Pathology and HOD
JIK Department of Histopathology,
Sindh Institute of Urology and Transplantation (SIUT),
Karachi, Pakistan.

Email address: drmubaraksiut@yahoo.com

PJKD 2020;4(4):347-351

Banff classification of renal allograft pathology has evolved enormously over the past 30 years and has become a multidisciplinary exercise. With this evolution, it has also increased in complexity and level of difficulty. It is no longer possible for a sole histopathologist without input from other clinical colleagues and pathologists, such as immunologists, to accurately diagnose and classify renal transplant pathology, especially the rejection. In this pictorial, we aim to provide an illustrated presentation of the Banff classification categories and practical tips and tricks to identify and report the lesions. This will be useful for better understanding of the renal transplant pathology not only for trainees and residents of nephrology and histopathology but also for practicing pathologists and nephrologists.

Banff category 2. Antibody-mediated changes

In this part, we will discuss the diagnosis and characterization of acute/active antibody-mediated rejection (AMR). In part A, we discussed hyperacute and accelerated acute types of AMR. It was thought during much of the early period of transplantation till early 1990s that antibodies cause only hyperacute and accelerated acute types of rejection and are not important in acute or chronic graft damage and dysfunction. However, with the widespread use of Banff classification coupled with better and newer antibody detection methods, and most importantly, the discovery and widespread use of C4d, it became apparent that antibodies are also important players in the causation of acute and chronic graft injury. With the help of above-mentioned ancillary techniques, criteria were developed for the diagnosis and classification of acute/active AMR during 2001 Banff meeting, which was published in 2003. For the first time, pathological criteria for the diagnosis and classification of AMR were developed. These are shown in Table 1. With this, the Banff classification became truly multi-disciplinary in nature, as it not only included histopathological criteria but also immunofluorescence and immunologic criteria for correct diagnosis of acute AMR. In the absence of these ancillary studies, some cases of acute AMR may be misdiagnosed. From Table 1, it is apparent, as also discussed in part A, that the main target of AMR is the circulatory system of the grafts, especially, the microcirculation, i.e., glomerular and/or peritubular capillaries in the case of kidney transplants. However, in contrast to hyperacute and accelerated acute types, in acute AMR, the character and intensity of glomerulitis and peritubular capillaritis is different. These are usually mild and comprise of either majority of neutrophils or majority of mononuclear cells or a mixture of both. This likely depends on the duration post-transplant at which acute AMR develops or the timing of the biopsy after graft dysfunction. Acute AMR may concur with borderline category, acute T-cell mediated rejection or interstitial fibrosis/tubular atrophy (IFTA). Table 2 depicts the pathological classification of acute AMR.

As is apparent from these tables and figures, AMR spans a whole spectrum of morphological lesions in the graft parenchyma ranging from acute tubular injury (ATI) to severe form of arteritis (v3), with the main changes being found in the vascular compartment, including the microcirculation. The focus of Banff classification has now shifted to AMR diagnosis and classification and diagnostic and classification criteria are being refined as more and knowledge accumulates. Molecular arrays are also being investigated for their potential use in early diagnosis of AMR.

Table 1. The immunopathological and serologic criteria for the diagnosis of acute antibody-mediated rejection in kidney allografts.

Diagnostic criteria	Findings
Morphological criteria of acute graft injury	Acute tubular injury Capillaritis- glomerular and peritubular Arterial- v3 arteritis
Immunopathological criteria of antibody and complement deposition and/or action	C4d positivity in peritubular capillaries Immunoglobulins and/or complements in peritubular capillaries or arterial lesions
Serologic criteria of circulating antibodies in the serum	Presence of circulating antibodies in blood against donor HLA or other donor antigens such as endothelial antigens

Table 2. Pathological classification of acute/active antibody-mediated rejection (fulfilling the criteria of C4d positivity and with circulating donor specific antibody)

Type 1	ATN-like
Type 2.	Capillary-glomerulitis, peritubular capillaritis (polymorphonuclear and/or mononuclear leukocytes in peritubular capillaries)
Type 3	Arterial – transmural inflammation/fibrinoid change

A series of representative images of biopsies with category 2 (acute AMR) of Banff classification are illustrated in Figures 1 to 6.

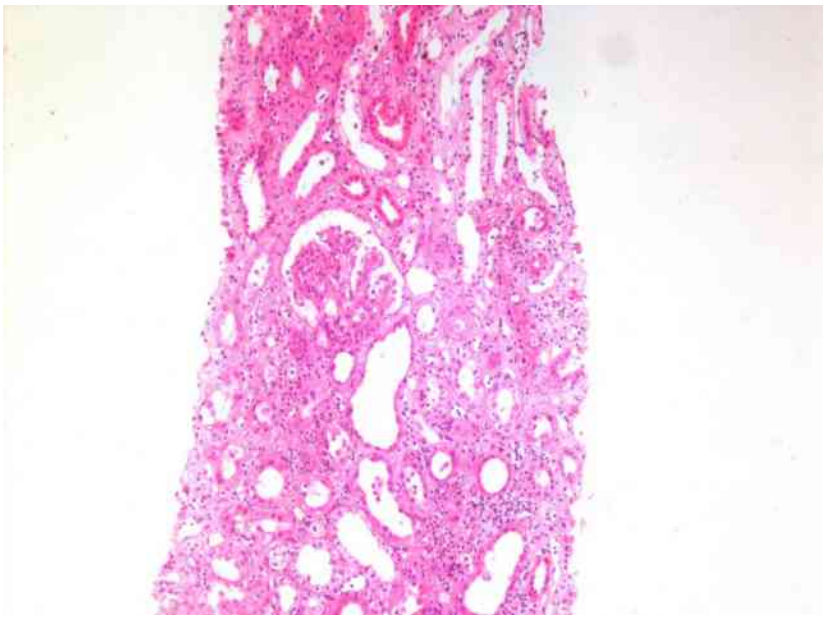

Figure 1. Low-power photomicrograph showing a representative area of a renal allograft biopsy done for acute graft dysfunction. At this magnification, the biopsy shows features of acute tubular injury (ATI), mild interstitial inflammation and edema. The glomerulus shows mild acute ischemic change. At this power, it is not possible to further characterize the nature of the lesion. (H&E, ×100).

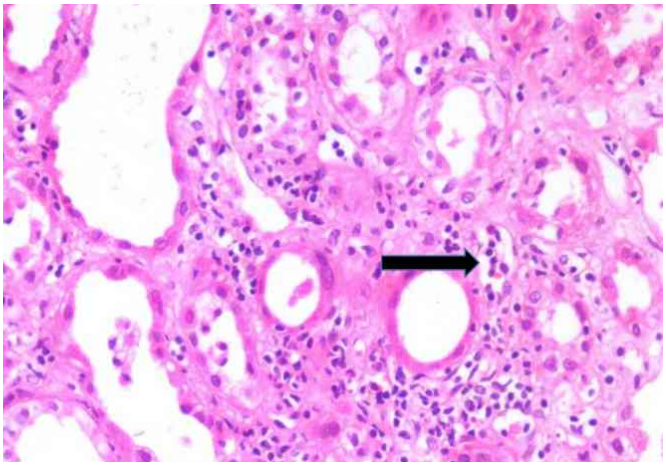

Figure 2. Medium-power photomicrograph of the same biopsy shown in Figure 1. There is mild interstitial infiltrate, acute tubular injury and one peritubular capillary showing more than 4-5 inflammatory cells in the lumen, consistent with peritubular capillaritis (arrow). Moderate acute tubular injury (ATI) is also seen, with a few tubules containing cellular debris in the lumen. (H&E, ×200).

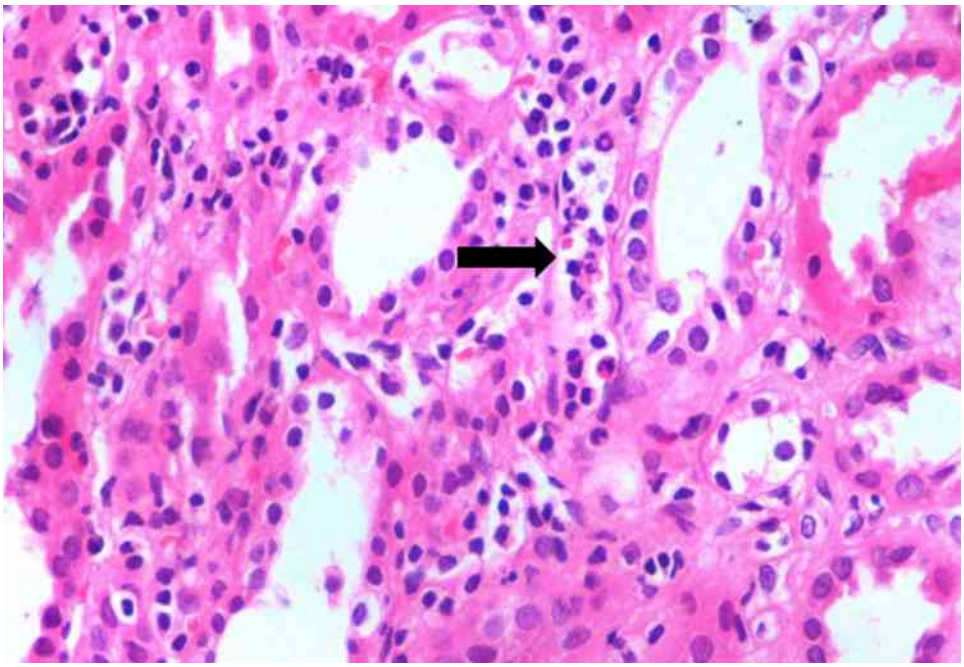

Figure 3. High-power photomicrograph showing a capillary with many inflammatory cells in the lumen. This will be categorized as peritubular capillaritis (ptc)-3 according to Banff criteria. Majority of inflammatory cells are neutrophils (arrow). The most severely affected peritubular capillary (PTC) is used for scoring the lesion. A number of other PTCs in the field show mild degrees of ptc. Ptc represents one of the components of microcirculation inflammation (MI) score (H&E, ×400).

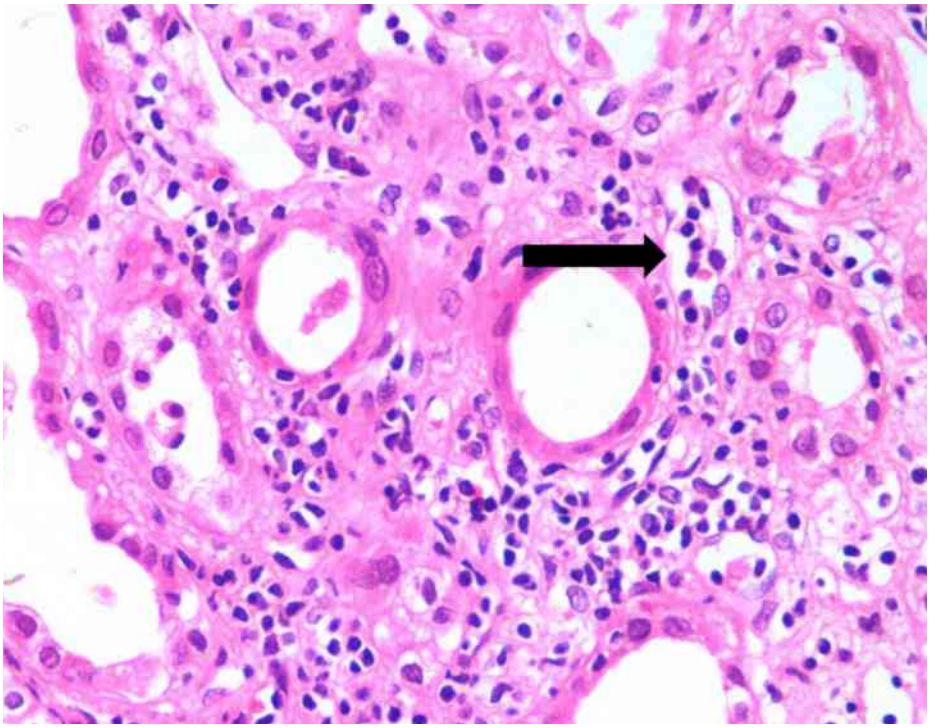

Figure 4. This is high-power photomicrograph of the same biopsy shown above. Ptc score in this case is ptc 2 and majority of cells in the lumen are mononuclear cells (arrow). There is also mild inflammatory cell infiltrate in the interstitium (H&E, ×400).

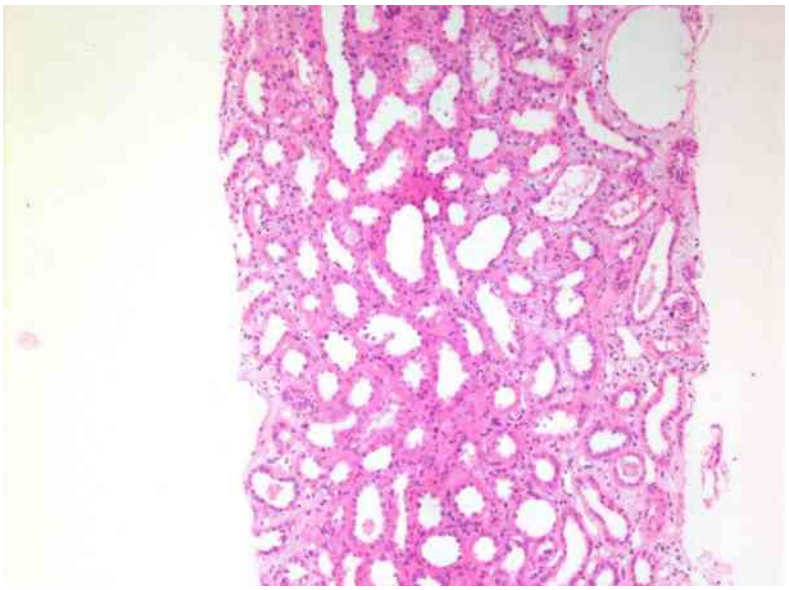

Figure 5. This is low-power photomicrograph of a representative area from a renal allograft biopsy done for acute rise in serum creatinine. There is moderate acute tubular injury (ATI) and generalized interstitial edema. Inflammatory cells are very scanty. Sometimes, antibody-mediated rejection (AMR) may present in this form. It can only be diagnosed as AMR if C4d and DSA are positive. This may represent a very early phase in the development of AMR or an unsampled example of some form of vascular rejection. (H&E, ×100).

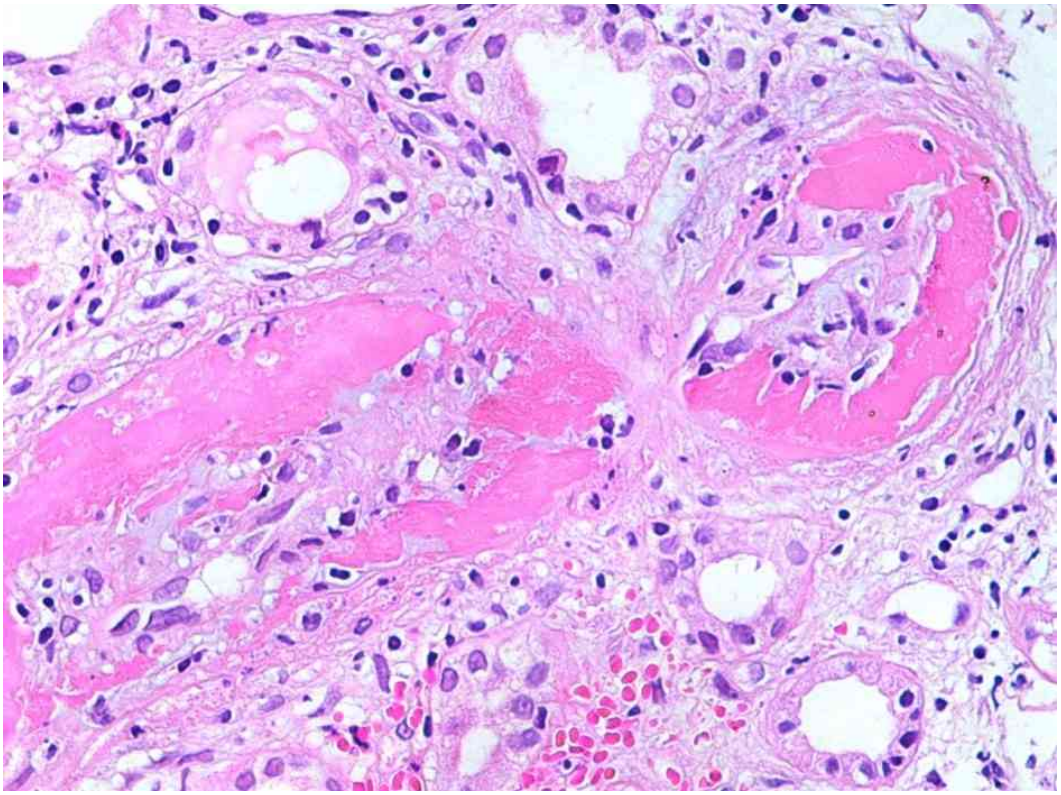

Figure 6. This is high-power photomicrograph of the biopsy with an interlobular artery at the center of the field. There is extensive fibrinoid necrosis of the arterial wall along with a few inflammatory cells and almost complete occlusion of lumen. This lesion qualifies for v3 Banff lesion score and is typically associated with antibody-mediated rejection. There is also interstitial hemorrhage in the background. Varying degrees of tubulitis are also seen in two tubules in the upper part of the field (H&E, ×400).

Further reading:

1. Racusen LC,Colvin RB,Solez K, Mihatsch MJ, Halloran PF, Campbell PM, et al. Antibody-mediated rejection criteria - an addition to the Banff 97 classification of renal allograft rejection.Am J Transplant 2003;3(6):708-714.
2. Mubarak M, Kazi JI. Evolution of the diagnostic criteria of antibody-mediated rejection of renal allografts: Banff classification updates. Port J Nephrol Hypert 2013; 27: 137-42.
3. Garg N, Samaniego MD, Clark D, Djamali A. Defining the phenotype of antibody-mediated rejection in kidney transplantation: Advances in diagnosis of antibody injury. Transplant Rev (Orlando). 2017;31(4):257-267.
4. Amore A. Antibody-mediated rejection. Curr Opin Organ Transplant. 2015;20(5):536-42.