Kidney Pathology Series: Kidney Transplant

www.pjkd.com.pk

Kidney Allograft Interstitial Fibrosis and Tubular Atrophy Due to Specific Causes: *Bacterial Infection/Pyelonephritis*

Dr. Muhammed Mubarak

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

DOI: 10.53778/pjkd64216
Email address: drmubaraksiut@yahoo.com
PJKD 2022;6(4):34-38

Chronic sclerosing changes in the renal graft parenchyma constitute the most difficult challenge to the field of kidney transplantation. In fact, these have emerged as one of the most common causes of late graft loss and re-transplants. These changes in the graft parenchyma result from a wide variety of causes including both allo-immune and non-immune factors (Table 1). A complex and, sometimes synergistic, interaction among these complicates the matter further. Often, more than one causes contribute to chronic injury to the graft. It is important to identify all causes and their relative contributions to chronic allograft injury if these are to be treated effectively. The role of the renal allograft biopsy and renal transplant pathologist is very important in this context. The pathologist should be familiar with the specific features pointing to specific causes. All of the specific causes of interstitial fibrosis/tubular atrophy (IF/TA) can and should be recognized by the pathologist. While some investigators suggest that the renal allograft biopsy is not useful in analyzing graft dysfunction after 1 year, published literature reveals that the allograft biopsy leads to a change in management resulting in improved renal function in 8% to 38% of patients.

Chronic changes due to chronic calcineurin inhibitor (CNI) toxicity were discussed in the previous issue of this journal. In this issue, we discuss the chronic sclerosing changes in the kidney graft parenchyma caused by bacterial infections of the graft /pyelonephritis.

Table 1. Some common and specific causes of chronic allograft dysfunction

Chronic rejection
T cell-mediated
Antibody-mediated
Chronic calcineurin inhibitor toxicity
Infections including bacterial and viral infections
Development of recurrent glomerular or other diseases
Development of de novo diseases (e.g., diabetic nephropathy)
De novo arteriosclerosis (hypertensive vascular disease)
Renal artery stenosis
Progression of donor disease (arteriosclerosis, fibrosis)

IFTA due to bacterial infections

Rejection and infections are the two principal determinants of long-term graft and patient survival following a successful kidney transplantation. With the steady decline in the rate of rejection during the past few years, the risk of infection is rising. This is mostly due to the use of more potent immunosuppressive agents. Infections are important in that they not only cause graft loss but can also lead to patient death if not diagnosed and treated promptly and appropriately. This tutorial is focused on bacterial infections affecting the graft itself.

Bacterial infections of the graft parenchyma initially and mainly involve the medulla. Hence, the adequacy criteria have included medulla along with cortex in the renal allograft sampling guidelines. However, in

severe or advanced cases, the infection may spread to and involve the cortex. As with the rejection process, infections also induce inflammatory response by the host immune system. In contrast to rejection, the predominant inflammatory cells in bacterial infections are the polymorphonuclear neutrophils (PMNs) with a variable mixture of chronic inflammatory cells, depending on the time duration of infection. These cells first accumulate in the interstitium and later invade the tubules (neutrophilic tubulitis). The accumulation of PMNs in the tubular lumina is termed as tubular microabscesses. The latter constitute the histopathologic hallmark of bacterial pyelonephritis. However, they may be seen in some instances of ischemic injury or infarction. If PMNs are confined to the peritubular capillaries (PTC) or glomerular capillaries, they may signify antibody-mediated rejection or hemolytic uremic syndrome. All these differentials must be kept in mind whenever PMNs are found in abundance in renal allograft biopsies. Typically, bacterial infections present with acute graft dysfunction and usually respond to treatment. However, recurrent, or incompletely treated infections may lead to chronic allograft injury and IFTA. Like rejection, infections can occur any time after transplantation. The pathologists should be aware of the above histopathological features in order not to miss the diagnosis of graft infection. Figures 1 to 8 illustrate examples of bacterial pyelonephritis resulting in chronic scarring of the graft parenchyma.

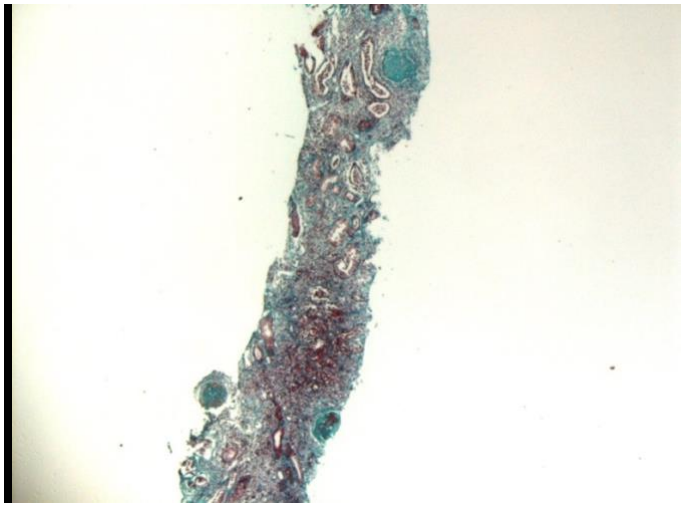

Figure 1. Low-power photomicrograph of a renal allograft biopsy showing marked chronic changes in the form interstitial fibrosis and significant loss of tubules. A few tubular lumina contain cellular debris even at this magnification. Three glomeruli included show global glomerulosclerosis (Trichrome stain, ×50).

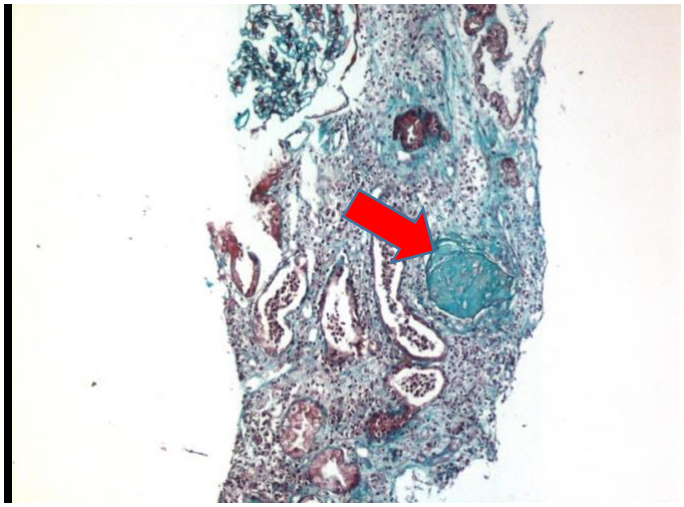

Figure 2. Low-power photomicrograph of the same renal allograft biopsy as shown in Figure 1 with one intact glomerulus and one globally sclerosed glomerulus (red arrow). Upto four tubules show clusters of inflammatory cells within their lumina. Chronic changes in the form of interstitial fibrosis and significant loss of tubules are also seen. (Trichrome stain, ×100).

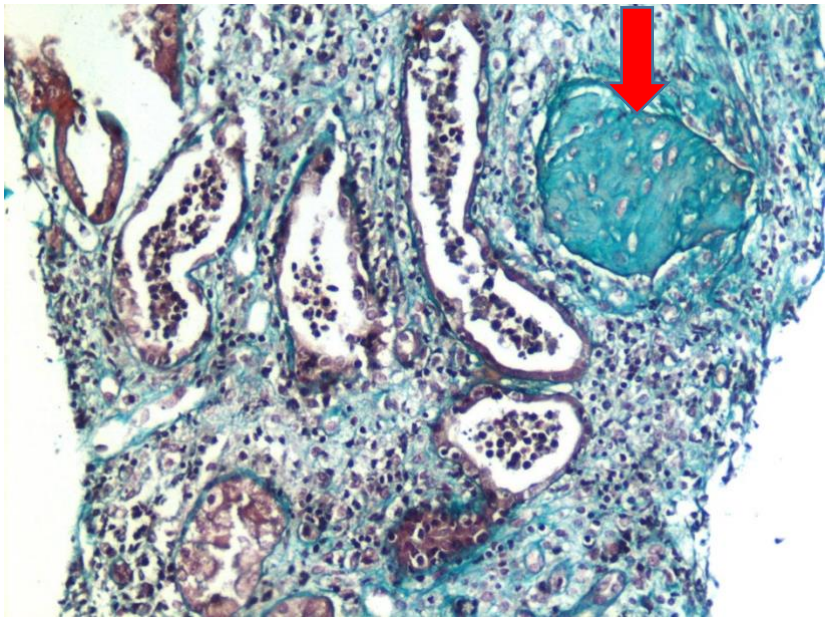

Figure 3. Medium-power photomicrograph of the same renal allograft biopsy as shown in Figure 1 with one globally sclerosed glomerulus (red arrow). Upto four tubules show clusters of inflammatory cells within their lumina. Chronic changes in the form of interstitial fibrosis and inflammation are also seen. (Trichrome stain, ×200).

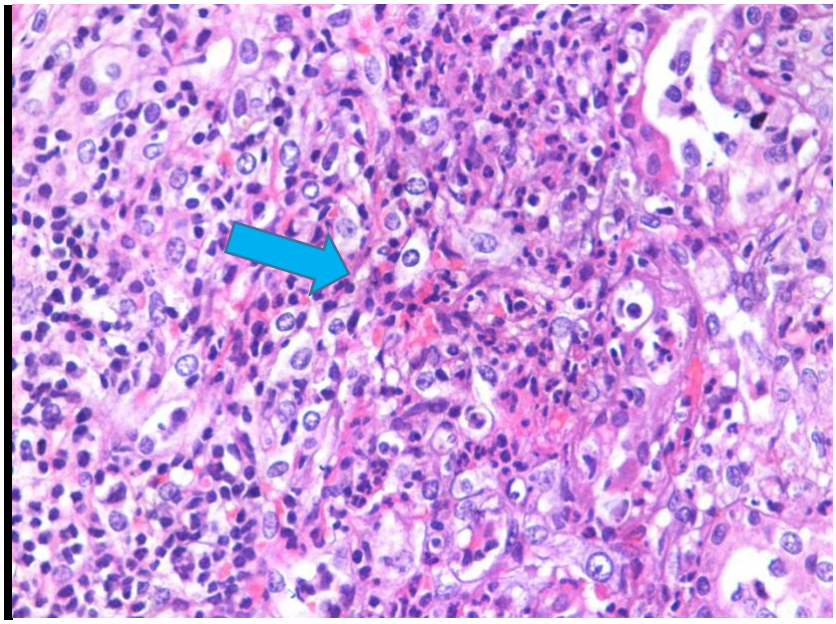

Figure 4. One representative area at high-power photomicrograph of the same renal allograft biopsy as shown in Figure 1 with dense mixed inflammatory cell infiltration in the interstitium. Many polymorphonuclear neutrophils (PMNs) are also seen. (H&E stain, ×400).

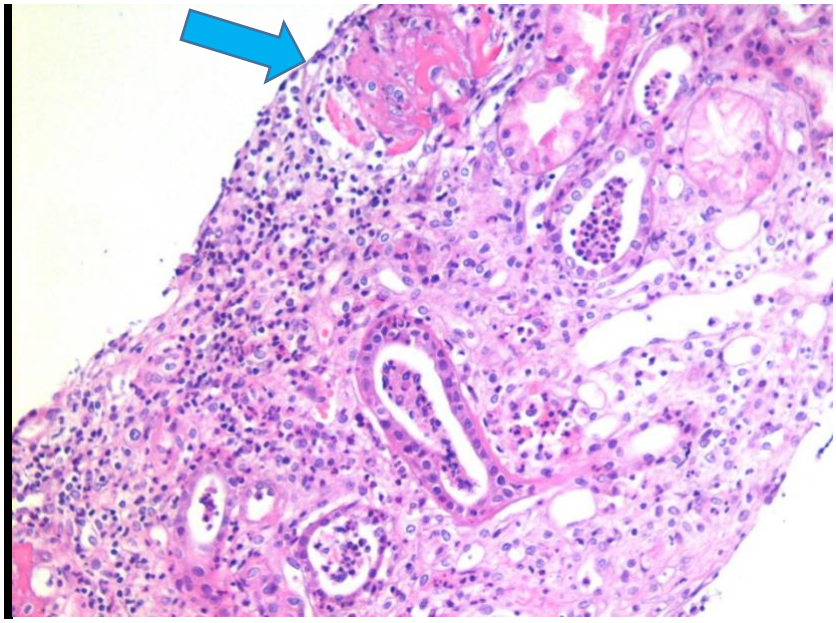

Figure 5. Another representative area at high-power photomicrograph of the same renal allograft biopsy as shown in Figure 1 with dense mixed inflammatory cell infiltration in the interstitium. Many polymorphonuclear neutrophils are also seen. Upto five tubules show clusters of PMNs within their lumina. One globally sclerosed glomerulus (blue arrow) is also present in the field. (H&E stain, ×200).

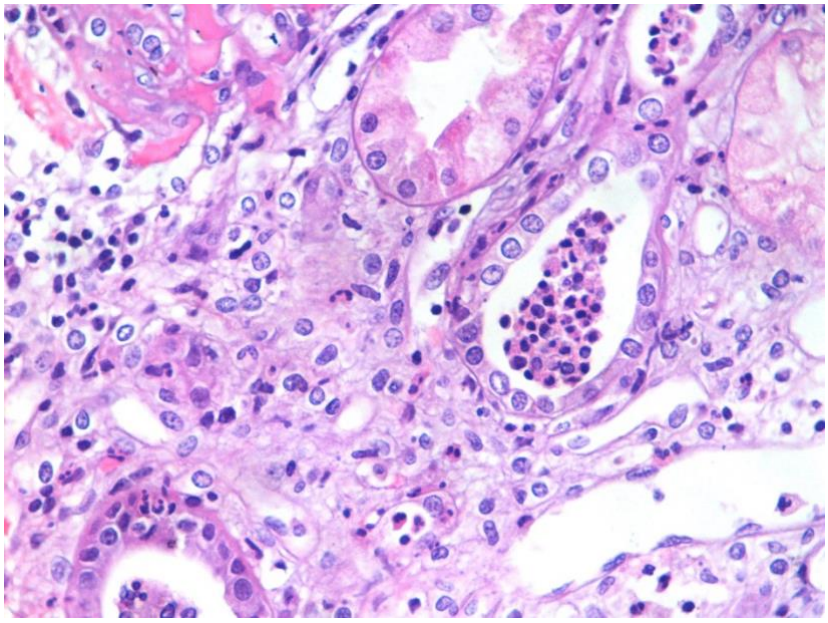

Figure 6. High-power view showing tubular microabscesses in three tubules. Interstitium is fibrotic and infiltrated by mixed inflammatory cells including a few neutrophils. (H&E stain, ×400).

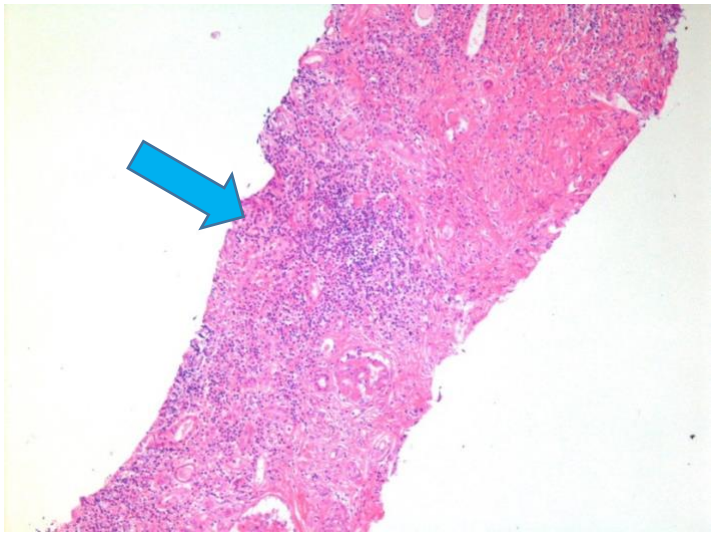

Figure 7. Low-power photomicrograph of another renal allograft biopsy showing severe chronic changes. A poorly formed lymphoid aggregate in the center of the field (arrow) suggests recurrent pyelonephritis as the underlying cause. Elsewhere tubular microabscesses were detected in the same biopsy. (H&E stain, ×100).

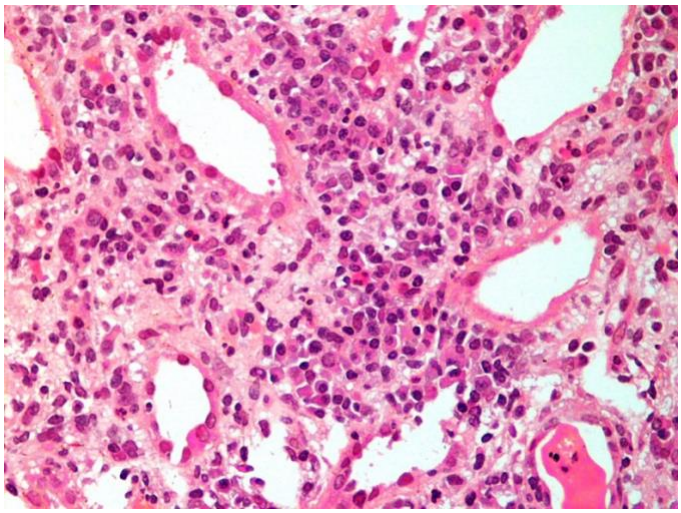

Figure 8. Medium-power photomicrograph of another renal allograft biopsy showing dense mixed inflammatory cell infiltration in the interstitium with many plasma cells. Presence of tubular microabscesses elsewhere in the biopsy suggested recurrent infection as the cause of this mixed inflammatory cell infiltrate. (H&E stain, ×200).

Further reading:

1. Solez K, Colvin RB, Racusen LC, Siss B, Halloran PF, Birk PE, et al. Banff ' 05 meeting report: differential diagnosis of chronic allograft injury and elimination of chronic allograft nephropathy (CAN). Am J Transplant 2007;7:518-26.
2. Racusen LC, Solez K, Colvin RB, Bonsib SM, Castro MC, Cavallo T, et al. The Banff 97 working classification of renal allograft pathology. Kidney Int. 1999;55(2):713-23.
3. Maanaoui M, Baes D, Hamroun A, Khedjat K, Vuotto F, Faure E, et al. Association between acute graft pyelonephritis and kidney graft survival: A single-center observational study. Am J Transplant. 2021;21(11):3640-3648.
4. Kazi JI, Mubarak M. Biopsy Findings in Renal Allograft Dysfunction in a Live Related Renal Transplant Program. J Transplant Technol Res 2012;2:108. doi:10.4172/2161-0991.1000108
5. Powers HR, Hellinger WC, Cortese C, Elrefaei M, Khouzam S, Spiegel M, et al. Histologic acute graft pyelonephritis after kidney transplantation: Incidence, clinical characteristics, risk factors, and association with graft loss. Transpl Infect Dis. 2022;24(2):e13801.
6. Singh R, Geerlings SE, Peters-Sengers H, Idu MM, Hodiamont CJ, Ten Berge IJ, et al. Incidence, risk factors, and the impact of allograft pyelonephritis on renal allograft function. Transpl Infect Dis. 2016;18(5):647-660.
7. Mathews T, Pushkar D, Kaul A, Bhaduaria D, Prasad N, Patel M, Behera M, Yachha M, Kushwaha R, Srivastava A. Early versus Late acute graft pyelonephritis: A retrospective analysis of graft and patient outcomes. Transpl Immunol. 2022 ;75:101657.