Letter

Re: Diagnosis of Interstitial Fibrosis and Tubular Atrophy in Kidney Allograft: Implementation of MicroRNAs

Dear Editor,

Chronic allograft nephropathy (CAN), like its successor category of interstitial fibrosis/tubular atrophy (IFTA), is a purely descriptive term used to denote the microscopical appearances of chronic sclerosing lesions observed on dysfunctional or surveillance kidney allograft biopsies.[1] However, the widespread use of the term led to a misconception in the minds of many, that it was a specific disease entity. This led to the formal replacement of the term by the Banff classification in its 2005 meeting by the "IFTA, not otherwise specified (NOS)" category.[2] Another important aim of this change was to encourage the transplant pathologists to look for and identify the specific causes of late graft dysfunction on kidney allograft biopsies and not just simply dump all the chronic lesions into the paper wastebasket category of CAN, so as to guide the optimal patient management and improve the long-term graft outcomes. The problems of nomenclature and classification aside, the chronic sclerosing changes are quite frequent on kidney allograft biopsies and form the focus of the current research on kidney allograft pathology.[1,2]

In a recent article published by the *Iranian Journal of Kidney Diseases*, Zununi Vahed and collegaues[3] have reviewed this topic in detail and explored the role of microRNAs as potential noninvasive biomarkers for an early detection of chronic changes in the kidney allograft. This objective, of course, consists of the "holy grail" of the kidney transplant pathology. However, even more important than the above goal, should be the search for markers that help identify the specific diseases causing chronic changes in the allograft, which can then be treated more appropriately, finally translating into better long-term outcomes. It is claimed that the major barrier to improving the long-term outcomes of kidney transplantation is the incomplete or erroneous understanding of the causes of chronic allograft failure.[4]

We take this opportunity to draw the attention of the authors to their remarks in the opening sentence, in which they claim that the modern immunosuppression has made little difference to the lesions of IFTA. This is not an entirely true statement. Two recent studies have revisited the natural history of IFTA in the modern era of transplant recipient management.[5,6] Both studies show that the in "low-risk" transplant patients on modern immunosuppressive agents, the prevalence and progression of early inflammation and chronic lesions is low. In fact, Stegall and coworkers[5] showed a dramatic reduction in the prevalence of moderate to severe fibrosis of 13% and 17% at 1 year and 5 years after transplantation, respectively, as compared to the results of previous studies.[7] In addition, there was little progression in the severity of the chronic lesions during the study period. They also claim that these changes have little impact on the future function of the kidney allograft. Both studies highlight the role of graft implantation injury in the early "subclinical inflammation" and of specific diseases in the late kidney allograft failure.[5,6] These results are markedly different from those of the landmark study by Nankivell and colleagues[7] on the natural history of CAN, which found moderate to severe chronic changes in 24.7% and 89.8% of the biopsies at 1 year and 5 years posttransplantation. It is worth noting here that the majority of kidney recipients in the study of Nankivell and colleagues[7] received cyclosporine and azathioprine. Mengel and colleagues[6] assessed both the histopathology and molecular profile of 6-week surveillance biopsies from a cohort of 107 kidney transplant patients with stable graft function. They concluded that the molecular phenotype does not provide a rationale for routine protocol biopsies, both for detecting silent rejection and for predicting the future outcome. The evidence from the above two studies adds to the other recent findings related to protocol biopsies, including the declining incidence of silent inflammation, diminishing role of calcineurin-inhibitor toxicity, of the lack of improvement after protocol biopsies, and the emergence of a new understanding of the role of specific diseases and late noncompliance in chronic allograft failure.[8] El-Zoghby and colleagues[4]

also found a declining role of calcineurin-inhibitor toxicity and concluded that most cases of kidney allograft loss have an identifiable cause.

There is, therefore, a strong need for integrating and corroborating the morphological study of kidney allograft biopsies with the newly emerging technologies such as molecular genetic, omics, and donor-specific antibody studies to better identify the "specific disease phenotypes" of chronic allograft injury, which can perhaps, then, translate into better and personalized management of kidney transplant recipients and better long-term graft outcomes.[4] In our view, this integration is all the more important and relevant in the context of IFTA than in the setting of acute kidney dysfunction.

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Re: Usefulness of Serum Procalcitonin Level for Prediction of Vesicoureteral Reflux in Pediatric Urinary Tract İnfection

Dear Editor,

We have read with interest the recently published article entitled "Usefulness of serum procalcitonin level for prediction of vesicoureteral reflux in pediatric urinary tract infection" by Mortazavi and Ghojazadeh.[1] They aimed to evaluate the predictive value of procalcitonin in describing vesicoureteral reflux (VUR). They concluded that elevated procalcitonin level may be used for prediction of all grades of VUR in children with febrile urinary tract infection. We would like to thank the authors for their contribution.

Procalcitonin, a 116-amino acid propeptide of calcitonin, is synthesized by the parafollicular C cells of the thyroid and involved in calcium homeostasis. [2] Several studies have demonstrated that procalcitonin levels rise in inflammatory states following bacterial or fungal infections, tumors, trauma and surgery. Procalcitonin can be a useful tool for diagnosis of sepsis and it can be used as a guide for antibiotic therapy in individual patients as a surrogate biomarker.

Urinary tract infections are crucial in young children since they can lead to serious problems such as kidney infections, permanent renal damages and end-stage renal failure.VUR is one of the most important predisposing factors of urinary tract infections in children and if it is left untreated, it can cause renal tissue inflammation and kidney damages.[1] Recently, procalcitonin has been proposed as a novel biomarker for prediction of VUR.[1]

Nonspecific elevations in procalcitonin levels can typically be seen in situations such as massive