Real Cause of High Level of Urinary $\beta_2$-Microglobulin after Renal Transplantation

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Dear Sir,

In their article “What is the true cause of high level urinary $\beta_2$-microglobulin after renal transplantation”, Nishi et al. [8] did not mention cytomegalovirus (CMV) infection as a reason for urinary $\beta_2$-microglobulin (U-$\beta_2$-MG) excretion. As reported by Bäckman et al. [1], CMV infections are known to cause high serum levels of $\beta_2$-MG. Because this protein has a low molecular weight (11.7 kD), it should be found in the urine during CMV infections. In order to test this hypothesis, we performed a prospective study in 149 patients undergoing kidney transplantation (table 1). In these patients, we determined $\beta_2$-MG, immunoglobulin G (IgG), transferrin (Tf), albumin (Alb), C-reactive protein (CRP) and $\alpha$-MG in 24-hour urine using a highly sensitive immunoluminometric assay [9]. In all CMV infections (n = 42), an isolated U-$\beta_2$-MG excretion was detected [4], while in all rejections, a nonselective glomerular proteinuria associated with urinary CRP excretion was observed [3, 6]. In ciclosporin-induced nephrotoxicity (n = 10), $\alpha$-microglobulinuria was a characteristic feature [5]. We did not detect U-$\beta_2$-MG in rejections and ciclosporin nephrotoxicity constantly. U-$\beta_2$-MG cannot be accepted as a marker of rejection or tubulotoxicity. This protein is not detectable in the urine constantly under these conditions probably because it is not stable in 24-hour urine. The reason why U-$\beta_2$-MG is, indeed, measureable in CMV infection constantly is not known. However, $\beta_2$-MG may coat CMV [2] and may become stable and detectable by this mechanism. As demonstrated, detection of isolated U-$\beta_2$-MG in 24-hour urine allows to diagnose CMV infections after renal transplantation. What Nishi et al. [8] described as an unknown Table 1. Changes in the concentration of urinary proteins in patients after renal transplantation with cytomegalovirus infections, rejections or acute ciclosporin nephrotoxicity

Data are given as median, minimal- and maximal values. ± C shows the changes between the time of diagnosis and the individual baseline. All concentrations of urinary proteins were related to the individual urinary creatinine (mg protein/g creatinine at the time of diagnosis divided by the values prior to diagnosis). © 1993 S.KargerAG, Basel 0028-2766/93/0653-0501 $82.75/0
Fig. 1. Flow scheme of different marker proteins, especially of CRPu in urine (CRPu) and serum (CRPs) after renal transplantation.

cause of U%-MG 3 weeks after transplantation has to be considered a CMV infection. Furthermore, our method enabled us to diagnose CMV infection earlier (median: 7 days) than using pp 65 CMV-antigen as a serum marker [4] of this disease. U-%-MG, especially in 24-hour urine, is not a good marker of kidney transplant rejection. To intensify immunosuppressive therapy following the detection of high levels of U-ß2-MG may cause fatal consequences when CMV infection is present. Therefore, our flow scheme (fig. 1) for the determination of urinary proteins [7] may be helpful in the diagnosis of impaired renal function after kidney transplantation. It has to be understood, that proteins of different molecular weight have to be analyzed in order to find out whether an isolated excretion of U%-MG is detectable or U%-MG is excreted inconstantly in association with other proteins.

References