What Is a True Cause of High Level of Urinary Beta-2-Microglobulin after Renal Transplantation?

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Dear Sir,

Serum β_2 -microglobulin (S^3_8MG) and urinary β_2 -microglobulin (U^3_8MG) have been utilized as markers of graft rejection or ciclosporin nephrotoxicity in renal transplantation [1,2]. We experienced a renal transplantation between two identical twins. We compared the postoperative changes in S- and U^3_8MG in this case with those in 6 cases that received renal transplants from 1 haplotype-identical living donor. No clinical abnormalities indicating graft rejection were recognized in those 6 cases. We found an interesting difference between them.

For the confirmation of a true identical set of twins we examined HLA typing, 17 kinds of blood types and DNA fingerprint pattern with the myo probe. HLA typing and 17 kinds of blood types coincided completely. The DNA fingerprint technique is a new forensic method for the judgement of an individual, a parent and child and a set of identical twins [3]. Band patterns of DNA fingerprint with the myo probe were quite the same between donor and recipient. From those results, our patients were considered true identical twins. In the clinical course after transplantation, enough urination and rapid decrease in S-Cr were observed. As immunosuppressive agents, ciclosporin, azathioprine and prednisolone were given according to the regular usage in our hospital.

The increased S^3_8MG level before transplantation rapidly decreased within the first week post-transplantation in 6 control cases as well as in an identical twins case (fig. 1). And in contrast to the twins case, 6 control

cases continuously had a high excretion of U^3_8MG , more than 1,000 $\mu g/l$ for 2 weeks after transplantation. First, we suspected this high excretion of β_2MG was related to the following 4 factors: (1) the elimination of β_2MG accumulated in the HD period; (2) tubular damage occurred during operation; (3) the nephrotoxicity of ciclosporin, and (4) the rejection in the transplanted kidney. There was a report that increased S^3_8MG decreased within 3 days after renal transplantation [4]. In the identical twins case, an extremely low level of U^3_8MG less than 500 $\mu g/l$ was noticed from the first week after transplantation (fig. 1b), whereas the level of S^3_8MG was almost the same as in controls before and after the operation (fig. 1a). It is supposed that this interesting result may contribute to the special condition of a transplantation between true identical twins. Total operation time, cold and warm ischemic time were almost the same in the 6 control cases and this identical twins case. The changes in urine volume, Ccr and FeNa% (fig. 1c) after renal transplantation did not show much difference between them. The immunosuppressive

treatment was done in the same combination, and dosage consisted of ciclosporin, azathioprine and prednisolone at least in the first 4 weeks postoperation. In the transplantation between identical twins, logically, rejection cannot occur. However, the potential or sub-clinical rejection which occurred in the transplanted kidney might prominently increase the level of $U^3\%MG$ but not as much as that of $S^3\%MG$. In other words, local production [5]

Fig. 1. a-c The changes in $S^3\%MG$, $U^3\%MG$ and $FeNa\%$ before and after renal transplantation. RT= Renal transplantation; •• = twins case; ■■■ = controls.

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or shedding [6] of β_2MG from HLA structure caused by the potential rejection in the transplanted kidney might relate to the high elimination of $U^3\%MG$. Of course this is a presumption derived from only 1 rare case. However, we are compelled to think that the main cause of high level of $U^3\%MG$ may be the potential rejection. Another question is why $U^3\%MG$ increased again from the 3rd week after transplantation in an identical twins case. Our answer is that this phenomenon might relate to the tubular damage by ciclosporin. Backman et al. [7] reported that $S^3\%MG$ of stable recipients treated with ciclosporin was higher than of those treated with azathioprine [7]. If the rejection is suppressed completely without side effects, accumulated $S^3\%MG$ might be discharged within the first week, and the very low level of $U^3\%MG$ might continue from the first week after renal transplantation.

References

Prischl F, Gremmel F, Schwabe M, et al: Beta-2 microglobulin for differentiation between ciclosporin A nephrotoxicity and graft rejection in renal transplant recipients. *Nephron* 1989; 51:330-337.

Martinez L, Kychenthal CV, Mendoza S, et al: Tubular markers in renal transplant patients under ciclosporin. *Transplant Proc* 1990; 22: 2277-2279.

Gill P, Anderson J, Werrett DJ, et al: Forensic application of DNA fingerprints. *Nature* 1985; 318:577-579.

Acchiardo S, Kraus AP, Jennings BR: β_2 -microglobulin levels in patients with renal insufficiency. *Am J Kid Dis* 1989; 13:70-74. Kin K, Kasahara T, Itoh Y, et al: β_2 -microglobulin production by highly purified human T and B lymphocytes in cell culture stimulated with various mitogens. *Immunology* 1979; 137:47-54.

Kubo RT, Colon SM, McCallmon RT: Some biological properties of β_2 -microglobulin and its antibody. *Fed Proc* 1976; 35:1182-1187. Backman L, Ringden O, Björkhem I, et al: Increased serum β_2 -microglobulin during rejection, ciclosporine-induced nephrotoxicity, and cytomegalovirus infection in renal transplant recipients. *Transplantation* 1986; 42:368-371.

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Announcement

6th International Congress on Bone Morphometry

October 4-9, 1992, Lexington, Ky., USA

The 6th International Congress on Bone Morphometry will be held in Lexington, Ky., on October 4-9, 1992. The scientific program will encompass up-to-date information on new developments in the field of bone histomorphometry with special emphasis on new frontiers in bone morphometry, i.e., histoenzymology, in situ hybridization and immunocytochemistry. There will be a broad spectrum of sessions addressing new developments and problems related to quantification of bone formation, bone resorption, bone structure and bone volume, quantitative effects of growth factors and hormones on bone and critical quality control issues related to bone morphometry. Moreover, there will be special sessions on new approaches to osteoporosis, renal bone disease, bone changes occurring with immobilization, malignancy and other clinical disorders. Another attractive feature of the meeting are sessions on bone morphometry assessing osteogenesis and remodeling into and around ingrowth prosthesis and the usefulness of bone morphometry for dentists, orthodontists, oral surgeons and plastic surgeons. Workshops will be held to address the role of bone morphometry in studying bone biomechanics and new technical developments in the field. For registration information contact:

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