Renal Tubular Defect in Nephrotic Syndrome Associated with Focal Segmental Glomerulosclerosis

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Dear Sir, Table 1. Renal function studies

Tubular insult with various degrees of histopathologic expression has consistently been encountered in nephrotic syndrome associated with focal segmental glomerulosclerosis. However, relating evidence supporting tubular functional abnormality was sporadically documented of which its significance is generally underestimated by the clinician [1–3]. In this respect, we have, therefore, observed tubular functional defect attested during 10–12 h fasting in 18 children with clinically steroid-resistant nephrosis and histopathologically proven FSGS. As depicted in table 1, there was a trend of increased urinary excretions of all the solutes above those of the normal control values during active proteinuria. Nevertheless, the differences were statistically significant only in the fractional excretion of phosphate and uric acid. In addition, simultaneous assessments of effective renal plasma flow using ^{131}I -labeled para-aminohippurate and glomerular filtration rate using $^{99\text{m}}\text{Tc}$ -labeled DTPA during active proteinuria revealed a preponderantly low effective renal plasma flow compared to glomerular filtration rate yielding a high filtration fraction.

Therapeutic combination of prednisolone (1–2 mg/kg/day), dipyridamole (10–15 mg/kg/day), calcium channel blocker (Nifedipine, 1–3 mg/kg/day) and ACE inhibitor (0.5–2 mg/kg/day) had been medicated to all 18 nephrotics with the duration of treatment varying from 6 to 24 months. Interestingly, reassessments of renal functions following the therapeutic trial revealed a regression of enhanced tubular excretion of solute in conjunction with the improvement of renal hemodynamics.

Normal	FSGS	Remission
active		

CCr – Creatinine clearance; TP = total protein; FENa = fractional excretion of Na; FECa = fractional excretion of Ca; FEP04 = fractional excretion of phosphate; FEUA = fractional excretion of uric acid; ERPF = effective renal plasma flow; GFR = glomerular filtration rate; FF = filtration fraction; FSGS = focal segmental glomerulosclerosis.

The enhancement of renal tubular excretions of inorganic phosphate, uric acid, calcium and sodium would indirectly reflect some degrees of defect in the tubular transport mechanism of the

kidney. With respect to the high filtration fraction observed during active proteinuria, tubular injury may be mediated by the hemodynamic factor. Inasmuch as renal microcirculatory flow has already been compromised in the nephrotic syndrome by both the low effective renal plasma perfusion and the defective quality of blood which is not only hypercoagulable and hyperviscous, but also has reduced red cell deformability [4–6]; the preponderant reduction

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Habib R: Focal glomerulosclerosis. *Kidney Int* 1973;4:355–361.

Bouissou F, Barthe PH, Pierragi MTH: Severe idiopathic nephrotic syndrome with tubular dysfunction (report of 9 pediatric cases). *Clin Nephrol* 1980;14:135–141.

Llach F: Hypercoagulability, renal vein thrombosis, and other thrombotic complications of nephrotic syndrome. *Kidney Int* 1985;28:429–439.

Futrakul P, Poshyachinda M, Mitrakul C: Focal sclerosing glomerulonephritis. A kinetic evaluation of hemostasis and the effect of anticoagulant therapy. A controlled study. *Clin Nephrol* 1978;10:180–186.

Cecchin E, Marchi SD, Panarello G, et al: Rheological abnormalities of erythrocyte deformability and increased glycosylation of hemoglobin in the nephrotic syndrome. *Am J Nephrol* 1987;7:18–21.

Dunn MJ, Mene P: Interactions of thromboxane A2 and prostaglandin E2 in the control of glomerular mesangial responses. *Am J Nephrol* 1989;9(suppl 1):7–12.

Patrono C, Salvati P: Thromboxane biosynthesis and pharmacologic modulation in progressive glomerulosclerosis. *Am J Nephrol* 1989;9(suppl 1):13–16.

Neuwirth R, Satrino JA, De Candido S, Clay K, et al: Angiotensin II causes formation of platelet activating factor in cultured rat mesangial cells. *Circ Res* 1989;64:1224–1229.

in blood flow through the efferent arteriolar compartment as being reflected by the high filtration fraction would undoubtedly further intensify the insult to the functional and structural integrity of the tubular epithelium. Recently, several mediators capable of constricting efferent arteriole thereby yielding a high filtration fraction such as angiotensin II, thromboxane A2, platelet-activating factor and calcium have been implicated in the pathogenesis of progressive glomerulosclerosis in experimental animal models [7–9]. 6

The therapeutic benefit of this preliminarily clinical trial with drugs exerting a vasodilating effect, such as dipyridamole, ACE inhibitor and calcium channel blocker, as evidenced by the clinical improvement in glomerular function as well as tubular transporting capacity, would render support to the concept that the hemodynamic factor may be responsible for the tubular insult.

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