

Urinary CD 80 in Nephrotic Syndrome: A Biomarker to Distinguish Minimal Change Disease From Other Glomerular Diseases

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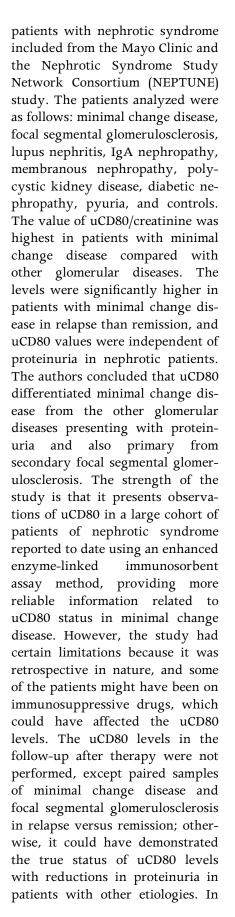
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ephrotic syndrome is the most common chronic kidney disorder with a remission and relapse course, and the response to corticosteroid treatment correlates with the prognosis of the disease. Minimal change disease and focal segmental glomerulosclerosis are the 2 common histopathologic lesions, besides other glomerular pathologies, found in a kidney biopsy of patients with idiopathic nephrotic syndrome.¹ The exact cause of minimal change disease is unknown; however, Reiser et al.² reported evidence of upregulation of B7-1 (also known as CD80) in podocytes induced by the injection of low-dose lipopolysaccharide in wild-type mice leading to proteinuria, whereas this effect was not found in mice lacking B7-1, which is indicative of a relationship between B7-1 expression and proteinuria. Subsequently, Ishimoto $et al.^3$ observed that

lipopolysaccharide injection caused proteinuria with the expression of CD80 by the podocytes. Additionally, CD80 mRNA expressions were also observed in response to Toll-like receptor 3 ligand polyinosinic-polycytidylic acid and Toll-like receptor 4 ligand lipopolysaccharide in patients with minimal change disease.4,5 Furthermore, it has been shown that sera of patients with minimal change disease in relapse were able to induce CD80 expression and its secretion by the podocytes.3

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In the recent past, several studies have demonstrated significantly increased levels of urinary CD80 (uCD80) in patients with minimal change disease in relapse than in remission, focal segmental glomerulosclerosis, and other glomerular diseases with good sensitivity (86.6%-99%), specificity (71.4%–100%), and areas under the curve (0.82-0.99) at different cutoff levels.^{5–8} In this issue of the journal, Gonzalez Guerrico et al.⁹ reported the utility a validated enzyme-linked of immunosorbent assay of uCD80 in



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addition, it was not shown whether the origin of uCD80 was from the kidney or filtered by the glomeruli due to increased levels in serum as a systemic response.

In contrast, Minamikawa et al.^{S1} reported that urinary CD80 is an unreliable diagnostic marker to differentiate among minimal change disease in relapse, focal segmental glomerulosclerosis, and other acquired and inherited kidney diseases, with the major limitation of small sample sizes in the study groups. In addition, Ling et al.⁵² showed that the raised uCD80 level as a prognostic biomarker with patients having >328.98 ng/g creatinine had a better response to immunosuppression (100%) vs. 34.5%) and a lesser proportion of patient progression to chronic kidney disease (2.9% vs. 41.4%) than below the cutoff level. The raised uCD80 excretion was found to have a decreased risk (relative risk 6.171, P = 0.013) of progression to chronic kidney disease in children with minimal change disease. The uCD80 also correlated significantly with proteinuria.^{5,S1}

CD80 is a transmembrane protein that is expressed on antigenpresenting cells or natural killer cells. It functions as a ligand and has important roles in T-cell activation or inactivation by binding with CD28 on T cells or cytotoxic T-lymphocyte–associated 4 on T-regulatory cells.^{S3} The podocytes can act as antigen-presenting cells, and a higher expression of CD80 can lead to reorganization of actin molecules in podocytes causing the disruption

of structures, which, in turn, can cause elevation of the podocytes' permeability, resulting in proteinuria.⁴ CD80 expression in glomeruli and its excretion in urine have been predicted for their response to abatacept therapy.^{\$4,\$5} Furthermore, it was also reported that uCD80 excretion in minimal change disease with positive CD80 staining in the glomeruli decreased after abatacept treatment with a temporary improvement in proteinuria.^{S4} Therefore, it appears that the origin of uCD80 may be from the podocytes.^{3,7} It has been emphasized that patients of idiopathic nephrotic syndrome expressing CD80 in their podocytes and showing increased urinary levels are steroid responsive and have long-term preservation of renal function.⁵⁶

The high uCD80 in nephrotic syndrome may be a potential urinary biomarker indicating minimal change disease, especially in children who mostly respond to steroid treatment, thus avoiding the need of a kidney biopsy.

DISCLOSURE

The author declared no competing interests.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF) Supplementary References.

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