Pediatr Nephrol (2014) 29:1467–1468
DOI 10.1007/s00467-014-2840-5

LETTER TO THE EDITORS

CD80 and suPAR in patients with minimal change disease and focal segmental glomerulosclerosis: diagnostic and pathogenic significance: Response

Gabriel Cara-Fuentes · Richard J. Johnson · Jochen Reiser · Eduardo H. Garin

Received: 14 April 2014 / Revised: 15 April 2014 / Accepted: 24 April 2014 / Published online: 11 May 2014
© IPNA 2014

Dr. Davin challenges our proposal on the utility of using serum suPAR and urinary CD80 levels to distinguish idiopathic focal segmental glomerulosclerosis (FSGS) from minimal change disease (MCD), which we base on the results of our study recently published in *Pediatric Nephrology* [1]. The basis of his argument relates to his supposition that CD80 is likely to be involved in FSGS since urinary CD80 was elevated in our patient cohort compared to normal controls. As evidence in support of his point of view he also refers to a recent study by Yu et al. that showed the presence of CD80 in glomeruli in some subjects with post-transplant FSGS [2]. These authors' observed that the latter patients had a resolution of proteinuria with CTLA4–Ig, which is a ligand for CD80 that blocks CD80-associated T-cell activation. Dr. Davin also suggests that the higher urinary CD80 levels in MCD may reflect the passage of soluble CD80 in the urine as a consequence of activation of the immune system during MCD flares.

We agree that FSGS may be associated with the staining of glomerular CD80 [2] and with mildly elevated urinary CD80 excretion [1]. However, in MCD there is a marked increase in urinary CD80 that results in minimal overlap between the two groups. Indeed, in 23 of our 26 FSGS patients the urinary CD80 values fell within 2 standard deviations of normal values, whereas only three of the 20 MCD patients in relapse fell into the same group. Furthermore, there was also a separation in suPAR levels. Segarra et al. similarly found that a serum suPAR level of >3,531 pg/ml had a 99 % ability to separate MCD and FSGS [3].

Dr. Davin suggests that higher CD 80 urinary levels in MCD than in FSGS might result from CD80 being released by T cells during the viral infections which usually trigger relapses in MCD. This suggestion is not supported by our early work which demonstrated that serum CD80 levels during relapse in MCD do not differ from those observed in MCD patients during remission and in normal controls [4].

The role of CD80 in podocyte diseases is still under active investigation and far from being definitive. There may also be additional differences in the role of CD80 in MCD and FSGS. For example, while CD80 may be present in glomeruli in FSGS, our recent experience suggests that the administration of CTLA4–Ig is not able to reverse the proteinuria (Alachkar et al. Letter to the Editor of the *New England Journal of Medicine*, March 27, 2014). Indeed, the study by Yu et al. [2] included the use of plasma exchange, which could also provide a reason for the beneficial response. In contrast, we found that the administration of CTLA4–Ig to two patients with MCD resulted in a transient but marked suppression of urinary CD80 excretion and urinary protein excretion (Garin et al., unpublished). In addition, the urinary excretion of CD80 in MCD is due to cell membrane-associated CD80—and not to soluble CD80.

We and others have found only a few FSGS patients showing staining of glomerular CD80 with mild increases in urinary CD80 excretion. Most of our patients did not show glomerular CD80 staining, and they had normal urinary CD80 excretion. We were surprised to see no data on urinary CD80 excretion in the publication of Yu et al., even in those patients who showed positive glomerular CD80 staining [2].

We do realize that more studies are needed on the sensitivity and specificity of serum suPAR and urinary CD80 in glomerular disease. In addition, studies on urinary suPAR may become increasingly valuable. Recently we did identify a patient with

G. Cara-Fuentes · E. H. Garin (✉)
Division of Pediatric Nephrology, Department of Pediatrics, University of Florida, Gainesville, FL, USA
e-mail: garineh@peds.ufl.edu

R. J. Johnson
Division of Renal Diseases and Hypertension, Department of Medicine, University of Colorado, Denver, CO, USA

J. Reiser
Department of Internal Medicine, Rush University Medical Center, Chicago, IL, USA

elevated levels of both serum suPAR and urinary CD80 who had a podocin mutation-associated FSGS. Thus, more studies are needed. However, our study and the study by Segarra [3] do suggest that serum suPAR and urinary CD80 are in general excellent markers for identifying idiopathic FSGS and MCD, respectively.

Conflict of interest Jochen Reiser is an inventor with pending or issued patents on novel therapies in proteinuric kidney disease. He stands to gain royalties from their future commercialization.

References

1. Cara-Fuentes G, Wei C, Segarra A, Ishimoto T, Rivard C, Johnson RJ, Reiser J, Garin EH (2013) CD80 and suPAR in patients with minimal change disease and focal segmental glomerulosclerosis: diagnostic and pathogenic significance. Pediatr Nephrol. doi:10.1007/s00467-013-2679-1
2. Yu CC, Fornoni A, Weins A, Hakroush S, Maiguel D, Sageshima J, Chen L, Ciancio G, Faridi MH, Behr D, Campbell KN, Chang JM, Chen HC, Oh J, Faul C, Arnaout MA, Fiorina P, Gupta V, Greka A, Burke GW 3rd, Mundel P (2013) Abatacept in B7-1-positive proteinuric kidney disease. N Engl J Med 369:2416–2423
3. Segarra A, Jatem E, Quiles MT, Arbos MA, Ostos H, Valtierra N, Carnicer C, Agraz I, Salcedo MT (2014) Diagnostic value of soluble urokinase-type plasminogen activator receptor serum levels in adults with idiopathic nephrotic syndrome. Nefrologia 34:46–52
4. Garin EH, Diaz LN, Mu W, Wasserfall C, Araya C, Segal M, Johnson RJ (2009) Urinary CD80 excretion increases in idiopathic minimal-change disease. J Am Soc Nephrol 20: 260–266