Letters and Replies

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Dialysis treatment and regulatory T cells

Sir,

We read with attention the paper by Hendrikx et al., recently published in Nephrology Dialysis and Transplantation [1]. The authors observed a lower number and an impaired function of both CD4+CD25bright+ and Foxp3+ T cells in end-stage renal disease patients, especially in haemodialysis (HD), when compared to healthy controls. These results are very interesting since it has been demonstrated that specific T cell populations, also known as regulatory T cells (Treg), play a key role in the control of the immune system [2,3]. Here, we report the results of a study which in contrast with the ones by Hendrikx et al. In order to evaluate the effects of dialytic treatment on Treg cells subset, we studied seven patients (60.4 ± 10.3 years, m/f: 4/3) on standard thrice-weekly bicarbonate HD with a low-flux membrane [cuprophane (CU)] for at least 6 months. A whole blood sample was harvested before and after the dialysis (PRE and POST, respectively). Peripheral blood mononuclear cells (PBMC) were isolated from blood samples by lymphoprep gradient density centrifugation. Flow cytometry was performed in order to evaluate Treg cells, using anti-CD4, CD25 and Foxp3 mAbs (BD Biosciences, San Jose, USA). According to flow cytometry results, we identified CD4+CD25bright+ and Foxp3+ cells.

Treg cell populations were quantified both as absolute number and as percentage of PBMC (n/%). Seven healthy sex–age-matched subjects (58.6 ± 7.6 years, m/f: 3/4) were the controls (CON).

There was a significantly higher absolute number and percentage of Foxp3+ cells in HD patients when compared to CON (124 ± 49 cells/3.0 ± 1.2%, P < 0.05 vs PRE), while there was no significant difference of Foxp3+ cells between PRE and POST (243 ± 131 cells/4.6 ± 1.8% vs 249 ± 96 cells/5.2 ± 2.8%, respectively). Similarly, CD4+CD25bright+ cells had significantly increased in number in PRE and POST (75 ± 46 and 87 ± 39 cells, respectively), compared to CON (51 ± 21 cells, P < 0.05 vs POST).

It is noteworthy that our data are contrasting with those by Hendrikx et al., who reported a lower number of Treg cells in HD patients. Some considerations could explain this discrepancy. Firstly, since biocompatibility influences inflammation and immune response [4], it is reasonable that the use of different membranes could play an important role in Treg cells modulation. Concerning this, our patients were treated with CU, a low biocompatibility membrane, while the devices used by Hendrikx et al. have not been reported. Moreover, it is possible that different individual and clinical factors—such as age, comorbidity, underlying nephropathy, etc.—could have effects on Treg cells, which are completely unknown so far.

In conclusion, we demonstrated that patients on HD with bioincompatible membranes (CU) present a state of chronic Treg cells induction, which is not affected by dialytic treatment. However, the contrasting results reported and the substantial lack of data about the mechanisms of Treg cells modulation in HD patients call attention to the requirement of larger studies.

Conflict of interest statement. None declared.

Editorial Note: Dr Hendrikx et al. had been invited to reply to this letter but we did not receive a response.

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Comment on ‘Membranous glomerulonephritis secondary to Borrelia burgdorferi infection presenting as nephrotic syndrome’

Dear Sir,

We read with interest the case of membranous glomerulonephritis secondary to Borrelia burgdorferi infection reported by Dr. Papineni et al. [1]. It is indeed interesting that, after the first reports of glomerulonephritis secondary to Lyme disease [2,3], new cases of apparently...
immune complex-mediated glomerulonephritis come to surface [1,4]. Although the actual frequency of Lyme disease-associated glomerulonephritis in humans is unknown as yet, it is our sense that this is most probably an under-diagnosed situation. An important factor that permits the diagnosis of the Lyme-associated glomerulonephritis to evade is the potentially chronic, remitting and relapsing course of the clinical manifestations of the causing infection. In view of the diagnostic obstacles and probably the low clinical suspicion for the search of Lyme disease, we believe that more cases of so-called 'primary' membranoproliferative glomerulonephritis (MPGN) or other glomerulonephritides might be associated with Lyme disease but are not diagnosed as such [5], a case which has also been documented in proteinuric dogs [6]. Regarding the treatment of Lyme nephritis, as long as the stimulation of the immune system caused by the infection seems to play a pivotal role in infection-associated glomerulonephritides, it would seem rational to treat such cases with a combination of antibiotics plus immunosuppressive therapy (corticosteroids, plasma exchange, interferon, monoclonal antibodies, etc.), in a way similar to the schemes used in the treatment of hepatitis C virus-related glomerulonephritis. Although such a treatment has already been reported to be effective in a case of Lyme nephritis [3], the existing data are inconclusive.

Conflict of interest statement. None declared.

Editorial Note: Dr. Papineni et al. had no further comments on this letter.

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MSK and dRTA: a puzzling association

Sir,

Carboni et al. have reported two intriguing cases [1]. We have a few concerns, however. The typical clinical phenotype of the recessive distal renal tubular acidosis (dRTA) presented by the two patients is very different from the one observed in characteristic medullary sponge kidney (MSK) patients. The latter frequently have defective distal acidification, but in its incomplete form, as we have recently reported [2]. Although in adulthood patients have osteopaenia, they do not manifest failure to thrive or have growth retardation in childhood [2]. Furthermore, sensorineural hearing loss has never been described in typical MSK patients.

The radiological diagnosis of MSK is more complicated than what is generally believed. Technical procedures may show urographic pictures resembling MSK. Thus, were the papillary precaliceal ectasias documented on films taken at least 10 min after injection of the contrast medium? Moreover, were they disclosed without compression manoeuvres or obstruction?

We agree with the authors that further studies on larger series are necessary to confirm their findings and possible causal relationship. We would add that both genetic and radiological studies on patients with typical MSK or with recessive dRTA should be performed.

At present, we would be very cautious in considering these two cases as MSK patients.

Conflict of interest. None declared.

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