NDT Plus (2010) 3: 104
Advance Access publication 6 November 2009

syndrome [1], necrotizing and crescenting glomerulonephritis [3,5], minimal lesion glomerulopathy [2], extracapillary glomerulonephritis with IgA deposits or active follicular necrosis against a background of glomerular sclerosis [4].

It is noteworthy that, as with this Crohn's disease case, favourable outcomes have been reported in all other rheumatoid arthritis cases. After adalimumab discontinuation and glucocorticoid [4] and/or immunosuppressive therapy [3,5], renal function recovered within a few weeks. Of interest, in one case proteinuria relapsed after adalimumab rechallenge [2].

In this case, the relative contributions of adalimumab and of the underlying Crohn's disease to the development of proteinuria cannot be exactly determined. However, it is questionable whether in this particular patient adalimumab induction scheme was the only factor able to induce proteinuria. We believe that the complete reversibility of proteinuria after adalimumab discontinuation points towards adalimumab as a triggering factor to a strongly predisposed for a renal dysfunction individual.

As there have been some concerns regarding safety issues during administration of anti-TNF-α agents, it is of importance to understand the mechanism(s) of their interference in the normal kidney function. By this way, we may able to properly screen and possibly identify high-risk groups before initiation of anti-TNF-α therapies. For the moment, careful patient selection for biological agents as well as regular follow-up can promptly diagnose and completely reverse rare or unexpected episodes.

Conflict of interest statement. None declared.

1st Department of Internal Medicine &
Hepato-Gastroenterology Unit
University Hospital of Ioannina
Ioannina, Greece
E-mail: etsianos@uoi.gr

Konstantinos H. Katsanos
Dionysios Theiakos
Ioannis Vagias
Dimitrios Christodoulou
Epameinondas V. Tsianos

1. Portuesi MG, Perosa P. Nephrotic syndrome in a patient with rheumatoid arthritis treated with adalimumab: a case report. *Rheumatismo* 2008; 60: 61–63
2. den Broeder AA, Assmann KJ, van Riel PL *et al*. Nephrotic syndrome as a complication of anti-TNFalpha in a patient with rheumatoid arthritis. *Neth J Med* 2003; 61: 137–141
3. Stokes MB, Foster K, Markowitz GS *et al*. Development of glomerulonephritis during anti-TNF-alpha therapy for rheumatoid arthritis. *Nephrol Dial Transplant* 2005; 20: 1400–1406
4. Saint Marcoux B, De Bandt M, CRI (Club Rhumatismes et Inflammation). Vasculitides induced by TNFalpha antagonists: a study in 39 patients in France. *Joint Bone Spine* 2006; 73: 710–713
5. Simms R, Kipgen D, Dahill S *et al*. ANCA-associated renal vasculitis following anti-tumor necrosis factor alpha therapy. *Am J Kidney Dis* 2008; 51: e11–e14

doi: 10.1093/ndtplus/sfp158

Lacking evidence for calcium-binding protein fetuin-A to be linked with chronic kidney disease-related pruritus (CKD-rP)

Sir,

Uraemic pruritus, now better known as chronic kidney disease-related pruritus (CKD-rP), is still a commonly experienced, tormenting and challenging symptom in patients with chronic kidney diseases [1].

There has been an ongoing discussion whether pruritus in chronic kidney disease is brought about by the common disturbance of calcium/phosphate homeostasis [2].

Recently it has been proposed that a vicious circle of metabolic derangements (malnourishment, inflammation, arteriosclerosis) may explain the exaggerated morbidity and mortality in a subset of haemodialysis patients [3]. Inflammation might be the most deleterious factor in this respect which, besides other factors, is related to the occurrence of CKD-rP and down-regulation of fetuin-A, an important calcium-binding circulating protein favouring tissue-calcifications in these patients [4].

Thus, we were interested in whether patients with CKD-rP display lower levels of serum fetuin-A.

Ten patients in a hospital-based haemodialysis centre complaining about CKD-rP were compared to another 12 patients who did not report to have suffered from CKD-rP at least 6 months prior to the interview. Patients with CKD-rP were asked to score the intensity of current pruritus using a visual analogue scale (VAS) ranging from 0 to 10. In both groups, 10 ml of blood was taken immediately after puncture of the arterio-venous fistula, and fetuin-A, 25-hydroxyvitamin D_3 (25[OH]D_3), total protein, albumin, calcium (corrected for serum albumin), phosphate, and high-sensitivity CRP (hsCRP) were measured.

Independent *t*-tests (continuous variables) and a χ^2-test (gender) evaluated whether there were significant ($P < 0.05$) differences between patients with and without CKD-rP.

The mean pruritus intensity of patients with CKD-rP was 5.9 ± 1.9. After identifying one univariate outlier (hsCKP $= 35.6$) in the group of patients without CKD-rP, CRP was significantly higher in patients with CKD-rP. We failed, however, to find significant differences in serum-calcium, phosphate, fetuin A and 25-OH-Vitamin D3 between the two groups (Table 1). Additionally, there was no relationship between the intensity of CKD-rP and the metabolic factors measured (including CRP) in patients suffering from pruritus.

Although our study approach has methodological limitations (small number of patients, no matched pairs) the results suggest that neither calcium-binding protein fetuin-A levels nor 25(OH)D_3 values were noticeably different in patients with CKD-rP compared to patients without CKD-rP. On the other hand, the marker for inflammation, CRP, was found to be significantly higher in patients with CKD-rP as shown before [5]. We hence believe that other inflammation-driven processes need to be studied in

Table 1. Patient and clinical characteristics between the two groups. PTH (intact parathyreoid hormone), hsCRP (high-sensitivity C-reactive protein), 25(OH)D_3 (25-hydroxyvitamin D_3)

	CKD-rP $n = 10$ M (SD)	No CKD-rP $n = 11$ M (SD)	*P*
Kt/V	1.5 (0.40)	1.3 (0.28)	0.28
Age	66.2 (12.7)	66.5 (13.9)	0.48
Male [*n* (%)]	5 (50.0)	8 (72.7)	0.39
Female [*n* (%)]	5 (50.0)	3 (27.3)	
Time on haemodialysis in months	40.6 (30.5)	38.7 (50.1)	0.92
Current use of 1-OH-vitamin D	0.5 (0.5)	0.7 (0.5)	0.31
Current use of cinacalcet	0.3 (0.5)	0.5 (0.5)	0.28
PTH (ng/L)	317.5 (334.0)	525.8 (474.3)	0.26
Fetuin A (g/L)	0.4 (0.1)	0.4 (0.1)	0.53
Corrected calcium	2.3 (0.2)	2.2 (0.2)	0.45
Calcium (mmol/L)	2.2 (0.2)	2.2 (0.2)	0.48
Protein (g/L)	69.3 (4.7)	68.4 (4.5)	0.65
Albumin (g/L)	35.7 (3.3)	35.7 (5.9)	0.99
HsCRP (mg/L)	12.5 (9.8)	4.1 (3.0)	0.02
25(OH)D_3 (μg/L)	13.9 (4.0)	14.2 (6.3)	0.91
Phosphate (mmol/L)	1.8 (0.6)	1.8 (0.4)	0.73

the future in order to understand the pathomechanisms of CKD-rP.

Conflict of interest statement. None declared.

[1]Department of Nephrology
Deutsche Klinik für Diagnostik
Wiesbaden, Germany
[2]Clinical Social Medicine
University Hospital Heidelberg
[3]Endocrinology/Oncology
Limbach Laboratory, Heidelberg
[4]Clinical Social Medicine
Occupational and Environmental
Medicine, University Hospital
Heidelberg, Germany
E-mail: T_Mettang@t-online.de

Thomas Mettang[1]
Uwe Matterne[2]
Heinz Jürgen Roth[3]
Elke Weisshaar[4]

1. Pisoni RL, Wikstrom B, Elder SJ *et al*. Pruritus in haemodialysis patients: international results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). *Nephrol Dial Transplant* 2006; 21: 3495–3505
2. Momose A, Kudo S, Sato M *et al*. Calcium ions are abnormally distributed in the skin of haemodialysis patients with uraemic pruritus. *Nephrol Dial Transplant* 2004; 2: 2061–2066
3. Pecoits-Filho R, Lindholm B, Stenvinkel P. The malnutrition, inflammation, and atherosclerosis (MIA) syndrome—the heart of the matter. *Nephrol Dial Transplant* 2002; 17(Suppl 11): 28–31
4. Metry G, Stenvinkel P, Qureshi AR *et al*. Low serum fetuin-A concentration predicts poor outcome only in the presence of inflammation in prevalent haemodialysis patients. *Eur J Clin Invest* 2008; 38: 804–811
5. Kimmel M, Alscher DM, Dunst R *et al*. The role of micro-inflammation in the pathogenesis of uraemic pruritus in haemodialysis patients. *Nephrol Dial Transplant* 2006; 21: 749–755

doi: 10.1093/ndtplus/sfp161

Advance Access publication 16 December 2009

Membranous glomerulonephritis secondary to *Borrelia burgdorferi* infection presenting as nephrotic syndrome

Sir,

A few months following a tick bite an adult patient presented with progressive oedema, hypoalbuminaemia and nephrotic range proteinuria. Serology was positive for *Borrelia burgdorferi* and renal biopsy confirmed secondary membranous glomerulonephritis (MGN).

A 64-year-old male sustained a tick bite on his left leg whilst holidaying on an island near Stockholm. There was no localized reaction or febrile illness associated with the bite. Over the next few months he experienced progressive oedema. Blood tests showed elevated serum creatinine at 147 μmol (106 μmol 2 months prior to holiday), serum albumin 11 g/L and serum cholesterol/HDL ratio 28.8. Urine dipstick showed 4+ of protein and 1+ of blood. Twenty-four-hour urinary collection for protein excretion was 15.46 g/24 h (<0.15 g/24 h). Hepatitis serology and autoimmune screen were negative and complement levels were normal.

Initial enzyme immunoassay to *Borrelia* C6 peptide was reactive. This was followed by western immunoblot which was *Borrelia burgdorferi* IgG antibody positive and IgM antibody negative, consistent with recent infection. The patient was treated with doxycycline 100 mg twice daily for 1 month.

Ultrasound of the renal tract revealed normal sized kidneys and a renal biopsy was performed. Histological examination showed diffuse thickening of the glomerular basement membrane (GBM). Immunohistology demonstrated IgG and C3 in a diffuse granular intensive reaction along the GBM in a membranous pattern. Electron microscopy revealed large electron dense deposits on the mesangial surface.

The patient is on an angiotensin-converting enzyme inhibitor to reduce the intraglomerular pressure, thereby reducing the rate of his disease progression, and on warfarin therapy to reduce the risk of thrombotic complications. His oedema has subsided and the proteinuria has decreased to 650 mg/mmol/L on a recent urine PCR (protein/creatinine ratio) determined in our clinic.

Lyme disease is caused by the tick-borne spirochete *Borrelia burgdorferi* [1].

Clinical manifestations of Lyme disease include a slowly expanding skin lesion, erythema migrans, which occurs at the site of tick bite. The skin lesion is frequently accompanied by malaise, headache, arthralgia, fever or regional lymphadenopathy, followed within days or weeks by disseminated infection that affects the nervous system, heart or joints [2]. Infection with *Borrelia burgdorferi* is well described as a cause of glomerulonephritis in animals, particularly canines [3]. This is rarer in humans, and association of Lyme disease with membranoproliferative glomerulonephritis (MPGN) in humans has been described in the literature only twice [4,5].

Most membranous glomerulonephritis is idiopathic but MGN may be secondary to immunological conditions, infections (hepatitis B and C, malaria), neoplasms or drugs.