Letters

Advance Access publication 16 February 2009

eGFR—Why read tea leaves when you can make the measurement?

Sir,

In a recent issue of *Nephrol Dial Transplant*, Poggio and Rule discuss the many inherent problems associated with estimating GFR (eGFR) by evaluating the fluctuation of serum creatinine [1]. Unfortunately, all renal biomarkers to date are influenced by a wide range of non-renal factors that can vary across different patient populations, disease states, diet and drug intake—both prescribed and over the counter. A great deal of effort has been devoted towards the development of correction formulas to improve the diagnostic value of biomarker-based estimates, MDRD being one example. Given the large number of variables—both known and unknown—eGFR tests are not likely to achieve the high level of accuracy, reproducibility and reliability associated with a measurement-based test.

An accurate GFR test relies on measuring the renal clearance of a filtration probe under controlled conditions. Correctly administrated, a measured GFR test will provide the correct value. The general method to accurately measure GFR is simple and straightforward. The test requires a series of timed blood or timed blood and urine collections postadministration of the filtration probe and the test is completed in 4 h on average. Some nephrologists, many of whom have never performed this procedure, view the length of the test as a major clinical barrier. However, in terms of time, a measured GFR test is no longer than many other clinical diagnostic procedures used in other fields of medicine. At present, there are several different analytical methods available to measure the concentration of a filtration probe in collected samples. Most recently, an ELISA method that is both inexpensive and readily adaptable in most clinical laboratory settings has been reported [2].

Many recent papers suggest that there are urgent clinical settings where a measured GFR test is preferred, particularly in patient populations where kidney function is expected to be >60 ml/min/1.72 m², such as healthy kidney donors, patients on nephrotoxic drugs, applications in clinical trials and risk stratification for interventional cardiovascular procedures. Moreover, a GFR measurement can complement eGFR screening by providing a confirmatory test for early stages of CKD. Most papers discussing eGFR, including Poggio and Rule, state that an accurate GFR is important and eGFR values are unreliable in many clinical settings and that a measured GFR test is unfortunately "expensive and inconvenient." We believe that the technical impediments to obtaining an accurate GFR measurement have been removed and the field of nephrology can now advance to fulfilling its clinical needs with a measured GFR test using the diagnostic tools currently available.

Conflict of interest statement. None declared.

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

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1. Poggio ED, Rule AD. A critical evaluation of chronic kidney disease—should isolated reduced estimated glomerular filtration rate be considered a ‘disease’? *Nephrol Dial Transplant* 2008

doi: 10.1093/ndt/gfp064

Advance Access publication 30 March 2009

Acute nephritic syndrome after anti-VEGF therapy for renal cell carcinoma

Sir,

Two interesting recent publications in this journal reported biopsy-proven kidney damage after treatment with the vascular endothelial growth factor (VEGF) receptor blocker sunitinib [1,2]. We would like to report another case of acute renal failure during treatment with this drug, yet with a different histopathological picture.

A 61-year-old woman was treated with sunitinib (50 mg once daily) for a renal cell carcinoma that was metastasized to lungs and abdominal lymph nodes. At baseline, the serum creatinine was 84 µmol/L with normal urine sediment and no proteinuria. Twenty-five days later, she was admitted because of nausea and vomiting and a risen serum creatinine level (362 µmol/L). Discontinuation of sunitinib and fluid repletion resulted in decline of the creatinine level to 150 µmol/L, but in the following days, the renal function rapidly deteriorated and haemodialysis was started (Figure 1). The urine analysis showed nephrotic range proteinuria, leucocyturia and erythrocyturia. Laboratory tests did not reveal thrombotic microangiopathy (TMA) and were negative for auto-antibodies, and serum complement levels were in the normal range. The kidney biopsy contained 10 glomeruli, all with massive influx of neutrophils and...
swelling and proliferation of endothelial cells. No signs of TMA were observed. Immunofluorescence microscopy was strongly positive for complement C3 in a starry sky distribution, without concomitant immunoglobulin deposits. Electron microscopy showed electron dense deposits along the endothelial side of the glomerular basement membrane.

Our patient presented with an acute nephritic syndrome with renal failure after anti-VEGF therapy for a metastasized renal cell carcinoma. The kidney biopsy showed an acute exudative immune-complex glomerulonephritis as can be seen after infections, during cryoglobulinaemia or in early MPGN.

Toxicity of the newer anti-VEGF drug sunitinib seems the most likely explanation as no other cause could be identified. Another possibility would be a renal tumour-related glomerulonephropathy, a rare entity associated with a variety of unrelated histopathological diagnosis [3]. Formally, we cannot exclude this possibility but the acute onset of glomerulonephritis and time relationship with sunitinib treatment argue against such a diagnosis. With the growing use of anti-VEGF therapeutics, unexpected renal side effects, specifically TMA [4, 5], become apparent.

Our findings describe a histopathological picture that has not been reported before with the use of anti-VEGF blockers, specifically with the newest agent sunitinib. It has not been reported before with the use of anti-VEGF therapeutics, unexpected renal side effects, specifically TMA [4, 5], become apparent.

Our findings describe a histopathological picture that has not been reported before with the use of anti-VEGF blockers, specifically with the newest agent sunitinib. It adds on the recent findings of Bollee et al. [2] and Winn et al. [1] who reported cases of TMA and acute interstitial nephritis, respectively. Based on the information available now, different histopathological patterns can be elicited by sunitinib. Therefore, it seems advisable that during anti-VEGF therapy, kidney function and the urine sediment are monitored carefully and a kidney biopsy is taken when proteinuria or renal insufficiency develops.

Conflict of interest statement. None declared.

Editorial note: Drs Winn et al. had no further comments on this letter.

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doi: 10.1093/ndt/gfp140

Advance Access publication 30 March 2009

Unexpectedly high incidence of brucellosis in one university dialysis unit of North East Greece

Sir,

We enjoyed reading the paper by Tuba Turunc et al. [1] in which they reported a series of seven dialysis patients with brucellosis, and stated that brucellosis may be overlooked in patients with end-stage renal disease (ESRD) who undergo dialysis. Comprehensive relative reports are lacking from the literature.

We report here our experience with an unexpectedly high incidence of brucellosis infection in our Dialysis Unit, in patients receiving renal replacement therapies.

Eight of 124 dialysis patients developed brucellosis during the 1-year period, while according to our records, there were no other episodes among the 284 dialysed patients during the previous 5 years. During that 5-year period, diagnosis of brucellosis was reported in 21 hospitalized patients in our hospital (mean annual incidence 5.2/100000 population), and in a total of 1246 cases from the entire Greek regions according to the records of the Ministry of Health (mean annual incidence 2.3/100000 population). All the patients were fed unpasteurized milk and cheese. Common clinical manifestations were mild fever (100%), malaise (100%), lost of appetite (87.5%) and fatigue (100%). Diagnosis was established by PCR. The patients were treated with oral doxycycline and oral rifampicin for at least 6 weeks (for two of the patients, the treatment lasted for 8 weeks). The patients were followed up for 1 year. There were no relapses, and PCR were negative in all the patients.

Brucellosis is endemic in Greece, and it constitutes a serious public health and economic problem in some rural areas. Though the data from the Hellenic Center for Infections Diseases Control (H.C.I.D.C.) indicate a gradually declining annual incidence, this might not represent the definite situation due to imprecise recording of new Brucella cases [2]. In 2001, the Greek Ministry of Agriculture instigated an eradication programme for brucellosis in cooperation with the European Community. Between 2000 and 2007, the annual incidence of brucellosis (number of