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 depositions. 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 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.

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


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

Sir,

We enjoyed reading the paper by Tuba Turunç 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%), loss 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...
cases per 100000 population) in Greece showed a decreasing tendency: 5 in 2000, 3.7 in 2001, 3 in 2002, 2.2 in 2003, 2.1 in 2004, 3.1 in 2005, 2.6 in 2006 and 1.38 in 2007 [3]. However, exacerbations in annual incidence of brucellosis (17.3–1110 per 100000 population) were observed in certain rural areas of Greece, despite the widespread vaccine programmes [4]. This may be due to incomplete epidemiological surveillance or uncontrolled animal movements across borders and transportation of dairy products [5,3].

Brucellosis is an infectious disease that can affect anyone, especially those who are more susceptible to infections, such as dialysis patients, particularly when they are living in agricultural and veterinary areas, so it should be considered as a possible cause of infection in cases of unexplained, long-duration fever, who live in agricultural areas (even in European Union).

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Editorial note. Dr. Turunc et al. had no further comments on this letter.

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Letters and Replies
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Do patients with uric acid stones exhibit abnormal circadian blood pressure—a hypothesis

Sir,

Although several studies have reported that kidney stone disease and hypertension are associated with each other, the link between the two conditions has not been identified. Very recently, Losito et al. demonstrated that increased acid excretion may be one of the mechanisms linking hypertension and kidney stone formation [1]. Rendina et al. suggested that insulin resistance (IR) might be another common factor for the development of hypertension and kidney stones. IR directly influences urinary salt supersaturation by affecting urinary pH as well as calcium, phosphate, urate and citrate excretion [2]. IR may cause low urinary pH and formation of uric acid stone due to defective ammonia synthesis by the proximal tubule as well as decreased ammonium transport into the renal tubular lumen [3].

Blood pressure (BP) normally declines or dips by 10–20 mmHg at night, and individuals who fail to dip their average nighttime BP relative to their average daytime BP by at least 10% are termed as non-dippers [4]. It was previously demonstrated that in both diabetic and non-diabetic patients IR as detected by homeostasis model assessment was independently associated with nocturnal nondipping [5].

In the light of these findings we hypothesized that IR that is both related with uric acid stones and nocturnal nondipping may be one of the common mechanisms for the development of thesepathologies. Patients with uric acid stones may exhibit increased IR, which might result in abnormal circadian blood pressure profiles in these patients.

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Reply

Sir,

Afsar, Yilmaz and Eyileten, with reference to our paper [1], put forward the hypothesis that insulin resistance may be one of the mechanisms responsible for altered blood pressure profile in patients with uric acid kidney stone. In our