

Persistent Microscopic Hematuria in ANCA Associated Vasculitis: “Active” or “Abnormal” Urine Sediment? A Clinician’s Dilemma

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Received date: October 15, 2015; Accepted date: October 20, 2015; Published date: October 24, 2015

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Keywords: ANCA vasculitis; Hematuria

Persistent Hematuria in ANCA Vasculitis

The ANCA associated vasculitides (AAV) include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and Churg-Strauss syndrome (eosinophilic granulomatosis with polyangiitis, EGPA). Renal involvement is present in 20-50% of patients at presentation; 70-80% of patients will in time have renal involvement during the course of GPA and MPA. The typical histopathology is a pauci-immune focal and necrotizing crescentic glomerulonephritis [1]. Therapy consists of a staged treatment approach involving two treatment phases: remission induction, and remission maintenance. Treatment response is evaluated both clinically and by measurement of serum creatinine, inflammatory markers and urinary markers.

The absence of disease activity in clinical trials is determined systematically according to a validated and published disease activity score list. The disease activity parameters include hematuria, red blood cell and/or mixed cellular casts in urine sediment and rise in serum creatinine as markers of active renal vasculitis [2]. In clinical trials of systemic vasculitis, most patients improve within weeks of induction therapy and glucocorticoid tapering typically begins in the first 4 weeks. However, most patients with renal involvement continue to have hematuria and proteinuria at 4 weeks and beyond. In clinical practice, remission of renal vasculitis is defined as stabilization or improvement in serum creatinine and resolution of hematuria. The persistence of hematuria is considered by most clinicians to reflect active renal vasculitis even in the absence of other markers of disease activity; patients may be continued on the same immunosuppressive regimen or immunosuppressive therapy may be enhanced. Recent studies have raised the question: in patients in whom there are no other signs of active disease and a stable serum creatinine, might the finding of persistent hematuria mark disease damage and not active inflammation? [3,4]

The best approach to resolve the controversy of whether hematuria in these settings reflects continued disease activity vs. damage is to perform a repeat renal biopsy in patients who have persistent hematuria but are otherwise considered to be in remission. Due to prior lack of such studies, clinical decision making has relied on circumstantial data. Magrey et al. reported chronic persistent hematuria in 10 out of 25 patients with GPA with renal vasculitis [3]. The hematuria lasted from 6 to 38 months following achievement of clinical remission in these patients. Based on clinical, laboratory and

imaging measures that supported achievement of clinical remission, they concluded that persistent hematuria in these 10 patients was due to damage and confirmed inactive renal disease by biopsies in two patients. Geetha et al. reported renal biopsy findings in six patients with small vessel vasculitis who underwent repeat renal biopsy for chronic persistent hematuria who otherwise met criteria for remission. None of the six patients had active vasculitis on renal biopsy, again suggesting that persistent hematuria could represent damage [4]. In a report of 31 patients undergoing repeat biopsy for suspected renal flare, 13% of biopsies did not have active glomerulonephritis [5]. Furthermore, a recent retrospective analysis of the impact of hematuria duration on one year estimated glomerular function rate (e-GFR) in AAV patients concluded that hematuria persistence for more than 90 days from the time of renal biopsy was not associated with lower one year e-GFR [6].

The notion that persistent hematuria is always a sign of active glomerulonephritis in vasculitis patients who appear to be in remission by all other measures is flawed. Indeed, stable hematuria may represent damage, just as is the case for chronic but stable proteinuria. We suggest that if uncertainty remains about whether persistent hematuria is due to damage vs. active disease, a repeat renal biopsy should be considered to guide rather than obligate maintaining or increasing high dose immunosuppressive therapy.

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