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Letter to the Editor

LETTER TO THE EDITOR

Circulating active von Willebrand factor and immunoglobulin A nephropathy outcomes

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The von Willebrand factor (vWF) is a specific marker of endothelial cell injury [1]. Van der Vorm *et al.* [2] recently reported that circulating vWF, and even more so, active vWF, is elevated in patients with chronic kidney disease (CKD) and end-stage renal disease. Their interesting study emphasized the forgotten relationship between coagulation and CKD complications.

Circulating vWF derives mainly from endothelial cells and has been proposed as a marker of vascular damage in diabetes mellitus, sepsis, high blood pressure or pre-eclampsia [3]. Immunoglobulin A nephropathy (IgAN) is characterized by severe endothelial damage even before the onset of arterial hypertension and glomerular sclerosis [4]. This vascular damage plays a fundamental role in the progression to CKD. vWF levels were higher in 10 IgAN patients without proteinuria, renal insufficiency or arterial hypertension than in healthy volunteers. In 16 patients with IgAN and proteinuria, vWF levels were significantly higher than in patients with IgAN without proteinuria, and there was a positive correlation between vWF and proteinuria levels. Angiotensin-converting enzyme inhibitors decreased both proteinuria and vWF levels in 11 IgAN patients [5]. The increased levels of vWF were later confirmed in 61 IgAN patients [6]. Endothelial cells are clearly involved in the pathogenesis and progression of IgAN [7]. Indeed, thrombotic microangiopathy lesions were found in 2–53% of patients with IgAN and were associated with severe arterial hypertension and worse kidney outcomes [8]. Glomerular capillary wall injury triggers local inflammation involving the coagulation cascade and local complement activation, similar to the mechanisms involved in vasculitis. The cross-talk between complement and coagulation through their serine protease proteolytic cascades is probably key in developing glomerular and vascular injury. The expression of tissue factor (TF), the initiator of the extrinsic pathway of coagulation, is favoured by complement. Thrombin can cleave C3 with the generation of C3a and C5a. C3a and C5a may in turn induce the release of TF and factor X activation. The active C5b-9 complex induces release of vWF by endothelium and platelet activation and aggregation, causing a prothrombotic state [9, 10].

Since IgAN lacks serum markers that predict outcomes, plasma total or active vWF should be studied as a potential simple method for risk stratification in IgAN. However, active vWF levels have yet not been studied in the context of IgAN. We wondered how many patients in the van der Vorm *et al.* [2] study had IgAN and whether they behaved in line with other CKD patients.

CONFLICT OF INTEREST STATEMENT

None declared.

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