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## Re: Prognostic Factors in Crescentic Glomerulonephritis: a Single-Center Experience

Dear Editor,

I read the article "Prognostic Factors in Crescentic Glomerulonephritis A Single-Center Experience" by Ozturk and coworkers with great interest.<sup>1</sup> In this retrospective study, a group of patients with crescentic glomerulonephritis because of different kidney diseases were evaluated for poor prognostic factors that led them to end-stage renal disease. They determined that renal survival was poor in those with serum creatinine levels greater than 4.2 mg/dL on admission and those with more than 63% crescentic glomeruli of the total glomeruli.<sup>1</sup> The article is interesting and directs our consideration towards an important area in which early diagnosis and proper treatment could save the kidney. Crescentic glomerulonephritis is

an important area of new discoveries and ideas.

The value of pathology examination of the kidney is double in glomerular disease, first, to establish the diagnosis, and the second, to provide prognostic information. It is actually a snapshot of prior and ongoing events. The morphologic classification of glomerular disease and prognostic pathological features is not static, but it is rather undergoing modification to increase the prognostic precision in response to generation of new knowledge. Studies investigating the tubulointerstitial involvement in lupus nephritis (LN) and in antinuclear antibody glomerulonephritis have shown that the predictive value of tubulointerstitial inflammatory cell infiltration, fibrosis, and tubular atrophy is even greater than that of glomerular changes, and it is

a denominator of obliterated glomeruli. Vascular changes such as thrombotic microangiopathy changes also had the worst renal outcome and were highly predictive of decline in kidney function. These components are habitually neglected when we are just looking at the glomeruli to predict the prognosis.<sup>2-5</sup>

Another important consideration is the underlying pathophysiological mechanisms. For example, global LN (World Health Organization class IV) with intense subendothelial immune complex deposit (Wire loop) and intracapillary deposits (hyaline thrombi) could have superior prognosis than segmental LN (termed World Health Organization class III), if the latter is more vacuities in nature.<sup>2</sup> The same consideration is important when we interpret crescentic glomerulonephritis.

Several types of glomerular diseases are accompanied by cellular crescents. It is a multilayered accumulation of cells in the Bowman space. When it occludes the urinary outlet, the affected nephron undergo degeneration. However, tubular integrity is preserved if the urinary pole remains patent. At least 3 cell types have been proposed as the cellular origin of crescents. First, infiltrating macrophages have been proposed; however, several observations dispute this. Second, under specific circumstances, podocytes contribute to cellular crescent formation; however, the relative contribution of podocytes seems to be small. Finally, increasing lines of evidence support the parietal epithelial cells (PECs) as the predominant cell type in cellular crescent formation.<sup>6,7</sup> The Bowman capsule PECs function as progenitors for podocytes and tubular cells. Cells that express progenitor markers glycosylated CD133 (glycCD133) or CD24 are termed *adult parietal epithelial multipotent progenitors*. Parietal epithelial cells that express CD44 are considered activated PEC. They are also termed deregulated adult parietal epithelial multipotent progenitors and contribute to crescent and pseudocrescent formation. Interestingly, 50% to 75% of cells in pseudocrescents express PECs markers of glycosylated CD133 and CD24, but not the podocyte markers of nestin and podocalyxin. Migrating to the glomerular tuft and

predominantly producing extracellular matrix, PECs also contribute to glomerulosclerosis, while in crescentic glomerulonephritis, the proliferative feature of these cells are more prominent.<sup>8</sup>

Activated PECs also have a critical role in the pathogenesis of many forms of focal segmental glomerulosclerosis, and it has been shown that sclerotic segments are connected to the Bowman capsule via an adhesion that provides the entry site for PECs to the tuft.<sup>8</sup> Parietal epithelial cells are progenitors of podocytes and tubular cells. It is their plasticity and their deregulated response that turns them to become the dreadful cell of glomeruli.

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