Chapter 6: Focal segmental glomerulosclerosis (FSGS) in adults

This chapter makes treatment recommendations for adult patients who present with proteinuria and histologic lesions of focal segmental glomerulosclerosis (FSGS).

Definitions

The nomenclature surrounding the classification of FSGS has been inconsistent and confusing, in part because a histopathologic pattern of injury has also been considered as a distinct disease. Likewise, the traditional classification of FSGS does not reflect practicalities surrounding clinical presentation, and diagnostic and treatment approaches in patients with FSGS lesions on the kidney biopsy. Therefore, the Work Group proposed changes to the nomenclature of FSGS to improve clinical utility and provide clarity about the underlying pathophysiology. Figure 49 provides an overview of the proposed classification of FSGS, and Figure 52 lists the secondary causes of FSGS lesions on the kidney biopsy.

Primary FSGS

The terms "primary" and "idiopathic" FSGS have been used interchangeably, leading to a great deal of confusion around FSGS nomenclature. The Work Group suggests eliminating the use of "idiopathic" to describe any type of FSGS and endorses the following definitions for FSGS going forward.

We define primary FSGS as a clinical–pathologic syndrome in which light microscopy of the kidney biopsy demonstrates FSGS lesions, electron microscopy of the kidney biopsy demonstrates diffuse foot process effacement, and clinically the patients display NS. NS is defined as proteinuria >3.5 g/d plus hypoalbuminemia (<30 g/l), often, but not necessarily accompanied by dyslipidemia and edema. When considering a diagnosis of primary FSGS, there should be no other identifiable causes of FSGS. Although the clinical–pathologic syndrome of primary FSGS has been attributed to a circulating permeability factor, this factor has yet to be identified. Currently, the only form of FSGS that can be reasonably attributed to a circulating permeability factor is FSGS that recurs rapidly after a kidney transplant and can be successfully treated by plasmapheresis to remove the factor.

FSGS can also occur in the absence of a genetic or identifiable secondary cause, in the absence of NS, and without diffuse foot process effacement on electron microscopy of the kidney biopsy. This form of FSGS is distinct from primary FSGS based on its clinical and histologic manifestations. We propose calling this disease FSGS-UC (for undetermined cause). It is conceivable that patients with FSGS-UC have secondary or genetic forms of FSGS that have not yet been elucidated.

Secondary FSGS

When an FSGS lesion, with or without the presence of diffuse podocyte foot process effacement, is found in the setting of an established pathophysiologic process known to cause FSGS, we refer to this as secondary FSGS. The known/presumptive etiologies of secondary FSGS are listed in Figure 52.

Genetic forms of FSGS

FSGS lesions may develop in patients who have mutations in podocyte or glomerular basement membrane proteins. The search for a genetic cause is not routine in adults with FSGS

Figure 49 | Proposed classification of FSGS. FSGS, focal segmental glomerulosclerosis.