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Collapsing focal segmental glomerulosclerosis: Increasing the awareness

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ABSTRACT

Collapsing focal segmental glomerulosclerosis (cFSGS), also known as collapsing glomerulopathy (CG) is of considerable interest for a variety of reasons. Its incidence is on the rise, and in many parts of the world, it has emerged as one of the leading causes of end-stage renal disease (ESRD). There is currently no specific treatment and the response to standard immunotherapeutic agents is poor. Majority of the cases have been reported from the western countries, but the lesion is also being increasingly recognized in the tropical regions. It is imperative to increase the awareness of the lesion among the pathologists and the nephrologists from the developing countries for its accurate diagnosis and appropriate prognostication.

Implication for health policy/practice/research/medical education:

Collapsing focal segmental glomerulosclerosis (cFSGS), also known as collapsing glomerulopathy (CG) is of considerable interest for a variety of reasons. Its incidence is on the rise, and in many parts of the world, it has emerged as one of the leading causes of end-stage renal disease (ESRD). It is imperative to increase the awareness of the lesion among the pathologists and the nephrologists for its accurate diagnosis and appropriate prognostication.

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Introduction

The lesion of collapsing focal segmental glomerulosclerosis (cFSGS) has attracted considerable attention in recent years for a variety of reasons. Its incidence along with that of non-collapsing FSGS (ncFSGS) is increasing, not only in the developed countries,

but, also in the developing parts of the world (1-5). Its terminology and nosology are still unsettled (6-10). The concurrence of both collapsing and sclerosing glomerular lesions and the focal nature of the condition is responsible for its current classification as a variant of FSGS (9). Its definitional problems still remain unresolved (10,

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11). Almost all reported studies have shown that its clinicopathological profile is more severe and renal survival markedly reduced in comparison with ncFSGS (6-8, 12). Most important of all, the list of etiologic agents/associated conditions is continuously expanding (13-16). Although numerous advances have been made in understanding and unraveling the pathomechanisms of this disease, but the picture is still far from clear (2, 3). The disease not only affects native kidneys, but also frequently involves the transplanted kidneys, both as *de novo* and recurrent forms, frequently leading to graft loss (17-22). Although the vast majority of the cases have been reported from the western world, but the lesion is also being increasingly recognized and reported from the tropical regions of the world (22).

In the above context, Mohammadi Torbati describes a pictorial case report of cFSGS in a 32-year-old male with the clinical presentation of rapidly progressive renal failure and recent febrile illness in the photo-nephropathology section of the current issue of *Journal of Nephropathology* (24). The case study provides evidence for the growing recognition and reporting of the lesion in the developing countries. The author has elegantly depicted the pathological appearances of the lesion in different tinctorial stains of the renal biopsy. This case will be very useful for increasing the awareness and educating the young nephrologists and nephropathologists alike in the developing countries to identify and report the lesion. The case also highlights the need for keeping a high index of suspicion for the diagnosis of the lesion, as the characteristic collapsing glomerular lesion was found in only one of the several glomeruli included in the biopsy and could have easily been missed if not meticulously and carefully sought by the examining pathologist. The author has discussed the differential diagnosis of the lesion, which should be helpful in preventing the over- or under-diagnosis of the condition. It

would have been more useful if some immunohistochemical markers of podocyte differentiation, transdifferentiation, and proliferation, were used and presented in the report. The pathological features of the condition along with detailed immunoprofiling of the dysregulated podocyte phenotype have also been discussed in detail in several recent reviews of the condition (1-5).

The author has also briefly touched on the clinicopathological correlation of the condition. It may be pointed out here that the renal biopsy diagnosis of cFSGS is not the end-diagnosis. Rather, its detection on renal biopsy specimens should lead to a search for the growing list of etiological factors, before it can be labeled as idiopathic form of the disease (5). It is noteworthy that among the growing list of possible etiologies, ischemia has emerged as the number one cause, not only in the native, but also the transplanted kidneys (13, 20-23). The ischemia may be of vasculopathic or hypovolemic in origin. We have recently described a number of cases of cFSGS in association with patchy acute cortical necrosis of hemodynamic origin with no evidence of vasculopathy (13, 14). The case reported by Mohammadi Torbati has history of hypertension of 3-year duration, but there is no mention of the vascular changes on the renal biopsy. It is hard to escape the speculation that some sort of vasculopathy might be present in this case too. The other presenting feature of the condition with febrile illness is also well described in literature (25). In fact, five out of six patients in the original report by Weis et al. (6) also presented with non-specific febrile illness. The cause of the febrile illness could not be ascertained in the previous reports, but the possibility of some unknown viral infection was suggested (25).

With the growing evidence from the recent studies, it is also becoming apparent that the lesion is not a single entity. Rather, it represents a dramatic response pattern of renal parenchyma

in genetically conditioned patients to a wide variety of injurious agents. This has led to a reclassification of this lesion into three categories: idiopathic or primary, reactive or secondary, and genetic forms (10-14). It also implies that the course of the disease and the ultimate outcome will largely depend on the underlying cause (13, 14). Moreover, although, the disease is defined by the glomerular lesions, it is the extent and severity of acute and chronic changes in the tubulointerstitial compartment, which determines the prognosis of the condition (10). There are also subtle differences in the pathological features of the condition on renal biopsies depending on the underlying cause, which may be helpful in elucidating the cause of the condition (2, 3).

In conclusion, the author has done a commendable job in presenting a pictorial case study of an interesting renal lesion, whose incidence is on the rise through out the world. It is imperative for the nephropathologists in the developing countries to make themselves aware of the condition and to keep a high index of suspicion for its accurate diagnosis.

Conflict of interest

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