EDITORIAL

Mayo Clinic/Renal Pathology Society Consensus Classification of Glomerulonephritides: A Giant Leap in Right Direction

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The importance of renal biopsy in the diagnosis and management of medical renal diseases is well established. The renal biopsy procedure and its accurate interpretation is a multidisciplinary task that greatly depends on a close liaison among nephrologists, radiologists, technologists, and pathologists.[1] Till recent past, there was no international standardized system for reporting and classification of glomerular diseases.[2] Traditionally, glomerular diseases or glomerulopathies have been classified on the basis of pathological appearances of the lesions as observed under the light microscopy (LM) and correlating these appearances with immunofluorescence (IF) and ultrastructural findings to arrive at a specific diagnosis.[1] This approach was simple, straightforward and pathologist-friendly, but was not very helpful from the point of view of treating nephrologists.[2] Optimal treatment of any disease requires knowledge of the etiology; and if that is not known, the pathogenesis of the disease.[1,2] Etiology is of primary importance; however, since it is unknown in the vast majority of glomerular diseases, pathogenesis can also be helpful for the management of these diseases. Hence, there was a dire need for an etiology/pathogenesis-based classification of glomerulonephritis (GN).

Glomerulopathy is an all-inclusive term denoting abnormality in the structure or function of the glomeruli, whereas GN in this context refers to proliferative and inflammatory forms of glomerulopathies. Proliferative glomerulopathies lead to glomerular hypercellularity and result from either proliferation of resident glomerular cells and/or leukocyte infiltration.[2] Broadly speaking, it can be divided into the endocapillary and extracapillary forms. Some diseases can result in both intracapillary and extracapillary proliferations. The lack of standardized guidelines for classification and reporting of GN not only affects patient care but also hampers the comparison of data among different studies and conduction of multicenter clinical and basic research trials.

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The above mentioned need for an etiology/pathogenesis based classification of GN was addressed by a group of renal pathologists and nephrologists, in February 2015 under the auspices of Mayo Clinic/Renal Pathology Society (RPS) to develop a consensus-based etiology/pathogenesis-oriented classification of GN and harmonize the pathological reporting guidelines for GN.[2] Previously, this approach has been used in the development of a number of important pathological classifications which have now achieved international recognition and are widely used in clinical practices and trials worldwide.[3-8] The mainstay of the classification is IF microscopy or less commonly, immunohistochemistry (IH) in concordance with LM and electron microscopy (EM), which divides GN into five types based on pathogenesis: immune-complex GN, pauci-immune GN, antiglomerular basement membrane antibody (anti-GBM) GN, monoclonal immunoglobulin (Ig) GN, and C3 glomerulopathy.[2] These are the pathogenic types and not specific diseases. Various types of specific diseases are found in each of these types of GN. Among these, the immune-complex GN is the most prevalent type and associated with many primary as well as secondary glomerulopathies.[2]

The consensus report also describes guidelines for the standardized reporting of kidney biopsies in cases of GN. According to the document, the basic report construct should include the following reporting items: specimen type, diagnosis, comment, clinical data, gross description, LM description, IF results, EM findings, and addendum for any special investigations.[2] This reporting guideline underlines the importance of integrated or correlative approach to the diagnosis of glomerulopathies in general, and GN in particular. The investigators have provided detailed guidelines on each of these report items along with examples. This detailed description will help in improving the utilization of the guidelines by pathologists throughout the world and will improve interobserver reproducibility. The most important element of the report is the diagnosis, which has been divided into primary and secondary diagnosis. The primary diagnosis consists of three or four components in the following order: (1) disease entity or pathogenic type (the latter in case where specific disease is not known), (2) pattern of glomerular injury or LM appearance of the glomeruli, (3) scores or classifications of the specific disease, wherever

available, and (4) additional disease-related features. More than one primary diagnoses may also be listed, if that is the case. This construct will help in the clinicopathological correlation of the biopsy findings and will be useful for making the treatment decisions in individual patients. Additional lesions, if in the glomeruli, which are not pathogenetically related to the primary diagnosis, are listed under the heading of secondary diagnosis. Thus, the element of "Diagnosis" is exhaustive and an all-inclusive item of the classification, synthesized from integration of all other data items. The classification not only deals with glomerular lesions, but also emphasizes recording and scoring of the tubular and interstitial lesions as well as the vascular lesions.

The main strength of this classification is that it is focused to etiology or pathogenesis of GN and thus more useful clinically. It is also suitable for making entry into computerized databases, is standardized; and most importantly, it is patient-centered. It addresses a large group of glomerulopathies mediated by immune- or antinuclear antibody (ANCA)-mediated disorders. Moreover, it is also claimed to be a working document with flexibility and adaptability, as new data emerges in the field which is one of the most important features of any classification in this era of rapid advancements in the diagnostic field .[9,10]

Although the above classification covers a major bulk of glomerular diseases, there are many others which have not been addressed in this document. These include membranous nephropathy, podocytopathies such as minimal change disease (MCD) and focal segmental glomerulosclerosis (FSGS) as well as thrombotic microangiopathy.[2] The classification, although consensus-based and logical, is derived from expert opinion of the world-renowned authorities in the field and is not supported by actual data; as such, it is not evidence-based. Widespread use of the classification in actual clinical practice will be helpful in exposing its potential weaknesses and deficiencies and in refining and revisiting it.[10]

Mayo Clinic/Renal Pathology Society classification of GN represents a major advancement in the field of native renal pathology aimed at standardizing the approach to diagnosis, classification and reporting of GN. It is a working classification, likely to change in future, as new data accumulate from its widespread use.

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