

Journal of Nephrothology

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Oxford classification of IgA nephropathy: Broadening the scope of the classification

Muhammed Mubarak^{1,*}

¹ Histopathology Department, Sindh Institute of Urology and Transplantation, Karachi, Pakistan.

ARTICLE INFO

Article type:
Commentary

Article history:
Received: 6 Mar 2012
Accepted: 7 Mar 2012
Published online: 18 Mar 2012
DOI: 10.5812/jnp.4

Keywords:
IgA nephropathy
Glomerulopathy
Glomerulosclerosis

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

IgA nephropathy (IgAN) is the most common glomerulopathy worldwide. The most significant development in IgAN research in the recent past consists of promulgation of the Oxford-MEST classification. The classification represents an entirely unique approach in the classification of renal diseases. The ongoing and future research should address the issues of combining the clinical, laboratory, histopathological, molecular biological and genetic data, to devise algorithms for individualized decisions of treatment choice for patients with IgAN, and accurate prognostication.

Please cite this paper as: Mubarak M. Oxford classification of IgA nephropathy: Broadening the scope of the classification. J Nephrothology. 2012; 1(1): 13-16. DOI: 10.5812/jnp.4

Commentary

IgA nephropathy (IgAN) is the most common glomerulopathy worldwide (1). However, its prevalence in published renal biopsy series and clinicopathological features vary from region to region, and country to country (2). This is mainly due to differences in biopsy indications, the extent of pathological evaluation of renal biopsies and the nephrology practice, rather than true ancestral differences in the prevalence of the disorder (3). The disease is most prevalent in countries with population-based urinalysis screening programs. Similarly, the clinicopathological presentation of the disease is milder in

centers employing the urinalysis approach for the diagnosis of the disorder (2, 3).

Although, in the majority of patients, the disease is benign, IgAN is characterized by a slowly progressive course to end-stage renal disease (ESRD) in 30-40% of individuals over 20-years of follow-up (2). This progression is unpredictable in most instances. There are no entirely reliable factors which can accurately predict the progression in individual patients (4). Traditionally, the prognostication was carried out using the clinical and laboratory parameters. Pathological features on renal biopsy have remained largely

*Corresponding author: Dr. Muhammed Mubarak, Histopathology Department, Sindh Institute of Urology and Transplantation, Karachi-74200, Pakistan. Telephone: 009221 99215752, Fax: 009221 32726165
Email: drmubaraksiut@yahoo.com

controversial till recent past (5, 6). Consequently, one of the active areas of research in IgAN at present involves the determination of precise factors which can accurately and reliably predict the prognosis and response to treatment in individual patients (7).

There is relatively little information in literature on the population-based prevalence and clinicopathological features of IgAN in third world countries (3, 8-10). In particular, there are very few studies on the pathological characteristics of the disease according to the new Oxford-MEST classification from these parts of the world (8).

The most significant development in IgAN research in the recent past consists of promulgation of the Oxford-MEST classification (5, 6, 11, 12). The classification represents an entirely unique approach in the classification of renal diseases. Although, the classification is robust, evidence-based, prevalidated, and international in outlook, there were some limitations in the original cohort used for the study (11, 12). It was retrospective collected, included select cases, excluded milder and rapidly progressive cases, and there was no representation of south Asian or Middle Eastern countries. The authors of the original classification and other researchers suggested validating the classification in different settings and in prospective cohorts of patients with the disease in routine clinical practice (5, 6, 11, 12). In this context, a number of validation studies have been published and attest to the usefulness of this classification in the routine clinical practice and the better reproducibility of the classification (13-18). Slight deviations and differences have also been reported, reflecting the diversity of the cases of IgAN in different centers, but overall results are concurrent with the original Oxford study (13-18). Nasri et al. have done a commendable job by exploring the new aspects of IgAN pathology in Iranian patients (19). The authors have analyzed the clinicopatho-

logical features in relation to the Oxford classification of IgAN in 102 patients over three years of study. There are many strong points in the study. The number of patients analyzed is fairly large. The study population is racially homogeneous, consisting of Iranian patients except for two Afghans. No pre-biopsy treatment was given in any case, thus eliminating the confounding variable of treatment effect on the disease morphology and classification. The authors found a higher prevalence of segmental glomerulosclerosis and mild to moderate interstitial fibrosis/tubular atrophy (IFTA) in the study cohort. These same features were significantly more prevalent in males as compared with females, attesting to the poor outcome of the disease in male patients. Segmental glomerulosclerosis is frequently seen in IgAN in many parts of the world and is indeed the common pattern in third world countries. It is also an adverse prognostic indicator in the Oxford classification (3). The authors also found a fair correlation of crescents with serum creatinine (Spearman's $\rho=0.386$) and propose that this lesion should be included in the future versions of the Oxford classification (19). Indeed, the predictive value of this lesion could not be assessed in the original study cohort of patients used for the development of the original classification, because of its rarity (5). A number of other investigators have also addressed the issue of extracapillary epithelial proliferation in IgAN and suggested that, this lesion should be included in the next version of the Oxford classification of IgAN to widen the scope of the classification (13).

There are a number of limitations and caveats in the study too. The study is, in effect, a cross-sectional analysis of IgAN cases, and there is no information on the follow-up or outcome of the patients under study. One of the important objectives of the Oxford classification is the prognostication of the disease course in patients with IgAN, which has not been undertaken in

this study. We hope that the authors will continue their work on long-term follow-up of this cohort with properly defined outcomes for future analysis. There are also no data on the treatment of these patients. The authors also did not correlate the morphological features with immunofluorescence (IF) features. This aspect has been addressed recently by Bellur et al. in the original study cohort used for developing the Oxford classification (20).

The ongoing and future research should address the issues of combining the clinical, laboratory, histopathological, molecular biological and genetic data, to devise algorithms for individualized decisions of treatment choice for patients with IgAN, and accurate prognostication (11).

In summary, Nasri et al. deserve congratulations for shedding light on newer pathological aspects of IgAN in Iranian patients according to the Oxford classification. Such studies will go a long way in further refining the original Oxford classification and broadening its scope and ultimately helping the individualized patient management and prognostication throughout the world.

Conflict of interest

The authors declared no competing interests.

Funding/Support

None declared.

Acknowledgments

None declared.

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