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Original Research Article

IgA nephropathy clinicopathologic study following the Oxford classification: Progression peculiarities and gender-related differences

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ARTICLE INFO

Article history:
Received 30 October 2015
Received in revised form
5 October 2016
Accepted 10 November 2016
Available online 22 November 2016

Keywords:
Gender-related differences
Glomerular filtration rate
IgA nephropathy
Oxford classification of IgA nephropathy
Renal biopsy

ABSTRACT

Background and aim: Immunoglobulin A nephropathy (IgAN) is the most frequent glomerular disease worldwide and one of the main causes of chronic kidney disease. We aimed to investigate clinicopathological correlations in IgAN patients by gender.

Materials and methods: The study was based on a retrospective analysis of renal biopsy data and clinical manifestations of the disease. Consecutive 73 biopsy-proven IgAN cases of male (62%) and female (38%) patients were investigated. Renal biopsies were reviewed using the new Oxford classification assessing the MEST (mesangial hypercellularity, endocapillary hypercellularity, segmental sclerosis/adhesion, tubular atrophy/interstitial fibrosis) score. The most powerful IgAN prognostic risk factors, morphological (segmental glomerulosclerosis and tubular atrophy/interstitial fibrosis) as well as clinical (proteinuria and hypertension) were taken into account in the correlation analysis. The mean rate of renal function decline was expressed as a slope of eGFR during the follow-up (FU) dividing delta GFR with the FU years.

Results: The mean age of the patients was 33.7 years (range, 16–76). Follow-up data were available for 64 patients with the mean follow-up of 4.1 years. The mean proteinuria at biopsy was 0.79 g/24 h. The mean arterial pressure (MAP) was 94.5 ± 16.7 mmHg and 7% of the patients were hypertensive. The initial mean estimated glomerular filtration rate (eGFR) was 94.9 ± 30.7 mL/min, at the end of the follow-up it was 86.2 ± 27.1 mL/min. The mean rate of renal function decline was −3.4 ± 11.9 mL/min/1.73 m^2 per year in males ($P < 0.05$)

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Peer review under the responsibility of the Lithuanian University of Health Sciences.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.medici.2016.11.003

and -0.7 ± 5.3 mL/min/1.73 m^2 per year in females. The Spearman correlation analysis confirmed a higher MEST score in the whole cohort and in males correlated with disease progression. In patients with proteinuria below 1.0 g/24 h, disease progression was faster in males.

Conclusions: According to the correlation analysis of the main prognostic risk factors, affecting the progression of IgAN, we can conclude that IgA nephropathy in males progresses more rapidly compared to females.

1. Introduction

IgA nephropathy (IgAN), or Berger's disease, is recognized as the most widespread type of glomerulonephritis worldwide and as one of the main causes of chronic kidney disease (CKD) [1–5]. Morphologically, the disease is defined by the predominance of diffuse, mainly mesangial deposition of IgA, identified by immunofluorescence or immunohistochemistry and by a variable degree of glomerular damage by light microscopy; whereas the pathogenesis of the disease still remains largely unknown [2,5]. Mesangial IgA deposition might be present in about 5%–15% of healthy individuals, but only about 1 in 50 people with IgA deposits present with clinical disease [1]. IgAN is potentially progressive to end-stage kidney disease (ESKD); however, its clinical presentation and progression in individual patients is variable and its course is generally benign in cases without proteinuria, hypertension or the reduced glomerular filtration rate (GFR). Also, in IgAN, overweight/obesity, present at diagnosis, is associated with an increase in the major risk factors (hypertension, proteinuria and severe renal lesions) which translate into a worse final outcome [6].

The Oxford classification of IgAN, published in 2009 [3], aimed to define reproducible and useful renal biopsy-based prognostic indicators. The study was based on a retrospective analysis of 265 IgAN patients of different age groups from four continents where renal biopsies were reviewed by expert pathologists focusing on prognostic information provided by renal biopsy [3]. As a result, the Oxford classification of IgAN based on the MEST score (mesangial hypercellularity, segmental glomerulosclerosis, endocapillary hypercellularity, and tubular atrophy/interstitial fibrosis) was proposed to predict renal outcome independently from all clinical indicators at the time of biopsy and during the follow-up [3]. According to these guidelines, several papers of investigations involving large cohorts of IgAN patients have been published [7–10] and comparisons of different IgAN validation studies have been presented [11–14].

We present a retrospective analysis of biopsy-proven IgAN during an 11-year period with a follow-up of the disease progression in Estonian population. The IgAN cases were classified according the Oxford classification, clinical-morphological correlations and performance of the prognostic scoring system was evaluated, with special attention to potential gender-related differences. The aim of this study was to investigate clinicopathological correlations in IgAN patients by gender.

2. Materials and methods

2.1. Demographic data and setting

All native kidney biopsies ($n = 578$) performed between 2001 and 2010 at the Department of Pathology of Tartu University Hospital were retrospectively reviewed and the data of all patients with biopsy-proven IgAN from this period and also from the year 2011 were collected. IgAN formed the main part of primary glomerulopathies (35.5%) [15]. A total of 88 cases of IgAN during the 11 years were registered. To compose the patients' cohort, we followed the recommendations of the International Consensus of IgAN study – the Oxford's classification of IgAN [3,4] – and, thus, 73 IgAN cases were selected for the study. By design, our study included the whole spectrum of IgAN cases represented in clinical practice. Demographic data included data on gender and age at the time of biopsy. Children were defined as ≤18, adults as 19–65, and elderly patients as >65 years of age.

Only biopsy-proven IgAN cases (standard light microscopy and immunofluorescence in all cases were performed), defined by a predominant diffuse deposition of IgA in the glomerular mesangium (both children and adults, with any level of eGFR and any level of proteinuria or without it) were included in the study. Antihypertensive or immunosuppressive treatment was not considered as an exclusion criterion. Patients with renal biopsies including less than 8 glomeruli, secondary IgAN such as Henoch–Schönlein purpura, IgAN with the combination of advanced diabetes mellitus, and cases with less than 1 year of follow-up were excluded.

2.2. Pathology data

A simplified score sheet of the Oxford classification of IgA nephropathy study was used [3]. Each biopsy was scored by two independent pathologists according to the Oxford classification [3]: total number of glomeruli, mesangial hypercellularity, M0/M1 (< or equivalent to >50% of glomeruli showing >4 mesangial cells in one area); endocapillary proliferation, E0/E1 (present/absent), segmental glomerulosclerosis/adhesion, S0/S1 (present/absent); glomerular membrane duplication, necrosis, cellular/fibrocellular crescent were categorized as present or absent; tubular atrophy/interstitial fibrosis, T0/T1/T2 as arteriosclerosis as well, A0/A1/A2 were categorized as absent/mild (0%–25%), moderate (26%–50%) or severe (>50%); arteriolar hyalinosis was categorized as absent or present. A0–A2 and