IgA nephropathy superimposed on diabetic nephropathy: A case report with review of literature in eight Indian studies

Bifica Sofia Lyngdoh, Pakesh Baishya, Jaya Mishra, Evarisalin Marbaniang, Biswajit Dey

Department of Pathology, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences (NEIGRIHMS), Shillong, India

ABSTRACT

Diabetes mellitus is one of the foremost diseases in the modern era and diabetic nephropathy contributes to a major percentage of end-stage kidney disease. Although diabetic nephropathy is difficult to revert back, detection of nondiabetic renal disease (NDRD) is important to detect as most of them are treatable. We describe a case of a 62-year-old female with long-standing diabetes mellitus presenting with massive proteinuria and clinical features of nephrotic syndrome. The kidney biopsy showed class III diabetic nephropathy along with focal proliferative glomerulonephritis with crescent formations. The immunofluorescence study showed strong mesangial IgA deposition with the predominance of lambda stain. This confirmed the diagnosis of diabetic nephropathy with superimposed IgA nephropathy. We reviewed eight Indian studies herewith to demonstrate NDRD spectrum in the Indian diabetic scenario.

Keywords: Diabetic nephropathy, immunofluorescence, renal biopsy

Introduction

The worldwide prevalence and incidence of diabetes mellitus is increasing day by day and diabetic nephropathy (DN), which is a kidney-related complication of diabetes mellitus, has become one of the foremost causes of end-stage kidney failure worldwide. A renal biopsy performed on diabetic patients could manifest either as DN or nondiabetic renal disease (NDRD) alone, or as DN with superimposed NDRD. DN is difficult to revert back to a normal state. However, certain NDRD, such as IgA nephropathy, mesangial-proliferative glomerulonephritis, and membranous nephropathy are often treatable, even reversible. Therefore, differentiating between these diagnostic categories is of considerable importance as this can influence the therapy and prognosis of the patient. We report a case of DN superimposed with IgA nephropathy (IgAN) with the literature review of kidney biopsies in eight Indian studies on diabetic patients.

Case Report

A 62-year-old female, who was a known case type 2 diabetes mellitus with nephropathy, visited our outpatient department for a checkup. Physical examination was unremarkable. Her laboratory parameters showed serum albumin of 3.4 g/dL, serum creatinine of 1.2 mg/dL, and 24-hour urine protein of 10.1 gm/24 hr. She then underwent a renal biopsy.

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A gross examination of the renal biopsy showed a linear core of grey-white soft tissue measuring one cm. On microscopic examination, the sections studied showed mostly renal cortical tissue. A total of 10 glomeruli were sampled, out of which two showed segmental sclerosis, three glomeruli exhibited cellular crescent and one demonstrated a fibrous crescent. All the glomeruli exhibited glomerulomegaly with marked mesangial matrix expansion with diffuse (>50% glomeruli) formation of Kimmelstiel–Wilson nodules. The capillary lumens were still patent segmentally and the basement membranes were thickened. One glomerulus showed focal and segmental endocapillary proliferation. The tubulointerstitial compartment showed tubular atrophy and interstitial fibrosis (40–50%) of the cortex, which was confirmed by Masson Trichome staining. There was mononuclear inflammatory cell infiltration, mostly at the atrophied cortex. The vascular compartment comprised 10 complete and partial profiles of small- to medium-caliber arteries. The medium-caliber arteries showed moderate intimal hyperplasia with hyalinosis and the small-caliber arteries along with the arterioles showed vascular hyalinosis. [Figure 1a-d]

Immunofluorescence study showed IgG, IgM, C3, and Kappa to be negative whereas IgA showed strong (4+) mesangial staining. [Figure 2] Lambda also exhibited moderate mesangial staining. Upon correlating the microscopic findings and the immunofluorescence findings, a final diagnosis of DN (RPS Class III) with superimposed IgA nephropathy was made with an MEST-C score of M1E1S1T1C2 [Oxford classification of IgA nephropathy: M-Mesangial hypercellularity, E-Endocapillary proliferation, S-Segmental sclerosis, T-Interstitial fibrosis/Tubular atrophy, and C-Crescents].

Review of Studies Done on Indian Renal Biopsies in Diabetic Patients

The eight studies done in India, which were reviewed, included a total of 461 diabetic patients undergoing renal biopsy. [Table 1] In their study of 160 patients of type 2 diabetes mellitus with clinically suspected NDRD, who had undergone renal biopsy, categorized the patients as Group I, (isolated NDRD), Group II (NDRD with underlying diabetic glomerulosclerosis), and Group III (isolated diabetic glomerulosclerosis). Group I had 68 patients (42.50%), Group II had 48 patients (30%) and Group III had 44 patients (27.50%). Group I predominantly comprised

| Authors       | Year | Place            | No of Patients |
|---------------|------|------------------|----------------|
| John et al[8] | 1994 | Vellore          | 80             |
| Premalatha et al[9] | 2002 | Chennai          | 16             |
| Moger et al[10] | 2005 | Chandigarh       | 26             |
| Soni et al[11] | 2006 | Hyderabad        | 160            |
| Prakash et al[12] | 2007 | Varanasi         | 23             |
| Prakash et al[13] | 2015 | Varanasi         | 31             |
| Mohandas et al[14] | 2016 | Thrivunanthapuram | 54          |
| Gopaliyah et al[15] | 2017 | Mallapuram/Kochi | 71             |
| Total         |      |                  | 461            |

Figure 1: (a) Low power of renal biopsy showing glomeruli with crescents and KW nodules (MT, ×10). (b) Renal biopsy showing one glomerulus with cellular crescent and segmental sclerosis, and two glomeruli with KW nodules (PAS, ×10). (c) Glomerulus showing cellular crescent along with areas of segmental sclerosis (PAS, ×40). (d) Glomerulus showing segmental endocapillary proliferation (PAS, ×40)

Figure 2: Immunofluorescence showing strong mesangial IgA staining (×20)
membranous nephropathy (19.2%) and FSGS (11.8%), while acute interstitial nephritis (33.3%) and postinfective glomerulonephritis (33.3%) were the most common NDRD in Group II. Prakash et al. in their study of 23 renal biopsies done in 2007 found that 13 (56.2%) cases had isolated DN, seven (33.3%) cases had NDRD, and three (13%) cases had NDRD superimposed on DN. MN (two cases), FSGS (two cases), and mesangiocapillary glomerulonephritis (one case) were the nondiabetic glomerular diseases. The predominant tubulointerstitial lesions in their study were chronic pyelonephritis and ischemic interstitial nephropathy. Prakash et al. in their study of 31 renal biopsies done in 2015 revealed isolated DN in 12 (38.7%), pure NDRD in 13 (41.9%), and mixed lesions in the remaining six (19.4%) cases. Idiopathic membranous nephropathy was the most common NDRD noted in four (21%) cases. Renal amyloidosis and FSGS were observed in two patients each, respectively. Focal mesangial-proliferative, proliferative glomerulonephritis with vasculitis, minimal change disease, myeloma cast nephropathy, and chronic tubulointerstitial nephritis were noted in one case each. With two cases, diffuse proliferative glomerulonephritis was the most common NDRD superimposed on DN. With one case each, chronic tubulointerstitial nephritis, amyloidosis, minimal change disease, and crescentic glomerulonephritis were the other NDRDs. Mohandas et al. in their study of 54 diabetic patients showed 40 (74.1%) cases had NDRD, of which 24 (44.4%) cases were due to diffuse proliferative glomerulonephritis, six (11.1%) cases each was due to IgA nephropathy and membranous nephropathy. Thirteen cases had DN as the only pathology. Gopaliyah et al. studied 71 diabetic patients who underwent renal biopsy. The prevalence rates of NDRD, DN, and DN with NDRD were 50.71% (n = 36), 28.16% (n = 20), and 21.13% (n = 15), respectively. Among the participants with NDRD, 69.44% (n = 25) had primary glomerular diseases (PGDs), 16.67% (n = 6) had tubulointerstitial diseases, and 13.89% (n = 5) had secondary glomerular diseases. IgA nephropathy was the most common of PGDs affecting seven (28%), followed by postinfective glomerulonephritis in five (20%), membranous nephropathy in four (16%), FSGS in three (12%), and miscellaneous lesions in 10 (24%).

From the above studies done in India, it was found that membranous nephropathy was the most common pathology among the NDRD in studies done by Premalatha et al., Soni et al., and Prakash (2007) et al. whereas in a study done by Moger et al. diffuse proliferative glomerulonephritis was the most common pathology among the NDRD. Gopaliyah et al. in their study showed IgA nephropathy to be the most common histological finding whereas Prakash et al. (2015) in their study showed membranous nephropathy and focal segmental glomerulosclerosis to be the most common pathology noted among the NDRD group. John et al. and Mohandas et al. in their studies did not separate the NDRD from those lesions superimposed with DN. John et al. found minimal change disease and Mohandas et al. found diffuse proliferative glomerulonephritis as the common pathologies.

**Summary**

In diabetic patients, DN is not the only renal disease noted in the kidneys. Renal diseases other than DN can occur in type 2 diabetic patients and these renal diseases are known as NDRD, either alone or co-existing with DN. With an increasing diabetic population, the role of primary care providers will be crucial in successfully managing these patients.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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