

Idiopathic nodular glomerulosclerosis- a rare case

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ABSTRACT

Nodular glomerulosclerosis is considered a signature lesion of diabetes nephropathy, but when it occurs in the absence of diabetes, it is called Idiopathic Nodular Glomerulosclerosis (ING). Idiopathic nodular glomerulosclerosis is a very rare disease and has been associated with obesity, hypertension, and smoking. We report a case of ING presenting as end-stage renal failure requiring hemodialysis.

Key words: idiopathic, nodular glomerulosclerosis, nephropathy

INTRODUCTION

Nodular glomerulosclerosis is considered a pathognomonic sign of diabetic nephropathy.¹ Millions of patients worldwide are affected with this nephropathy.^{1,2} Idiopathic nodular glomerulosclerosis (ING) is very rare, and fewer than 50 cases have been reported in the English literature.³ It is considered a distinct nephropathy with light microscopy and ultrastructural changes that mimic diabetic nodular glomerulosclerosis but without impaired glucose metabolism or other specific disease characteristics.^{4,5} Here we report a case of ING in an obese patient presenting with end-stage renal disease.

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CASE

A 34-year-old Hispanic woman with an increased body mass index (BMI, 33.7 Kg/m²), hypothyroidism, and kidney disease presented to the emergency room with headache, generalized weakness, and new onset hypertension. She had no recent history of infection or use of OTC nonsteroidal anti-inflammatory drugs. During admission, she looked sick; her blood pressure was 150/80 mmHg. Funduscopic examination revealed vitreous hemorrhages and cataracts in both eyes.

The initial laboratory studies included serum creatinine 12.07 mg/dL, blood urea nitrogen 99 mg/dL, estimated glomerular filtration rate 4 mL/min/1.73 m², urine protein 14.1 g/24hr, serum albumin 2.3 g/dL, total proteins 5.4 g/dL, serum potassium 5.2 mmol/L, hemoglobin 8.5 gm/dL, hematocrit 24.8 %, and HbA1c 5.1%. Antiglomerular base membrane antibodies, C-ANCA, P-ANCA, atypical pANCA, complement C3 and C4 levels, hepatitis B surface antigen, and C antibody assays were either within normal limits or negative.

Renal biopsy revealed advanced nodular glomerulosclerosis with severe tubular atrophy with interstitial fibrosis, and severe arterio- and arteriole-sclerosis. By light microscopy the specimen had 17 glomeruli; 15 were globally sclerotic. Electron microscopy confirmed the sclerotic glomeruli were large with mesangial nodules, the glomerular basement membrane was diffusely thickened and wrinkled, and the capillaries were narrowed and obliterated due to the increased mesangial matrix. The fluoresceinated antibody stains showed linear capillary wall staining for IgG (1+) and albumin (1+). A Congo red stain was negative for amyloidosis. Given the lack of history of diabetes, the morphologic features were consistent with idiopathic nodular glomerulosclerosis (Figure 1A, 1B and 1C). She was started on intermittent hemodialysis and has been maintained on thrice weekly dialysis.

DISCUSSION

Idiopathic nodular glomerulosclerosis was first described by Alpers and Biava as a rare clinical-pathologic entity in five patients without diabetes mellitus.⁶ In 1999, Herzenberg *et al* used the term “Idiopathic nodular glomerulosclerosis” to describe the histopathologic findings of renal biopsy that mimic diabetic nodular glomerulosclerosis. Since then numerous associations have been linked with this rare entity.⁷ Exogenous factors, such as smoking, endogenous factors, such as hypertension, obesity, or hypercholesterolemia, biochemical events caused by hormonal responses or cytokines, and demographic factors, such as older age, white race/ethnicity, and male gender, have been linked to IGN.⁸⁻¹⁰

Although we have little information about this patient’s past history, the most interesting feature is her young age (34 years old). Most patients reported in the literature are white males with a mean age above 55 years and chronic hypertension and smoking.^{3,8-10} Our patient had none of these risk factors but was obese which is a common characteristic and risk factor for ING.^{8,9} Li *et al* reported a series of 15 patients and found 87% of them were overweight

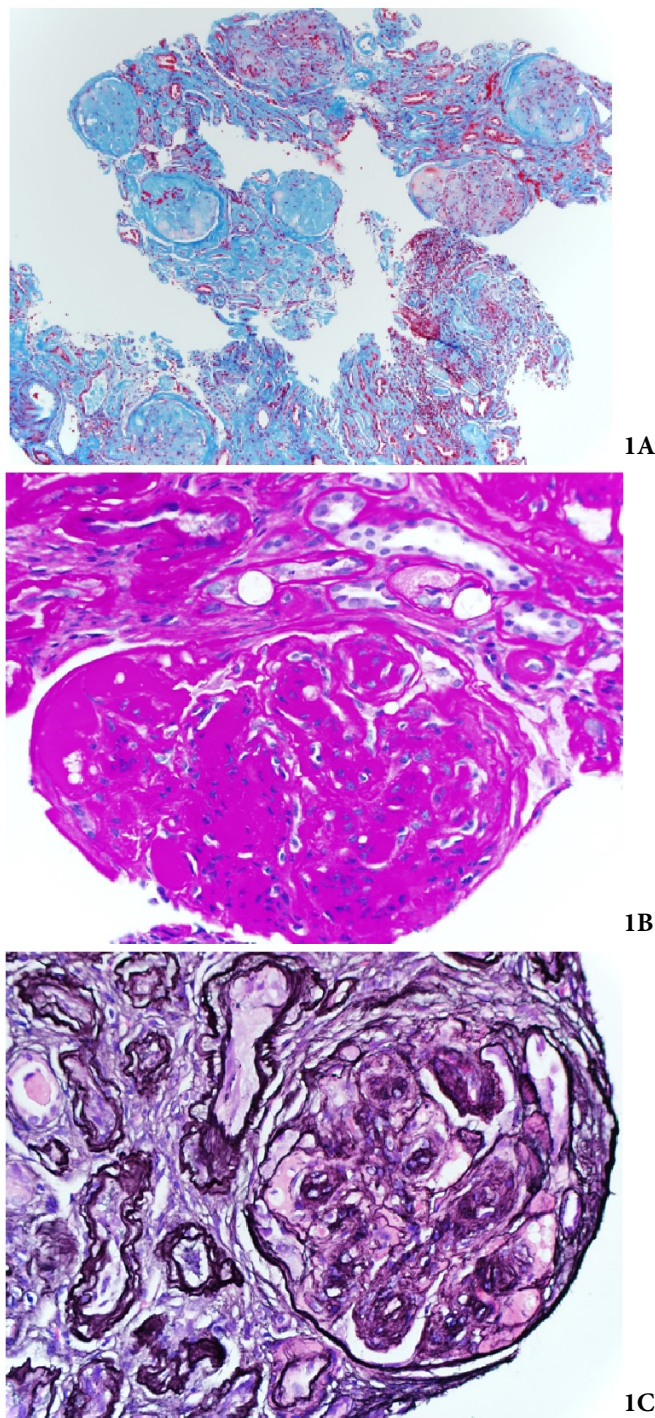


Figure 1A-C: Three small fragments of renal cortex with up to 17 glomeruli, 15 glomeruli are sclerotic. Many of the globally sclerotic glomeruli remain large with mesangial nodules still apparent. There is marked tubular atrophy and interstitial fibrosis (**1A** Trichrome x 100; **1B** PAS x 400; **1C** Jones x 400).

or obese.⁸ Jun Wu *et al* reported a series of 20 Chinese patients with 95% being overweight or obese.¹⁰ In 2001, Kambhan *et al* described obesity-related glomerulopathy, a syndrome that is increasing in prevalence due to the obesity epidemic worldwide.¹⁵ Obesity-related glomerulopathy presents the same pathologic features as ING, including glomerulosclerosis, mesangial matrix expansion, and thickening of the glomerular basement.

The Hb A1c was 5.1% which rules out diabetes mellitus (DM) in our patient, but an oral glucose tolerance test (OGTT) was not done. Nevertheless, one possible hypothesis is that some patients have lower thresholds for glucose induced kidney damage without overt DM.^{11,16,17} The ophthalmological examination in our patient might suggest a hyperglycemic state like latent diabetes mellitus or a non-persistent hyperglycemic state. Navaneethan *et al* compiled information of 42 ING patients. Among these patients, 35 underwent OGTT, and 12 patients had glucose intolerance. One third of these patients (including those with glucose tolerance and without glucose tolerance) had diabetic retinopathy changes.¹⁸ Most ING patients develop end-stage renal disease and require dialysis.^{7,8,10} The pathologic changes in our case are among the most severe in the reported cases, and more than 80% of the glomeruli studied were globally sclerotic with marked tubular atrophy and interstitial fibrosis.

In summary, our patient lacks some of the most common risk factors for ING, such as older age, male gender, chronic hypertension, and a smoking history, but she was obese and had features of diabetic eye disease. Idiopathic nodular glomerulosclerosis is a rare disease; more studies are needed to understand its pathogenesis and possible approaches to prevention.

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