

IgA nephropathy in African Americans: uncommon but possible

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Lesson

Though IgA nephropathy is relatively uncommon in African Americans, our case serves as a reminder that it needs to be considered in the differentials when these patients present with proliferative glomerulonephritis.

Keywords

IgA nephropathy, glomerulonephritis, African American

Introduction

Despite being the commonest primary glomerulonephritis in the world, IgA nephropathy is rarely reported among African Americans, who otherwise have high renal disease burden.¹ Traditionally, nephrology trainees have been taught that IgA nephropathy should be considered as the last differential for glomerulonephritis in African American patients unless they have human immunodeficiency virus (HIV) infection. This assumption is based on the ‘reported’ rarity of this disease in this population and the fact that African Americans make up more than 50% of the new cases of HIV infection in the United States.² Although focal segmental glomerulosclerosis is the most common glomerular lesion in HIV-related kidney disease, IgA nephropathy is frequently encountered in these patients.³ However, IgA nephropathy is being increasingly recognised in the non-HIV African American population.⁴ Factors such as level of disease awareness, access to appropriate diagnostic facilities and referral patterns may play a role in the under-diagnosis of IgA nephropathy in this population. Moreover, there are reports suggesting that these patients may have more severe disease at presentation.⁵ In addition to racial disparities in prevalence, IgA nephropathy exhibits a significant male preponderance, and herein, we report a rare case of IgA nephropathy in an African American woman.

Case report

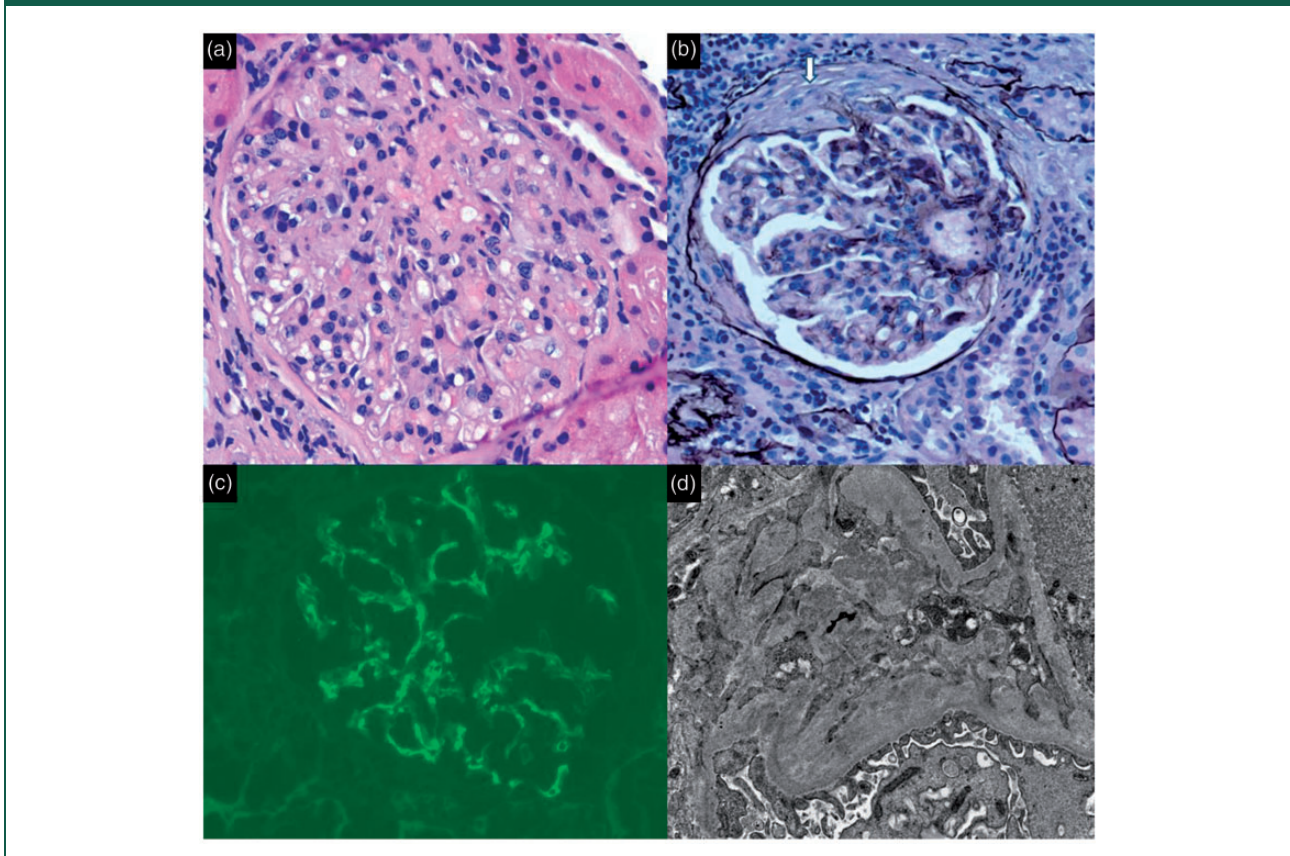
A 48-year-old African American woman was referred to our institution for further evaluation and

management of recently diagnosed IgA nephropathy. Her baseline serum creatinine was 1.2 mg/dL (ref: 0.5–1.1). She was initially evaluated at an outside facility three months prior to presentation, when the serum creatinine was 1.4 mg/dL with a urine protein–creatinine ratio of 1.7 g/g (ref: less than 150 mg/g) and 60/hpf red blood cells (ref: 0–5) in the urine. She did not have gross haematuria. A month later, her serum creatinine increased to 1.7 mg/dL, which prompted a renal biopsy. Unfortunately, the sample was inadequate, but it was suggestive of crescentic IgA nephropathy. Serologic tests for antinuclear antibodies, antineutrophil cytoplasmic antibodies, HIV and viral hepatitis were negative, and serum complements were within normal limits. In our clinic, the patient’s blood pressure was 110/78 mmHg while taking amlodipine 10 mg and losartan 25 mg/day. Serum creatinine was 1.4 mg/dL and urine protein–creatinine ratio was approximately 1.2 g/g. We elected to rebiopsy her to confirm the diagnosis of crescentic IgA nephropathy in a non-HIV-positive female African American patient, and the possibility of treatment with an alkylating agent. This time, an adequate sample was obtained and, interestingly, it was consistent with IgA nephropathy (Figure 1). As there were fibrocellular crescents in only 2 of the 11 glomeruli and the renal function remained stable, there was no indication for therapy with an alkylating agent. However, because of proteinuria exceeding 1 g/g despite being on an angiotensin receptor blocker, we treated her with a tapering course of prednisone. Six months later, her urine protein–creatinine ratio reduced to 437 mg/g and serum creatinine remained relatively stable at 1.6 mg/dL.

Discussion

Primary IgA nephropathy occurs at any age, with clinical onset in the second and third decades of life being the most common. There is a male preponderance ranging from 2:1 in Japan to 6:1 in northern

Figure 1. Renal biopsy demonstrating (a) mesangial hypercellularity (H&E 40×), (b) a fibrocellular crescent (silver stain 20×), (c) immunofluorescence IgA staining and (d) prominent mesangial deposits on electron microscopy.



Europe and the United States.⁶ IgA nephropathy is most prevalent among men of Southeast Asia, accounting for about 50% of all glomerular diseases in Japan. In Europe and the United States, it occurs with greatest frequency in Caucasians and is remarkably rare in Blacks.⁷ It has been suggested that the risk of IgA nephropathy might be influenced by the IgA2 allotype and the rare Black patients with IgA nephropathy may be homozygous for the A2m(1) allele which predominates in Whites. However, Crowley-Nowick et al. tested this hypothesis in a multicentre study with 27 Black IgA nephropathy patients and found that the presence of the A2m(1) allele did not increase the risk for IgA nephropathy, and the presence of the A2m(2) allele or homozygosity for this allele did not protect Blacks from the development of IgA nephropathy.⁸ It is now recognised that the regional differences in screening for kidney disease and kidney biopsy practices contribute to variations in disease prevalence. For example, in Japan, routine screening for urinary abnormalities is performed in all school-aged children, and symptom-free individuals with microscopic

haematuria are more likely to undergo renal biopsy, leading to an increased diagnosis of IgA nephropathy. On the other hand, in the United States, Canada and the United Kingdom, renal biopsy is not routinely recommended for patients presenting with isolated haematuria or mild proteinuria unless accompanied by worsening renal function.⁶ Moreover, factors such as socioeconomic status, healthcare literacy and access to diagnostic facilities may play a role.

In addition to differences in the prevalence, recent reports suggest that African American patients with IgA nephropathy may present with atypical and more severe features such as nephrotic syndrome.⁵ Of note, it is estimated that IgA nephropathy presents with gross haematuria in about 40–45% of patients, microscopic haematuria and proteinuria in about 35–40% and nephrotic syndrome or acute kidney injury in the remainder.⁷ Available evidence suggests that accelerated decline in renal function is associated with proteinuria more than 1 g/day in a dose-dependent fashion and independent of other risk factors.⁹ Therefore, in patients with proteinuria more than

1 g/day, despite three to six months of optimised supportive care (including Angiotensin converting enzyme inhibitors or angiotensin receptor blockers and blood pressure control), and GFR > 50 mL/min/1.73 m², current guidelines recommend a six-month course of corticosteroid therapy.¹⁰ We treated our patient with prednisone based on this guideline. Crescentic IgA nephropathy, by definition, is IgA nephropathy with crescents in more than 50% of glomeruli in the renal biopsy with rapidly progressive renal deterioration. Such cases carry poor prognosis, and treatment with alkylating agents (cyclophosphamide) is recommended in addition to steroids.

While definitive conclusions about epidemiology of a disease cannot be drawn from a single case study, we want to emphasise that IgA nephropathy is uncommon but does occur in African Americans and needs to be considered in the differentials when they present with proliferative glomerulonephritis. Early identification and prompt initiation of treatment may result in favorable outcomes. Future research should focus on race-based comparison of presenting complaints, renal biopsy lesions and response to treatment in patients with IgA nephropathy. It may also be worthwhile to investigate the incidence of this disease in patients with 'mixed' racial and ethnic backgrounds.

Declarations

Competing Interests: None declared.

Funding: None declared.

Ethics approval: Informed consent for publication was obtained from the patient for publication of this case study.

Guarantor: AK.

Contributorship: All authors were involved in the care for the patient (AK, WLC, DHE and JT). AK drafted the initial version of manuscript, performed literature search and approved the final manuscript. WC has provided the pathology images and pertinent information. DE assisted in drafting the manuscript and approved

the final manuscript. JT was the attending physician on the case, reviewed the manuscript for critically important intellectual content and approved the final version for submission.

Acknowledgements: None.

Provenance: Not commissioned; peer-reviewed by Zehra Eren.

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