

A Case Report of Immunoglobulin A-dominant Acute Postinfectious Glomerulonephritis in a Patient with a Horseshoe Kidney

Woods SA^{1*}, Trivedi DD², Naseer A^{2,3}, Huch KM^{1,2,3} and Gyamlani G^{2,3}

¹Department of Internal Medicine, University of Tennessee Health Science, Memphis, USA

²Division of Nephrology, University of Tennessee Health Science, Memphis, USA

³Veterans Affairs Medical Center, Nephrology Section, Memphis, USA

Abstract

Immunoglobulin A-dominant acute postinfectious glomerulonephritis (IgA-dominant APIGN) is an increasingly recognized morphologic variant of APIGN. In contrast to classic APIGN, in which there is glomerular deposition of IgG and/or C3, IgA is the sole or dominant immunoglobulin deposited in IgA-dominant APIGN. Patients present with declining glomerular filtration rate (GFR), proteinuria, and microscopic hematuria. Horseshoe kidney (HSK) is a relatively common renal anomaly. To this point, the co-occurrence of HSK and IgA-dominant APIGN has not been reported in the literature. Here, we report a case of IgA-dominant APIGN in a patient with HSK resulting in the need for temporary hemodialysis.

Keywords: Immunoglobulin A; Postinfectious glomerulonephritis; Horseshoe kidney

Introduction

Acute post-infectious glomerulonephritis (APIGN) is an immune-complex mediated glomerulonephritis that follows an extra-renal infection. Classically, APIGN has been a post-streptococcal glomerulonephritis (PSGN) occurring predominantly in children following pharyngitis or impetigo. This is still the predominant scenario in developing countries [1]. However, over the years, the spectrum of disease in developed countries has changed such that the disease is more likely to occur in persons older than 60 years (0.9 cases per million versus 0.4 cases per million) [2] and the inciting pathogen is more likely to be *Staphylococcus* than *Streptococcus* with incidences of 46% and 16%, respectively [3]. Within the last 15 years, there has been discovery of a new morphological variant of APIGN known as immunoglobulin A-dominant acute postinfectious glomerulonephritis (IgA-dominant APIGN), which is characterized by diffuse endocapillary proliferative glomerulonephritis with dominance or sole deposition of IgA rather than the classic IgG immunoglobulin in the subepithelial layer of the glomerulus [4,5]. Factors associated with IgA-dominant APIGN appear to be male gender, older age, and staphylococcal infection [6]. It often manifests as acute or rapidly progressive renal failure with proteinuria, and the mainstays of treatment are antimicrobial therapy, steroids, and supportive care with outcomes including complete renal recovery (16-38%), persistent renal dysfunction without renal replacement therapy (20-43%), progression to ESRD (27-41%), and death (4-13%) [5,6].

In contrast to APIGN, there has been no significant evolution in the epidemiology of the horseshoe kidney (HSK). It remains the most common renal fusion abnormality with an incidence ranging from 1:400-1:700 persons [7-9]. HSK results from fusion of the right and left metanephros during fetal development, and evidence suggests that defects in genes involved in the development of the renal capsule, namely *Foxd-1*, are responsible for the failure of the early metanephros to separate from the midline and body wall to form two distinct kidneys flanking the midline [10,11].

Although the association has not been formally investigated, there does not appear to be an increased risk of glomerular disease associated with horseshoe kidney. A recent literature review by Hu et al delineated the glomerular pathologies which have been identified in a HSK thus far [12]. Here, we add to that list with a case report of IgA dominant

APIGN in a patient with a HSK. To our knowledge, this is the first case described in the literature.

Case Report

A 63 year-old African American male with a past medical history of diabetes mellitus, hypertension, and dermatitis presented with complaints of dyspnea upon exertion and anasarca for five days. The nephrology service was consulted for evaluation of non-oliguric acute kidney injury as evidenced by a serum creatinine increase to 2.7 mg/dL from 1.2 mg/dL measured five months prior to admission, associated with microscopic hematuria and nephrotic-range proteinuria with a urine protein to creatinine (UPC) ratio of 7243 mg/g. The patient had a recent flare of his dermatitis which was treated with a short course of steroids.

Examination revealed a hypertensive patient with anasarca, an erythematous, scaly rash on the neck, shoulders, and chest, and a non-erythematous, ichthyotic rash of his lower extremities.

Serologic studies were unremarkable with the exception of an elevated anti-DNAse level. Serum complement levels were within normal limits (C3 127 mg/dL and C4 36 mg/dL). Blood and urine cultures had no growth. Renal ultrasound revealed a horseshoe kidney without other abnormalities. The dermatology service diagnosed the rash as acquired ichthyosis. Because of progressively worsening renal failure necessitating hemodialysis without a clear etiology, a percutaneous renal biopsy was obtained under CT guidance.

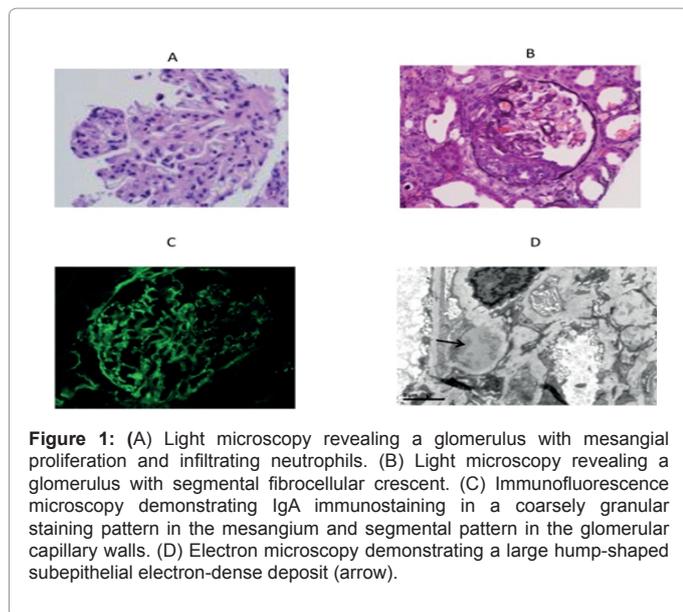
Light microscopy (LM) (Figure 1A and 1B) revealed 21 glomeruli including five with segmental cellular crescents and three with global sclerosis. The glomeruli had minimal mesangial proliferation, scattered

***Corresponding author:** S. Alexander Woods, University of Tennessee Health Science Center, 956 Court Street, Suite H314, Memphis, TN 38163, USA; E-mail: swoods29@uthsc.edu

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neutrophils within the capillary lumina, and extensive tubular damage. Immunofluorescence (IF) (Figure 1C) demonstrated 2+ segmental granular mesangial staining with IgA and C3, 1+ kappa light chain staining, and trace IgM and lambda light chain staining. IgG and C1q staining were absent in the glomeruli. Electron microscopy (EM) (Figure 1D) demonstrated electron-dense deposits in the mesangial distribution and scattered hump-like electron-dense deposits in the subepithelial distribution.

These findings were consistent with IgA-dominant APIGN due to a presumed staphylococcal skin infection superimposed upon a streptococcal skin infection. The patient received two weeks of antibiotic therapy consisting of piperacillin/tazobactam for 5 days and ampicillin/sulbactam for 9 days. He underwent hemodialysis for two weeks after which he regained sufficient renal function for discontinuation of dialysis. Follow-up of the patient in the clinic four weeks later revealed continued renal convalescence with a creatinine of 2.5 mg/dL and a UPC ratio of 2236 mg/g. At one-year follow-up, the patient's creatinine had improved to 1.4 mg/dL with a UPC ratio of 700mg/g.

Discussion

IgA-dominant APIGN is an increasingly recognized morphologic variant of APIGN, particularly in persons greater than 65 years of age (17% of cases) [3]. Skin is the most common site of infection (26-51% of cases) followed by lung and abscesses from sites other than skin. Additional sites of infection reported include the urinary tract, bone, heart, and upper respiratory tract. Staphylococcal species account for the majority of infections (70%). Streptococcus, enterococcus, and gram-negative species are responsible for 6-9% of cases, and the remainder of cases have no identifiable pathogen (21-24%) [3,5,6]. Often, the source of infection is not clinically obvious because of long latency periods between the time of infection and the development of glomerulonephritis (up to 16 weeks). Previous studies have reported an association between IgA-dominant APIGN and diabetes, noting that the higher circulating concentrations of IgA in diabetics may predispose them to the IgA-dominant variant [3-6]. However, based upon the analysis of cases identified by Nasr et al and Koo et al. the incidence of diabetes in patients with IgA-dominant APIGN is 34-55%,

revealing that diabetics likely do not have a greater predisposition to IgA-dominant APIGN than non-diabetics [3,5,6].

Patients often present with hypertension, renal failure, nephrotic-range proteinuria, and hematuria. Hypocomplementemia has been identified in up to 69% of patients [5].

Diagnosis is made by renal biopsy. Histologic patterns identified on LM include endocapillary proliferative and exudative GN (63% of patients), pure mesangial proliferative GN (33%), and crescentic GN (4%). Immunofluorescence reveals IgA as the sole or dominant immunoglobulin deposited in 96% of cases, and staining for C3 is of higher intensity relative to IgA in 55% of cases and of equal intensity in 36% of cases. Additionally, staining for kappa light chains is equal to or stronger than staining for lambda light chains in 69% of reported cases. Electron microscopy reveals mesangial electron-dense deposits and subepithelial humps in 96% and 83% of cases, respectively [5].

The differential in staining of IgA, C3, and light chains aids in the differentiation of IgA-dominant APIGN from IgA nephropathy. The former more frequently has lower-intensity staining for IgA than C3 and less mesangial staining for lambda than kappa light chains [3,13].

Our patient was an elderly diabetic male who presented with hypertension, anasarca, and non-oliguric acute kidney injury. Renal biopsy showed features of crescentic and mesangial proliferative GN on LM (Figure 1A and 1B). Immunofluorescence staining of IgA and C3 was equivalent at 2+ staining, and light-chain stain demonstrated greater kappa light chain deposition relative to lambda light chain thus differentiating IgA-dominant APIGN from IgA nephropathy (Figure 1C). EM revealed subepithelial and mesangial electron dense deposits. There were only scant subepithelial deposits seen on EM which may have resulted in a negative IF staining in the area of glomerular basement membrane. These pathological findings were consistent with other reported cases of IgA-dominant APIGN.

Our patient also had a horseshoe kidney (HSK). This is a common congenital anomaly and has been associated with an increased incidence of hydronephrosis [14,15], nephrolithiasis [9,14,16-18], UTI [14] and certain malignancies [19-21]. Several types of glomerular diseases have been reported to occur in HSK [12,22-29] and though there has not been a formal study designed to specifically address this association, studies addressing either HSK or glomerulonephritis individually have not identified an association of the two [1-7,9]. In light of the frequent incidence of HSK and the need for renal imaging prior to biopsy for diagnosis of glomerular disease, we might expect that if an association existed, it would have presented itself in the studies of glomerular disease conducted thus far. The lack of association may reflect the fact that HSK malformation results from abnormalities of the renal capsule, not the parenchyma. For this reason, the renal parenchyma of a HSK may be at the same risk for glomerular disease as that of a normal kidney. However, because HSK poses a relative contraindication to renal biopsy, providers may be hesitant to pursue a definitive diagnosis, and thus the incidence of biopsy-proven glomerular disease in HSK may be underestimated [25].

In our case, we suspect that the occurrence of IgA-dominant APIGN in a HSK is a matter of coincidence, and that this case supports the supposition that the renal malformation of HSK neither protects nor predisposes to glomerular disease, but rather holds the same risk for glomerular disease as that of the general population. However, a formal study to address the incidence of glomerular disease in patients with HSK relative to the general population is needed to elucidate the true association between the two entities.

In conclusion, IgA-dominant APIGN is an increasingly recognized morphologic variant of APIGN, and HSK remains a common renal malformation. We report a case of IgA-dominant APIGN occurring in a patient with a HSK. To our knowledge, this is the first case reported in the literature.

References

- Rodriguez-Iturbe B, Musser JM (2008) The current state of poststreptococcal glomerulonephritis. *J Am Soc Nephrol* 19: 1855-1864.
- Coppo R, Gianoglio B, Porcellini MG, Maringhini S (1998) Frequency of renal diseases and clinical indications for renal biopsy in children (report of the Italian National Registry of Renal Biopsies in Children). Group of Renal Immunopathology of the Italian Society of Pediatric Nephrology and Group of Renal Immunopathology of the Italian Society of Nephrology. *Nephrol Dial Transplant* 13: 293-297.
- Nasr SH, Fidler ME, Valeri AM, Cornell LD, Sethi S, et al. (2011) Postinfectious glomerulonephritis in the elderly. *J Am Soc Nephrol* 22: 187-195.
- Nasr SH, Markowitz GS, Whelan JD (2003) IgA-dominant acute poststaphylococcal glomerulonephritis complicating diabetic nephropathy. *Hum Path* 34: 1235-1241.
- Nasr SH, D'Agati VD (2011) IgA-dominant postinfectious glomerulonephritis: a new twist on an old disease. *Nephron Clin Pract* 119: c18-25.
- Koo TY, Kim GH, Park MH (2012) Clinicopathologic Features of IgA-Dominant Postinfectious Glomerulonephritis. *Korean J Pathol* 46: 105-114.
- Allen AC (1951) Horseshoe kidney. In: Allen AC (ed) *The kidney: Medical and surgical diseases*. Grune & Stratton, Inc., New York, USA.
- Campbell MF (1954) Embryology and anomalies of the urogenital tract. In: Campbell MF (ed) *Urology*. W.B. Saunders Company, Philadelphia.
- Weizer AZ, Silverstein AD, Auge BK, Delvecchio FC, Raj G, et al. (2003) Determining the incidence of horseshoe kidney from radiographic data at a single institution. *J Urol* 170: 1722-1726.
- Schedl A (2007) Renal abnormalities and their developmental origin. *Nat Rev Genet* 8: 791-802.
- Levinson RS, Batourina E, Choi C, Vorontchikhina M, Kitajewski J, et al. (2005) Foxd1-dependent signals control cellularity in the renal capsule, a structure required for normal renal development. *Development* 2005 132: 529-539.
- Hu P, Jin M, Xie Y, Chen P, Zhang X, et al. (2014) Immunoglobulin A nephropathy in horseshoe kidney: case reports and literature review. *Nephrology (Carlton)* 19: 605-609.
- Chui SH, Lam CW, Lewis WH, Lai KN (1991) Light-chain ratio of serum IgA1 in IgA nephropathy. *J Clin Immunol* 11: 219-223.
- Glenn JF (1959) Analysis of 51 patients with horseshoe kidney. *N Engl J Med* 261: 684-687.
- Shimkus EM, Mekhanna I (1993) [Hydronephrosis in a horseshoe kidney]. *Urol Nefrol (Mosk)* : 48-51.
- Stamatelou KK, Francis ME, Jones CA, Nyberg LM, Curhan GC (2003) Time trends in reported prevalence of kidney stones in the United States: 1976-1994. *Kidney Int* 63: 1817-1823.
- Evans WP, Resnick MI (1981) Horseshoe kidney and urolithiasis. *J Urol* 125: 620-621.
- Lampel A, Hohenfellner M, Schultz-Lampel D, Lazica M, Bohnen K, et al. (1996) Urolithiasis in horseshoe kidneys: therapeutic management. *Urology* 47: 182-186.
- Mesrobian HG, Kelalis PP, Hrabovsky E, Othersen HB Jr, deLorimier A, et al. (1985) Wilms tumor in horseshoe kidneys: a report from the National Wilms Tumor Study. *J Urol* 133: 1002-1003.
- Krishnan B, Truong LD, Saleh G, Sirbasku DM, Slawin KM (1997) Horseshoe kidney is associated with an increased relative risk of primary renal carcinoid tumor. *J Urol* 157: 2059-2066.
- Buntley D (1976) Malignancy associated with horseshoe kidney. *Urology* 8: 146-148.
- Chen A, Ko WS (1990) Horseshoe kidney and membranous glomerulonephropathy. *Nephron* 54: 283-284.
- Fujimoto S, Hirayama N, Uchida T, Iemura F, Yamamoto Y, et al. (1992) Horseshoe kidney and membranous glomerulonephritis with cold activation of complement. *Intern Med* 31: 625-628.
- Alagözülü H, Candan F, Gültekin F, Bulut E, Elagoz S (2001) Horseshoe kidney and nephrotic syndrome due to idiopathic membranous nephropathy. *Intern Med* 40: 1259-1260.
- Abson C, Jones M, Palmer A, Persey M, Gabriel R (1991) Horseshoe kidney, focal and sclerosing glomerulonephritis and primary hypothyroidism. *Nephron* 58: 124.
- Kayataş M, Urün Y (2007) Two cases with horseshoe kidney in association with nephrotic syndrome: is there a causal relationship between two conditions? *Ren Fail* 29: 517-518.
- Rivera F, Caparrós G, Vozmediano C, Bennouna M, Anaya S, et al. (2010) [„Horseshoe kidney”, renal adenocarcinoma and nephrotic syndrome]. *Nefrologia* 30: 596-598.
- Matyus J, Kovacs J, Ujhelyi L, Karpati I, Dalmi L, et al. (1996) Interferon therapy in cryoglobulinemic membranoproliferative glomerulonephritis associated with hepatitis C virus infection. *Orv Hefil* 137: 2527-2530.
- Kavukçu S, Sahin B, Türkmen M, Soylu A, Lebe B, et al. (2003) Horseshoe kidney with mesangioproliferative glomerulonephritis and goiter. *Turk J Pediatr* 45: 350-352.