

CASE REPORT

AN UNUSUAL CASE OF IGA-DOMINANT POSTINFECTIOUS GLOMERULONEPHRITIS: A CASE REPORT AND REVIEW OF THE LITERATURE

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We report a case of IgA-dominant postinfectious glomerulonephritis in a 49-year-old man presenting with acute kidney injury, nephrotic range proteinuria and hematuria. He suffered from ischemic heart disease, cardiac insufficiency, mitral regurgitation, tricuspid insufficiency, septal aneurysm and hypertension. Renal biopsy revealed segmental and focal endocapillary and mesangial hypercellularity, and thickening of the glomerular capillary wall. Immunofluorescence showed co-dominant strong coarse granular immunostaining of IgA, IgG and C3 mainly along the glomerular capillary wall. On electron microscopy some large subepithelial hump-shaped deposits were present. In summary, this case demonstrates the presence of a broad spectrum of glomerular histological findings in postinfectious glomerulonephritis.

Key words: IgA-dominant glomerulonephritis, postinfectious glomerulonephritis, renal biopsy.

Introduction

Glomerular injury can occur in a number of infections. Poststreptococcal glomerulonephritis is a classic example of postinfectious glomerulonephritis with diffuse proliferative and exudative glomerular histology, IgG and C3 immunostaining and subepithelial humps. It is widely accepted that the incidence of poststreptococcal glomerulonephritis has decreased in the past three decades in developed countries [1, 2, 3]. The disease is now more frequent in the elderly, especially in association with intravenous drug use or alcoholism [4]. Immunoglobulin A-dominant postinfectious glomerulonephritis (IgA-dominant PIGN) is a recently defined entity often associated with staphylococcal infections [5, 6, 7, 8]. This lesion is usually found in adult patients with diabetes, or an-

other form of chronic illness [9]. The more extensive use of renal biopsy has demonstrated the presence of a broad spectrum of glomerular histological findings in PIGN [10]. The pattern of glomerular disease is not uniform, and the same organism has been shown to produce different morphologic appearances in different patients or in different geographic areas. Moreover, uncharacteristic clinical presentation involving subclinical infections highlights the important diagnostic role of renal biopsy [11].

Case report

A 49-year-old man presenting acute renal failure, nephrotic range proteinuria and hematuria was admitted to the Department of Nephrology. He suffered from ischemic heart disease, cardiac insufficien-

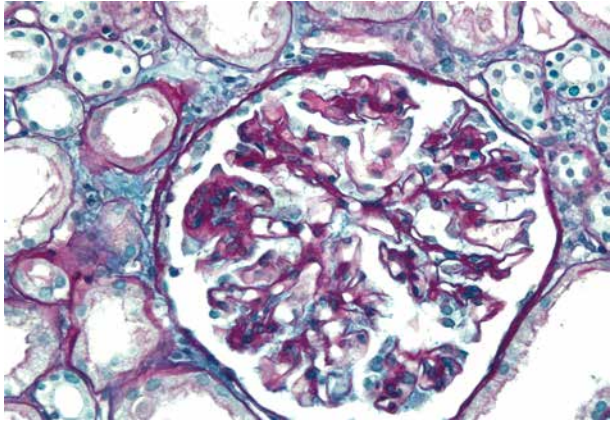


Fig. 1. Glomerulus with mild segmental mesangial and endocapillary hypercellularity. PAS staining. Magnification 400×

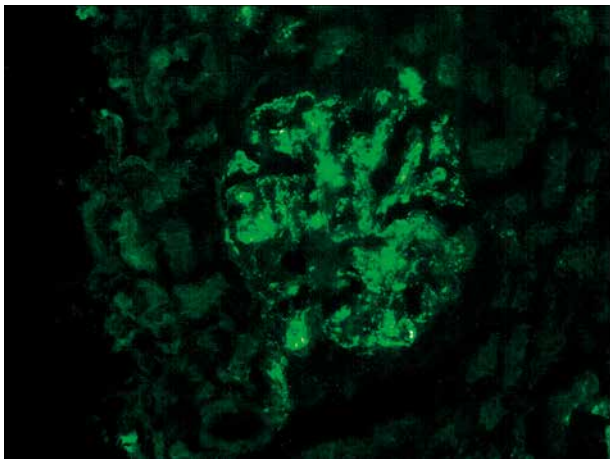


Fig. 2. Immunofluorescence. Strong (+3) granular immunostaining for IgA in the mesangium and capillary loops. Fluorescein isothiocyanate-conjugated anti-human IgA (Dako). Magnification 200×

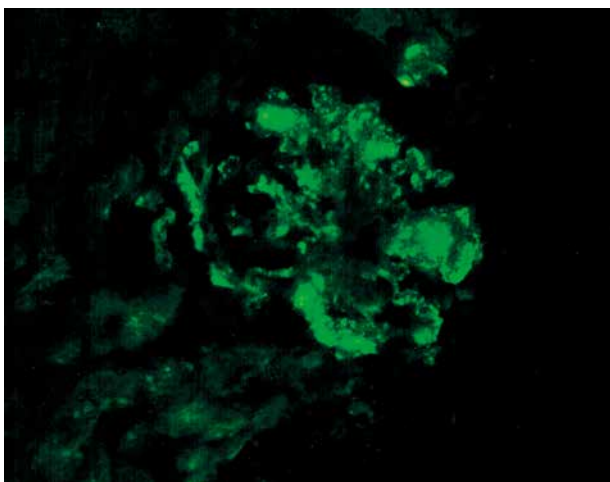


Fig. 3. Immunofluorescence. Strong (+3) granular immunostaining for IgG in the mesangium and capillary loops. Fluorescein isothiocyanate-conjugated anti-human IgG (Dako). Magnification 200×

cy, mitral regurgitation, tricuspid insufficiency, septal aneurysm and hyperlipidemia. On clinical examination he had swelling of the legs and hypertension. At admission the patient did not have documented infection. Serology showed HBsAg, HCV, and HIV negative. Urinalysis showed proteinuria (5.6 g/24 h) and hematuria (10-15 erythrocytes per high-power field). Laboratory findings showed hemoglobin of 10.5 g/dl, red blood cell (RBC) count 3,230,000/mm³, white blood cell (WBC) count 15,000/mm³ (polymorphs 90%, lymphocytes 6.4%, monocytes 2.3%), serum creatinine 2.94 g/dl. Urine culture examination was negative. Renal biopsy was performed. The samples were embedded in paraffin and sectioned at 2 μm, followed by HE, Masson, periodic acid-Schiff, periodic acid-silver methenamine, and Congo red staining. For immunofluorescence study (IF), the samples were sectioned in frozen conditions, followed by staining for IgG, IgA, IgM, C3, C1q, kappa and lambda light chain. The electron microscopy (EM) examination was done with a JEM 1011 electron microscope after routine staining. Light microscopy showed 15 glomeruli with mild, focal and segmental mesangial or endocapillary hypercellularity (Fig. 1), and thickening of the capillary loops. Interstitial lesions were scanty and included focal inflammatory infiltrates composed of lymphocytes, and mild focal fibrosis. Immunofluorescence evaluation in 10 glomeruli showed co-dominant strong coarse (+3) granular positivity for IgA (Fig. 2), IgG (Fig. 3) and C3 along the capillary wall and mesangium with weaker (+2) immunostaining for kappa light chain and slight (+1) immunostaining for lambda light chain. Immunostaining for IgM and C1q was negative. Electron microscopy revealed in glomeruli subepithelial hump-shaped deposits (Fig. 4) and intramembranous (Fig. 5) or me-

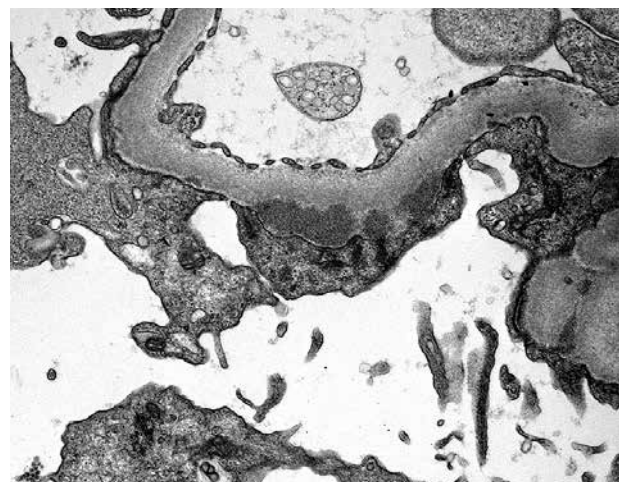


Fig. 4. Electron microscopy. Hump-like subepithelial deposits and diffuse effacement of foot processes. Uranyl acetate and lead citrate stain. Magnification 10 000×

sangial deposits. Based on the renal biopsy findings IgA-dominant postinfectious glomerulonephritis was diagnosed.

Discussion

IgA dominant PIGN is a relatively recently recognized entity, and it is important to distinguish it from IgA nephropathy, with which it can easily be confused [9, 12, 13, 14, 15, 16, 17, 18, 19]. The most frequent histological pattern of glomerular injury in IgA-dominant PIGN is endocapillary and exudative glomerulonephritis, identical to that seen in poststreptococcal glomerulonephritis; however, pure mesangial proliferative glomerulonephritis was described in 33% of reported patients with this disease [6]. In the study of Hsieh *et al.* [11] an atypical pattern of focal mesangial proliferation accounted for a striking proportion of IgA-dominant PIGN cases and, moreover, was increasingly recognized over time. It is thought that glomerular IgA dominant or co-dominant deposition is more frequently seen in atypical histological pattern [20]. Koyama *et al.* [21] reported a variable renal histology ranging from mild mesangial proliferative glomerulonephritis to diffuse mesangiocapillary glomerulonephritis with crescents, and mesangial and capillary wall staining for IgA and IgG (usually co-dominant) as well as for C3 in cases of glomerulonephritis due to methicillin-resistant *Staphylococcus aureus* infections. The literature data indicate that IgA-dominant PIGN is not peculiar to staphylococcal infection. In the study of Wen and Chen [13] seven patients with IgA-dominant PIGN were afflicted with non-staphylococcal infection: two streptococci, and five gram-negative bacteria. In the series of Bu *et al.* [22] 55 patients with IgA-dominant PIGN had documented staphylococcal infection, and the remaining infected patients tested positive for HIV in 3 patients, *Streptococcus* and *Klebsiella* and *Escherichia coli* in 2 each, *Rickettsia*, and *Acinetobacter baumannii*, *Chlamydia pneumonia* and hepatitis A virus in 1 patient each. Moreover, it is noteworthy that in the study of Bu *et al.* in 10 patients with IgA-dominant PIGN no pathogens were detected. The most common sites of infection in IgA-dominant PIGN are the skin and visceral abscess. The average duration of the incubation period is estimated to be about 4 weeks [5, 9, 16, 23, 24], although in some cases the infection may be identified at the time of renal biopsy because the infection was unrecognized for some time [25]. Clinical presentations of IgA-dominant PIGN are typically acute kidney injury with proteinuria, hematuria, and hypocomplementemia [22]. Several investigators have reported that IgA-dominant PIGN mainly affected diabetic patients [5, 14, 16, 23, 24], but in the study of Bu *et al.* [22] diabetes mellitus and hypertension were present in about 23% of pa-

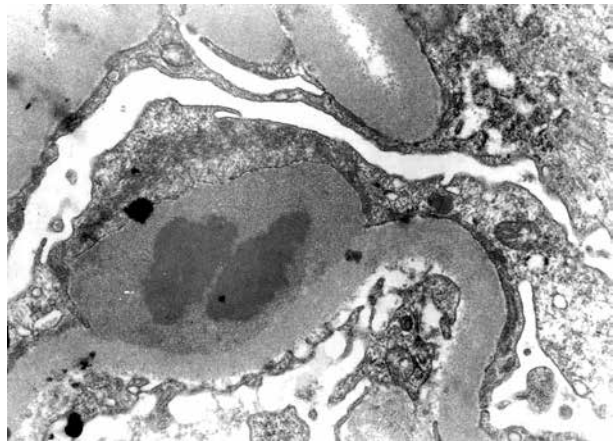


Fig. 5. Electron microscopy. Hump-shaped large subepithelial deposits and effacement of foot processes. Uranyl acetate and lead citrate stain. Magnification 20 000 \times

tients, malignancy in 15.4% of patients and heart diseases in 16.7%. In renal biopsy in patients with IgA-dominant PIGN immunofluorescence examination revealed coarse granular staining for IgA in the glomerular capillary wall and/or in mesangial areas with co-deposition of C3 and IgG in the majority of cases [22]. On electron microscopy electron-dense deposits are mesangial, subendothelial and subepithelial including varying numbers of humps [16, 22]. It must be stressed that IgA-dominant PIGN must be distinguished from IgA nephropathy (IgAN) because of different treatments and prognosis of these diseases. Clinical and histological features that favor IgA-dominant PIGN over IgAN include initial presentation in older age, acute renal failure at presentation, undercurrent culture-documented staphylococcal infection, depressed serum complement, diffuse endocapillary hypercellularity with prominent neutrophil infiltration on light microscopy, stronger staining for C3 than IgA, lack of lambda predominance on IF, and the presence of subepithelial humps on EM [5, 16, 23, 24]. The etiology of IgA-dominant PIGN is not clear, but Koyama *et al.* [21] speculated that bacterial superantigen played an important role in the pathogenesis of this entity. Superantigens are proteins that may be detected in several pathogenic microbes including *Staphylococcus*. They are powerful activators of immune systems and stimulate the production of T cells, and induce antibody production including IgA [21, 26].

The first choice of treatment for IgA-dominant PIGN should be antibiotic therapy [22], although Okuyama *et al.* [27] reported a case of a 48-year-old man who failed to respond to antibiotic treatment alone, but responded to steroids in addition to antibiotics. Bu *et al.* [22] documented that the outcomes of patients with IgA-dominant PIGN are variable. The renal function of half of the patients improved, about 12% of patients had persistent renal dysfunc-

tion, about 20% progressed to ESRD, and about 14% died.

The presented case does not entirely meet all criteria of IgA-dominant PIGN, because of the lack of clinically proven infection, but it should be taken into consideration that the infection may be subclinical. The patient suffered from ischemic heart disease and cardiac insufficiency, and on admission to hospital his laboratory data exhibited a high WBC count with 90% polymorphs, strongly suggesting infection. It is possible that in this case the detailed laboratory examination will reveal the pathogens that are responsible for the disease, or possibly the patient had a subclinical infection preceding admission to the hospital.

In summary, this case shows that atypical histological and clinical features can constitute diagnostic challenges in PIGN. However, the presence of IgA-dominant or co-dominant strong immunostaining in immunofluorescence examination and subepithelial hump-shaped deposits on electron microscopy strongly suggest recognition of IgA-dominant PIGN, despite the lack of documented infection at the time of presentation.

The authors declare no conflict of interest.

The study was supported by grant of Medical University of Łódź Nr 503/6-038-01/503-61-001.

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