Case Report

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IgA nephropathy with leucocytoclastic vasculitis

Lin-Yan Wei[1,2], Chao Liu[2], Ya-Li Zhang[2,#] and Guo-Liang Li[1,2,#]

Abstract

Leucocytoclastic vasculitis is a rare type of allergic disease caused by immune complexes. IgA nephropathy is a glomerulopathy characterized by recurrent episodes of gross haematuria or microscopic haematuria and IgA deposition in the glomerular mesangial region. IgA nephropathy complicating leucocytoclastic vasculitis is rare documented. We present a case of IgA nephropathy in a 47-year-old woman with leucocytoclastic vasculitis and discuss the clinical and pathological data, aiming to promote the diagnosis and treatment of this specific clinical manifestation.

Keywords

Leucocytoclastic vasculitis, allergic vasculitis, IgA nephropathy, haematuria, oedema, urine occult blood, kidney biopsy

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Introduction

Leucocytoclastic vasculitis (LCV), also known as allergic vasculitis (AV), is a type III allergic disease caused by immune complexes, infections, and medications. It is a typical small-vessel (small arteries/veins and capillaries) vasculitis that may be confined to the skin or exhibit systematic manifestations involving other organs, the most common of which is the kidney, comprising approximately 20% of LCV cases.[1] IgA nephropathy (IgAN) is a glomerulopathy

[1]Department of Cardiovascular Medicine, First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China
[2]Department of Nephrology, First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China

[#]These authors contributed equally to this work.

Corresponding author:
Guo-Liang Li, Department of Cardiovascular Medicine, First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, China.
Email: liguoliang_med@163.com

that is characterized by recurrent episodes of gross haematuria or microscopic haematuria and IgA deposition in the glomerular mesangial region. IgAN in patients with LCV is rare described. Here, we present a case of LCV and concomitant IgAN in a 47-year-old woman and discuss the clinical and pathological data in the case. We hope to promote the diagnosis and treatment of this specific clinical manifestation.

Case report

A 47-year-old woman presented with extensive palpable purpuric lesions and areas of necrosis and haemorrhagic blisters on her bilateral lower extremities, 15 months prior to admission. Previous laboratory examination showed IgA 4.65 g/L, erythrocyte sedimentation rate (ESR) 31 mm/hour, urine red blood cell 288.2 /μL. Skin biopsy was highly suggestive of LCV. After treatment with ampicillin and methylprednisolone, the lesions were resolved.

The patient on admission complained of oedema of the lower extremities and urinary foam. Physical examination was unremarkable except for moderate pitting oedema of the bilateral lower extremities. Laboratory test results are shown in Table 1. Kidney biopsy showed mesangial proliferation (Figure 1), with glomeruli focal segmental hyperplasia and sclerosis (Figure 2), accompanied by crescent formation; immunofluorescence showed IgA granular/mass-like deposition (Figure 3), consistent with the characteristics of IgA nephropathy.

The patient received a diagnosis of LCV and IgAN. After the initial treatment of corticosteroids (1 mg/kg/day of oral prednisone for 1 week, slowly tapered over the following 3 weeks) and other symptomatic treatment, the oedema of the lower extremities and rash resolved.

At 1- and 3-month follow-ups, notable regression was recorded: urine protein was 1+, urine occult blood 1+, blood haemoglobin 95 g/L, no lesions or oedema of the lower extremities.

Table 1. Laboratory test results.

Item	Result	Reference interval
Blood haemoglobin	79 g/L	115–150 g/L
Urine occult blood	1+	–
Urinary protein	0.26 g/24 h	0–0.15 g/24 h
Serum protein electrophoresis		
Albumin	55.30%	55.8–66.1%
β-1 globulin	8.80%	4.7–7.2%
β-2 globulin	6.80%	3.2–6.5%
γ globulin	17%	11.1–18.8%
Immune function		
IgA	4.60 g/L	0.7–3.8 g/L
IgG	12.10 g/L	7–16 g/L
IgM	0.97 g/L	0.4–2.3 g/L
Complement C3	1.07 g/L	0.8–1.85 g/L
Complement C4	0.22 g/L	0.1–0.4 g/L
Infectious index		
Hepatitis B core antibody	6.50 COI	<1.00
Hepatitis B e antibody	0.47 COI	>1.00
Hepatitis B virus DNA	<1.00E+002 IU/ml	<1.00E+002 IU/ml

COI, cut-off index.

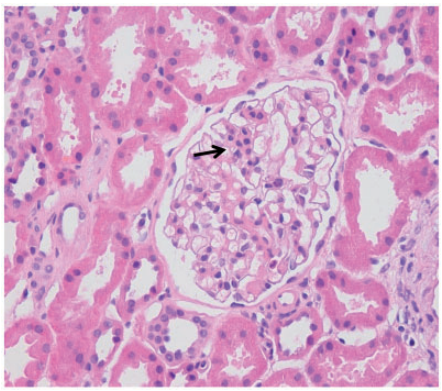

Figure 1. Kidney biopsy showing intermittent moderate proliferation of mesangial cells. The arrow indicates proliferation of mesangial cells (haematoxylin & eosin stain).

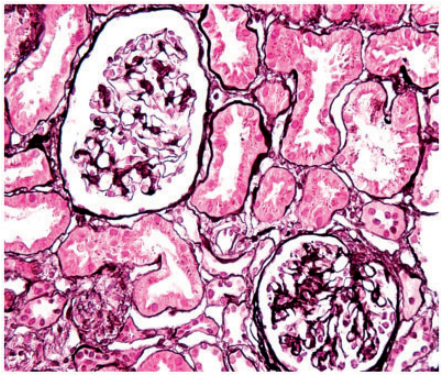

Figure 2. Mesangial proliferation, focal segmental hyperplasia and sclerosis of glomeruli, and immune complex deposits in the mesangial region (periodic acid methenamine silver + Masson stain).

The patient's family gave written consent for the publication of her clinical data. The study was approved by the ethics committee of the First Affiliated Hospital of Xi'an Jiaotong University.

Discussion

The LCV of our patient was initially diagnosed in another hospital and it is unfortunate that we could not obtain a skin biopsy

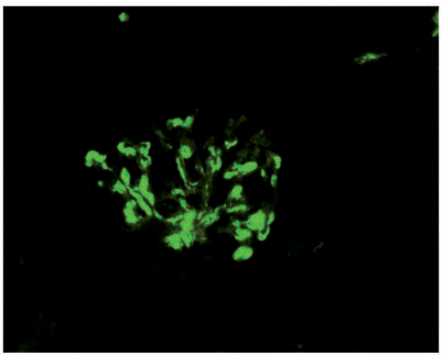

Figure 3. IgA deposits in the mesangial region (immunofluorescence detection).

specimen or report. However, her clinical manifestations, laboratory tests, and response to hormone therapy are all in accordance with the original diagnosis. Further, a diagnosis of Henoch-Schönlein purpura (HSP) was excluded based on the following four points. (1) HSP is more common in children and teenagers. (2) The pathological changes of HSP are mostly located in the superficial dermis and primarily invade the small blood vessels of the dermal papilla, so these lesions are relatively simple and mainly manifest as purpura; the pathological changes in a case of LCV are deeper, such that the entire layer of dermis and subcutaneous tissue can be involved, with a rash that is usually pleomorphic and severe: blood blisters, necrosis and ulcers may occur on purpura and purpura macular papules. (3) HSP is a type of systemic vasculitis that can be eliminated by the absence of joint or abdominal pain. (4) More than half of the HSP patients exhibit haematuria, proteinuria, nephrotic syndrome, and, in some cases, renal failure; thus, HSP is more prone to renal damage than LCV, and the damage is more serious with a poorer prognosis.

Vasculitis diseases often lead to kidney involvement because of the special distribution of renal blood vessels. Systemic lupus

Table 2. Summary of cases.

No	Year	Age	Sex	Possible cause	Skin lesions	Renal injury	Treatment	Outcome
1[4]	1982	45	Male	Ankylosing spondylitis	Purpuric rash on legs.	Serum creatinine: 76 μmol/L, Haematuria: 30 000 red cells/min Albuminuria: 0.75 g/24 h.	NSAID	The skin lesions persisted for a few weeks; haematuria disappeared during the following year.
2[5]	1989	35	Male	Inflammatory bowel disease, ankylosing spondylitis	Purpuric skin lesions on left legs.	Urine analysis: >20 red blood cells, some hyaline casts per high power field. Protein excretion: 0–6 g/24 h.	Bed rest, ibuprofen	The skin lesion gradually healed. Urine analysis intermittently showed red blood cells. Proteinuria did not increase.
3[4]	1991	50	Male	Ankylosing spondylitis	Diffuse purpura over forearms and legs.	24-h proteinuria: 1 g.	Piroxicam	Purpura subsided in two months and he was subsequently lost to follow up.
4[6]	2008	65	Female	Sjögren's Syndrome	Palpable skin rash and bilateral leg oedema.	Creatinine 8.5 mg/dL, urinary protein: 3.6 g/day, microscopic haematuria.	Glucocorticoids, maintenance haemodialysis	Skin lesions dramatically improved, no improvement in renal function.
5[7]	2008	48	Male	Warfarin sodium	Reddish-purple macules and patches in lower extremities.	Trace protein and microscopic haematuria, acute renal failure.	Warfarin was withdrawn	Improved and discharged from hospital, but recrudesced 3 days later and died.
6[8]	2011	65	Female	*Bartonella henselae* infection	Extensive palpable purpuric lesions, necrosis, haemorrhagic blisters on legs.	Acute renal failure, creatinine level: 1.8 mg/dL, and proteinuria increased to 16 g in 24 h, microhaematuria.	Intravenous methylprednisolone	Skin lesions dramatically improved, renal function recovered.
7[9]	2012	45	Female	Antiphospholipid antibody syndrome with tuberculous lymphadenitis	Crusted lesions on the dorsal feet with purulent exudates and interdigital maceration.	Microscopic haematuria, urinary erythrocytes: 90% total dysmorphic cells, 19% acanthocytes; proteinuria: 255 mg/24 h.	Ciprofloxacin, Fluconazole, aspirin and warfarin	Significant improvement of skin lesions. but haematuria and proteinuria remained positive.

erythematosus/HSP-related kidney damage can manifest as IgA nephropathy;[2] antineutrophil cytoplasmic autoantibody-associated vasculitis[3] can combine with IgA nephropathy. As an important type of vasculitis disease, LCV can also cause kidney damage, typically manifesting as microscopic haematuria and proteinuria. Individuals with LCV are characterized by a high propensity for renal dysfunction, including chronic renal failure. Several previous literatures have referred to the pathological changes in LCV-related renal injury, among them only seven cases in six articles included IgA deposits found in renal biopsies of patients with concurrent LCV.[4–9] The clinical characteristics of the cases are summarized in Table 2. Four of the previous cases were caused by rheumatism, two cases were caused by infection, and one was caused by medicine; however, the onset of lesions and renal injury occurred with no obvious cause in our patient. All of the prior patients developed severe lesions on the lower extremities, as well as haematuria and proteinuria, similar to the case in our report. Of the previous seven patients, one improved and was withdrawn from warfarin. This patient was discharged from the hospital but recrudesced 3 days later and died. Of the remaining six patients, four dramatically improved through treatment for primary diseases and two improved through hormone therapy. The present case underwent initial treatment with corticosteroids and had recovered well at follow-up.

For our patient, since the lesions initially occurred with haematuria, renal involvement was indicated; this was further confirmed by the findings of oedema of the lower extremities, urinary foam, moderate anaemia, urine occult blood +, a small amount of urine protein, increased serum IgA, and biopsy supporting the pathological diagnosis of IgAN. IgAN and LCV-induced lesions occurred simultaneously and both showed a remarkable response to the glucocorticoid treatment. We hypothesize that the concurrence of these two conditions is not a matter of coincidence; therefore, we speculate that the IgAN was induced by LCV with the following possible explanation. Serum IgA immune complexes increase in LCV; immune complexes with specific sizes then combine with receptors on the surface of mesangial cells and deposit in the mesangial area; these deposits activate complement, stimulate the proliferation of mesangial cells, promote the secretion of mesangial matrix and cytokines, and eventually cause IgAN. However, the specific mechanisms underlying IgAN induction by LCV remain unclear.

There are no uniform treatments for LCV, but a combination of adrenal cortical hormone and cytotoxic drugs are used empirically. In this patient, the oedema, rash, urine occult blood, and urinary protein were alleviated by comprehensive treatment strategies, including prednisone (20 mg/day), combined with other symptomatic treatment. Thus, renal function should be further characterized when haematuria appears in LCV patients. LCV often includes renal involvement; effective treatment as early as possible can significantly improve the prognosis.

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Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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