Hypocomplementemic urticarial vasculitis syndrome with gastrointestinal vasculitis and crescentic membranoproliferative glomerulonephritis without immune complex deposits

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Received: 18 February 2019 / Accepted: 19 September 2019 / Published online: 4 October 2019
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Abstract

Hypocomplementemic urticarial vasculitis syndrome (HUVS) is a small vessel vasculitis characterized by hypocomplementemia and urticaria-like exanthema. Some cases also display abdominal pain and membranoproliferative glomerulonephritis (MPGN) with immune complex deposits. We treated a case of HUVS with biopsy-proven gastrointestinal vasculitis and atypical histological findings in a kidney biopsy. The 36-year-old Japanese man, who was previously diagnosed with diffuse panbronchiolitis, visited our hospital due to transient urticaria-like exanthema and rapid deterioration of kidney function. On admission, the skin lesion was found to be only pigmentation, showing no vasculitis by skin biopsy. In laboratory findings, renal dysfunction with hematuria and proteinuria and hypocomplementemia were observed. Gastrointestinal vasculitis was proven by endoscopy and biopsy of the mucosa. Kidney biopsy revealed MPGN with crescents. No immune complex deposits were observed by immunofluorescence or electron microscopy. Additional examination revealed high titers of anti-C1q antibody. The patient was diagnosed with HUVS and treated with corticosteroids and plasma exchange. Although renal function and gastrointestinal vasculitis partially improved, infectious pneumonia frequently recurred. His renal dysfunction began to progress again and reached end-stage kidney disease. This is the first case of HUVS with biopsy-proven gastrointestinal vasculitis and MPGN without immune complex deposits. Notably, in some case of HUVS, anti-C1q antibody may activate the alternative complement pathway without immune complex deposits, resulting in renal injury.

Keywords Alternative complement pathway · Anti-C1q antibody · Kidney biopsy · Gastrointestinal endoscopy · Urticaria-like exanthema

Introduction

Hypocomplementemic urticarial vasculitis syndrome (HUVS) is a small vessel vasculitis characterized by hypocomplementemia and urticaria-like exanthema [1]. Two major criteria and at least 2 minor criteria are required for confirmation of the HUVS diagnosis [2]. Major criteria are hypocomplementemia and urticaria-like exanthema. Minor criteria include leukocytoclastic vasculitis, arthralgia or arthritis, ocular inflammation, glomerulonephritis, abdominal pain, and anti-C1q antibody positivity. Abdominal pain as a minor criterion may be accompanied by nausea, vomiting, and diarrhea [3]. This suggests that HUVS can be responsible for gastrointestinal inflammation, but neither endoscopic nor histological findings of gastrointestinal lesions in HUVS have been reported. Renal involvement occurs in 14–50% of HUVS patients [4, 5]. Renal disease in HUVS is often mild,

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although dialysis may be required in severe cases. Particularly, if kidney biopsy shows crescentic glomerulonephritis, renal failure tends to rapidly progress to end-stage kidney disease. In all previous case reports, immune complex deposits were observed in glomerulonephritis. Cutaneous lesions in HUVS are caused by leukocytoclastic vasculitis in the dermal layer, and skin biopsy is, therefore, useful to diagnose HUVS. However, it is often difficult to prove vasculitis in skin because skin lesions can resolve rapidly. Although elevation of serum anti-C1q antibody is one of the minor criteria, it is difficult to measure because currently only specific research institutions can measure it. Herein, we report the first case of HUVS with vasculitis of gastric mucosal epithelium proven by upper gastrointestinal endoscopy, and with crescentic MPGN without immune complex deposits by immunofluorescence and electron microscopy.

Case report

A 36-year-old Japanese man visited our hospital because of rapid deterioration of his kidney function. When he had been diagnosed with diffuse panbronchiolitis at another hospital 2 years previously, urticaria-like exanthema had transiently occurred on his lower legs. At the time, his serum creatinine level elevated to 1.7 mg/dL and urinalysis had demonstrated proteinuria and microscopic hematuria. Kidney biopsy in the previous biopsy had shown mesangial proliferative glomerulonephritis without deposition of immunoglobulin and complement. His renal dysfunction had been progressed after that and he was, therefore, admitted to our hospital.

Although he had a history of diffuse panbronchiolitis, other symptoms of HUVS such as dyspnea, abdominal pain, visual disorder, and arthralgia were not evident. On admission, his height was 168 cm, body weight 63.3 kg, body temperature 36.6 °C, and blood pressure 138/88 mmHg. Physical examination revealed breath sound, heart sound, abdomen and nervous system were all normal. However, he had bilateral leg edema due to renal failure, and skin pigmentation on his lower legs from resolved urticaria-like exanthema (Fig. 1). Urinalysis revealed 3+ occult blood and 2+ proteinuria. Urinary protein excretion was 3.7 g/g·Cr. A full blood examination showed white blood cells 6540/ μ L, red blood cells $421 \times 10^4/\mu$ L, hemoglobin 11.6 g/dL, hematocrit 37.3%, and platelets $40.3 \times 10^4/\mu$ L. Upon visual examination, neither atypical leukocytes nor fragmentation of red blood cells were observed. Serum biochemical analyses revealed total protein 7.2 g/dL, serum albumin 3.2 g/dL, blood urea nitrogen 47 mg/dL, serum creatinine 3.37 mg/dL (estimated glomerular filtration rate 18 mL/min/1.73 m²), sodium 138 mmol/L, potassium 4.5 mmol/L, chloride 104 mmol/L, calcium 8.6 mg/dL, phosphate 4.8 mg/dL, and C-reactive protein 0.57 mg/dL. Anti-double-stranded DNA

Fig. 1 Pigmentation from resolved urticaria-like exanthema on the lower legs. Skin pigmentation on the lower legs was evident, although a skin biopsy from this area showed no vasculitis findings

antibody increased up to 16.2 IU/mL (normal < 10 IU/mL), but decreased to within the normal range upon re-examination. Antinuclear antibody, anti-U1-ribonucleoprotein antibody, myeloperoxidase anti-neutrophil cytoplasmic antibody (ANCA), proteinase-3 ANCA, anti-glomerular basement membrane antibody, anti-Sjögren syndrome-related antigen (SS)-A antibody, anti-SS-B antibody, and cryoglobulin were all negative. Hepatitis B virus surface antigen, anti-hepatitis C virus antibody, anti-human T-lymphotropic virus 1 antibody, and tuberculosis by the T-SPOT.TB assay[®] were also all negative. Serum levels of C3, C4, and total serum hemolytic activity (CH50) were 20 mg/dL (normal 71–135 mg/dL), 24 mg/dL (normal 11–34 mg/dL), and 25.1 U/mL (normal 31.6–57.6 U/mL), respectively. The serum level of C1q was 9.6 mg/dL (normal 8.8–15.3 mg/dL). His circulating immunocomplexes (C1q solid phase assay) were over 50 μ g/mL (normal < 3.0 μ g/mL), and the result could be caused by serum anti-C1q antibody. His circulating immunocomplexes by another assay (monoclonal rheumatoid factor assay) revealed 3.5 μ g/mL (normal < 4.2 μ g/mL). We measured anti-C1q antibody concentration by enzyme-linked immunosorbent assay (ELISA), and his serum anti-C1q antibody level was over 500 (51,965 U/mL for reference purpose only, normal < 10 U/mL). Computed tomography scanning revealed diffuse panbronchiolitis, but no other abnormal findings in the abdomen. Ultrasonography showed normal size of bilateral kidneys (right 12.0 $\times$ 3.7 cm and left 10.8 $\times$ 4.4 cm). Skin biopsy of the area of pigmentation on the lower legs was performed but could not prove leukocytoclastic vasculitis. Esophagogastroduodenoscopy showed

granular mucosa with focal erythema at the greater curvature of the stomach (Fig. 2a). Histopathological examination demonstrated neutrophilic infiltration of gastric mucosa and blood vessel walls (Fig. 2b). We tried to detect C1q in the vessel wall of gastric biopsy by immunohistochemistry, but

Fig. 2 Esophagogastroduodenoscopy findings. **a** Granular mucosa at greater curvature of the stomach before corticosteroid therapy. **b** Biopsy-proven vasculitis with neutrophil infiltration before corticosteroid therapy. Hematoxylin and eosin stain, $\times 200$ magnification. **c** C1q could not be detected in the gastric mucosa by immunohistochemistry, $\times 200$ magnification. **d** The granular mucosal lesion was improved after corticosteroid therapy

could not do (Fig. 2c). A percutaneous kidney biopsy was performed on the 13th day after admission to determine the cause of urinary abnormality and kidney dysfunction. Light microscope observation revealed global glomerulosclerosis in 22 of 49 glomeruli, with moderate interstitial fibrosis and severe inflammation (Fig. 3a). Twenty-seven non-sclerotic glomeruli showed uniform proliferative changes: moderate to severe mesangial proliferation, mesangial matrix increase, and mild to moderate endocapillary hypercellularity. In 19 glomeruli, cellular to fibrocellular crescent formation was observed (Fig. 3b). Double contours of the glomerular capillaries were also observed (Fig. 3c). Vascular lesion was not observed in kidney artery (Fig. 3d). Immunofluorescence studies revealed IgG (–), IgA (–), IgM ($\pm$), C3 (1+), C1q (1+) and fibrinogen ($\pm$) in the glomerular mesangium and the capillary wall (Fig. 3e–f). Ultrastructural examination showed focal foot process effacement of the glomerular epithelial cells and mesangial interposition but did not show electron dense deposits (Fig. 3g). These findings suggested membranoproliferative glomerulonephritis (MPGN) with prominent crescents. Considering these findings, we diagnosed the patient with HUVS.

Three daily doses of intravenous methylprednisolone (1000 mg each) were administered, followed by oral prednisolone (0.6 mg/kg/day). His serum creatinine declined from 5.6 to 2.2 mg/dL, and urine protein–creatinine ratio decreased to 1.2 g/g Cr. The granulation of the gastric mucosa evident by gastrointestinal endoscopy disappeared (Fig. 2d). After 22 days of steroid treatment, the patient developed bacterial pneumonia; therefore, we administered

Fig. 3 Kidney biopsy. **a** Kidney tissue showing moderate interstitial fibrosis and severe inflammation. Periodic acid Schiff stain, $\times 100$ magnification. **b** Glomerulus showing mesangial proliferation and endocapillary hypercellularity with cellular crescents. Periodic acid Schiff stain, $\times 400$ magnification. **c** Glomerular proliferative lesion and double contour of glomerular capillaries are observed. Periodic acid silver methenamine stain, $\times 400$ magnification. The double contour is shown at higher magnification. **d** Vascular lesion was not

observed in kidney artery, Masson trichrome stain, $\times 400$ magnification. **e** Glomerular depositions of C3 (1+) are observed in the mesangial area and capillary loop by immunofluorescence staining. **f** Glomerular depositions of C1q (1+) are observed in the mesangial area and capillary loop by immunofluorescence staining. **g** Electron microscopic reveals focal foot process effacement of the glomerular epithelial cells and mesangial interposition (arrow heads), but not electron dense deposits

antibiotics and rapidly reduced the level of corticosteroid. Hypocomplementemia was prolonged and high serum levels of anti-C1q antibody remained, resulting in progressive renal dysfunction. We tried plasma exchange and his serum anti-C1q antibody was temporally decreased immediately after apheresis (7,449 U/mL for reference purpose only), but promptly rose on the next day (100,257 U/mL for reference purpose only). We had to cease plasma exchange and were unable to add immunosuppressants due to the recurrent pneumonia. After 15 months of beginning corticosteroid treatment, the patient reached end-stage kidney disease (Fig. 4). Although he had no vasculitis symptoms for 3 years after initiation of hemodialysis, his serum level of anti-C1q antibody had remained high (96,700 U/mL for reference purpose only).

Discussion

Here, we report the case of a patient diagnosed with HUVS accompanied by endoscopic biopsy-proven vasculitis of the gastric mucosa and crescentic MPGN without immune complex deposits by electron microscopy. We achieved a partial therapeutic effect and gastric vasculitis was ameliorated by corticosteroid and plasma exchange treatment. However, we were not able to use more intensive immunosuppressive therapy because of recurrent pneumonia, and the patient progressed to end-stage kidney disease.

This is the first case reported of biopsy-proven gastric mucosal vasculitis associated with HUVS. Although the

criteria for HUVS include abdominal pain, little has been reported on gastrointestinal vasculitis in HUVS. Although the patient had never complained of abdominal pain, the gastrointestinal endoscopic and biopsy findings suggested the vasculitis of HUVS. When the patient was admitted in our hospital, his skin lesion was only pigmentation without vasculitis proven by biopsy despite the evident vasculitis in gastric mucosa. His urticaria-like exanthema appeared and disappeared repeatedly, so it was difficult to catch up his skin vasculitis when the urticaria-like lesion vanished. Even after urticaria-like exanthema has resolved, endoscopic biopsy of the gastrointestinal mucosa may also be useful for diagnosing HUVS. Moreover, endoscopic findings might better indicate the activity of this disease because they were improved after corticosteroid therapy in this case.

We tried to detect C1q in the vessel wall of gastric biopsy because kidney biopsy showed glomerular C1q deposits by immunofluorescence. Unfortunately, we could not prove the C1q deposition in the vessel wall of the gastric mucosa. We think that the sliced sample might not include vasculitis lesion or the protocol of immunohistochemistry experiment could not proper for paraffin-embedded sample of the stomach.

Renal involvement occurs in 14–50% of HUVS patients [4, 5]. Glomerular lesions in HUVS are variable and include MPGN, mesangial proliferative glomerulonephritis, and membranous nephropathy [6]. Anti-C1q antibodies form antigen–antibody complexes in the blood and are deposited in the vessel walls. The complexes activate complement through the classical pathway which induces

Fig. 4 Clinical course. *mPSL* methylprednisolone, *PSL* prednisolone, *CFPM* cefepime, *LVFX* levofloxacin, *CAZ* ceftazidime, *PE* plasma exchange, *HD* hemodialysis, *Cr* serum creatinine, *Up/Ucr* urinary protein to urinary creatinine ratio

leukocytoclastic vasculitis in a variety of organs [7]. Immune complex deposition in the glomerular endothelium has been reported previously in HUVS with MPGN cases [8–10]. However, our case did not have subendothelial electron dense deposits by electron microscopy and had normal serum C1q level, despite prominent elevation of anti-C1q antibody and decreased serum complement. These findings suggest that not immune complex but activated complement might injure glomeruli and cause MPGN. Our case displayed normal plasma C4 levels and low plasma C3 levels, suggesting activation of the alternative pathway. Renal diseases induced by complement activated through the alternative pathway, such as C3 glomerulopathy and endothelium injury in atypical hemolytic-uremic syndrome, also show MPGN-like glomerular lesion, resembling our case [11]. However, in our case, neither fragmentation of red blood cells, thrombocytopenia, histological findings of endothelial injury, nor C3 glomerular deposition were observed. Thus, it seems to be problematic to classify this case into C3 glomerulopathy or atypical hemolytic-uremic syndrome. C3 glomerulopathy associated with monoclonal gammopathy has been reported and the overproduction of immunoglobulins could activate the alternative pathway [12]. Thus, in our case, overproduction of anti-C1q antibody might cause the activation of alternative pathway. From the above reasons, the pathology of HUVS may be associated with dysfunction of the alternative pathway of complement. Therefore, more cases are required to confirm the etiology of glomerulonephritis without immunocomplexes in HUVS.

In general, renal dysfunction in HUVS is often mild, although cases demonstrating MPGN with crescents are progressive. Some of these cases were successfully treated with corticosteroids and cyclophosphamide followed by mycophenolate mofetil [13]. Notably, in another report, a patient treated with intravenous methylprednisolone, cyclophosphamide, and plasmapheresis was transferred to the intensive care unit with severe gram-negative sepsis. Cyclophosphamide and plasmapheresis therapies for the patient were discontinued and maintenance hemodialysis therapy was initiated [10]. We were also unable to use immunosuppressants due to recurrent pneumonia and our patient's renal dysfunction progressed to end-stage kidney disease.

Plasma anti-C1q antibody level is very useful for the diagnosis of HUVS [4], especially when skin biopsy has no evidence of vasculitis as in this case. Furthermore, the anti-C1q antibody level is also useful for estimating the activity of the vasculitis. This case maintained high levels of anti-C1q antibody despite the corticosteroid and plasma exchange therapies, then progressed to end-stage kidney disease. There have been no reports on the level of anti-C1q antibody in HUVS patients treated with dialysis. The present case had continuously high levels of anti-C1q antibody even 3 years after the initiation of hemodialysis. We would,

therefore, like to follow his plasma C1q antibody level and evaluate whether he has any vasculitis symptoms except for renal disease such as exanthema and gastrointestinal lesions. Especially, we should prove the vasculitis in the skin by biopsy because we have not done yet. The problem is that plasma anti-C1q antibody level can only be measured by particular research institutions. We measured it ourselves using a commercial ELISA kit (ORGENTEC, Mainz, Germany). Therefore, there is an urgent need to establish a standardized clinical assay for the measurement of anti-C1q antibody concentration.

HUVS is sometimes accompanied by chronic obstructive pulmonary disease (COPD) [14, 15]. However, diffuse panbronchiolitis as a HUVS pulmonary involvement has not been reported. The autopsy of a patient with HUVS without pulmonary disease demonstrated leukocytoclastic vasculitis in alveolar wall arterioles [16]. Therefore, HUVS with pulmonary lesions is not necessary for COPD. We could not confirm whether the diffuse panbronchiolitis in our patient was caused by HUVS as we did not perform a lung biopsy. Notably, corticosteroid and plasma exchange therapies did not improve his pulmonary symptoms but rather resulted in recurrent pneumonia.

Corticosteroids, immunosuppressants such as azathioprine, cyclophosphamide, cyclosporine, mycophenolate mofetil and methotrexate, dapsone [17], intravenous immunoglobulin therapy [18], and plasma exchange [10] have been trialed for treating HUVS; however, the best treatment modality for HUVS has yet to be defined. Notably, recurrent HUVS after kidney transplantation resulting in a poor prognosis has also been reported [19], highlighting the need for improved treatment options. Recently, rituximab has shown greater effectiveness than other immunosuppressants [5]. Similarly, a case of HUVS successfully treated with omalizumab has also been reported [20]. As these above treatments are related to immunosuppressive therapies, we were unable to utilize them because of the recurrent pneumonia in our patient.

In summary, we treated a case of HUVS with gastrointestinal vasculitis by endoscopic examination and crescentic MPGN without immune complex deposits by electron microscopy. This case suggests that gastrointestinal endoscopy is a useful tool for the diagnosis of HUVS and that complement activation without immune complexes might be associated with glomerulonephritis in HUVS. Furthermore, measurement of the plasma level of anti-C1q antibody is useful for the diagnosis of HUVS, and we should measure it when we encounter patients with hypocomplementemia and renal dysfunction, even if a skin biopsy lacks evidence of vasculitis.

Acknowledgements We thank Ms. Hideko Noguchi for her excellent technical assistance. We thank Simon Teteris, PhD, from the Edanz

Group (www.edanzediting.com/ac), for editing the English text of a draft of this manuscript.

Compliance with ethical standards

Conflict of interest All the authors have declared that no conflict of interest exists.

Human and animal rights This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Written informed consent was obtained from the patient included in this case study.

References

- McDuffie FC, Sams WM, Maldonado JE, Andreini PH, Conn DL, Samayoa EA. Hypocomplementemia with cutaneous vasculitis and arthritis possible immune complex syndrome. *Mayo Clin Proc.* 1973;48:340–8.
- Schwartz HR, McDuffie FC, Black LF, Schroeter AL, Conn DL. Hypocomplementemic urticarial vasculitis: association with chronic obstructive pulmonary disease. *Mayo Clin Proc.* 1982;57:231–8.
- Sanchez NP, Winkelmann RK, Schroeter AL, Dicken CH. The clinical and histopathologic spectrums of urticarial vasculitis: study of forty cases. *J Am Acad Dermatol.* 1982;7:599–605.
- Wisniewski JJ, Jones SM. Comparison of autoantibodies to the collagen-like region of C1q in hypocomplementemic urticarial vasculitis syndrome and systemic lupus erythematosus. *J Immunol.* 1992;148:1396–403.
- Jachiet M, Flageul B, Deroux A, Le Quellec A, Maurier F, Cordoliani F, et al. The clinical spectrum and therapeutic management of hypocomplementemic urticarial vasculitis: data from a French nationwide study of fifty-seven patients. *Arthritis Rheumatol.* 2015;67:527–34.
- Wisniewski JJ, Baer AN, Christensen J, Cupps TR, Flagg DN, Jones JV, et al. Hypocomplementemic urticarial vasculitis syndrome clinical and serologic findings in 18 patients. *Medicine (Baltimore).* 1995;74:24–41.
- Venzor J, Lee WL, Huston DP. Urticarial vasculitis. *Clin Rev Allergy Immunol.* 2002;23:201–16.
- Cadnapaphornchai MA, Saulsbury FT, Norwood VF. Hypocomplementemic urticarial vasculitis: report of a pediatric case. *Pediatr Nephrol.* 2000;14:328–31.
- Saeki T, Ueno M, Shimada H, Nishi S, Imai N, Miyamura S, et al. Membranoproliferative glomerulonephritis associated with hypocomplementemic urticarial vasculitis after complete remission of membranous nephropathy. *Nephron.* 2001;88:174–7.
- Balsam L, Karim M, Miller F, Rubinstein S. Crescentic glomerulonephritis associated with Hypocomplementemic Urticarial Vasculitis Syndrome. *Am. J. Kidney Dis. National Kidney Foundation, Inc.;* 2008;52:1168–73.
- Servais A, Frémeaux-Bacchi V, Lequintrec M, Salomon R, Blouin J, Knebelmann B, et al. Primary glomerulonephritis with isolated C3 deposits: a new entity which shares common genetic risk factors with haemolytic uraemic syndrome. *J Med Genet.* 2007;44:193–9.
- Ravindran A, Fervenza FC, Smith RJH, Sethi S. C3 glomerulopathy associated with monoclonal Ig is a distinct subtype. *Kidney Int.* 2018;94:178–86.
- Enríquez R, Sirvent AE, Amorós F, Pérez M, Matarredona J, Reyes A. Crescentic membranoproliferative glomerulonephritis and hypocomplementemic urticarial vasculitis. *J Nephrol.* 2005;18:318–22.
- Falk DK. Pulmonary disease in idiopathic urticarial vasculitis. *J Am Acad Dermatol.* 1984;11:346–52.
- Jones MD, Tsou E, Lack E, Cupps TR. Pulmonary disease in systemic urticarial vasculitis: the role of bronchoalveolar lavage. *Am J Med.* 1990;88:431–4.
- Mitsuiki K, Hirakata H, Oochi N, Nagashima A, Onoyama K, Abe M, et al. Nephrotic syndrome due to membranous glomerulopathy in hypocomplementemic urticarial vasculitis syndrome—a case report. *Nihon Jinzo Gakkai Shi.* 1994;36:863–70.
- Fortson JS, Zone JJ, Hammond ME, Groggel GC. Hypocomplementemic urticarial vasculitis syndrome responsive to dapsone. *J Am Acad Dermatol.* 1986;15:1137–42.
- Yamazaki-Nakashimada MA, Duran-McKinster C, Ramirez-Vargas N, Hernandez-Bautista V. Intravenous immunoglobulin therapy for hypocomplementemic urticarial vasculitis associated with systemic lupus erythematosus in a child. *Pediatr Dermatol.* 2009;26:445–7.
- Grimbert P, Schulte K, Buisson C, Desvaux D, Baron C, Pastural M, et al. Renal transplantation in a patient with hypocomplementemic urticarial vasculitis syndrome. *Am J Kidney Dis.* 2001;37:144–8.
- Nucera E, Basta F, Buonomo A, Mezzacappa S, Margiotta DP, Antonelli Incalzi R, et al. A case of hypocomplementemic urticarial vasculitis syndrome successfully treated with omalizumab. *J Invest Allergol Clin Immunol.* 2017;27:382–4.

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