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A Case of Anti-Glomerular Basement Membrane Glomerulonephritis Complicated by Type 1 Diabetes Mellitus, Mimicking Urinary Tract Infection

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Female, 44
Final Diagnosis: Anti-glomerular basement membrane glomerulonephritis
Symptoms: Fever
Medication: —
Clinical Procedure: —
Specialty: Nephrology

Objective: Rare co-existance of disease or pathology

Background: Type 1 diabetes mellitus (DM) tends to complicate other autoimmune diseases. When considering renal dysfunction in patients with DM, diabetic nephropathy is a likely diagnosis. By contrast, anti-glomerular basement membrane (GBM) glomerulonephritis, an autoimmune disease, is one cause of rapidly progressive glomerulonephritis.

Case Report: We report the case of a 44-year-old woman diagnosed with anti-glomerular basement membrane (GBM) glomerulonephritis. The diagnosis was made on the basis of serological test results and pathological findings of a renal biopsy. Five years before admission, she was diagnosed with type 1 DM. At admission, she presented with a fever, chills, nausea, low back pain, and malaise, which were followed by progressive renal dysfunction. The initial presentation mimicked a urinary tract infection, which delayed the correct diagnosis.

Conclusions: Our patient's course strongly suggests that rapidly progressive glomerulonephritis should be considered as an early differential diagnosis in cases of progressive renal dysfunction, especially when accompanied by fever, regardless of the underlying disease.

MeSH Keywords: Anti-Glomerular Basement Membrane Disease • Diabetes Mellitus, Type 1 • Diabetic Nephropathies

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/902590

Background

Type 1 diabetes mellitus (DM) tends to complicate other autoimmune diseases such as thyroid disease and celiac disease [1]. When considering renal dysfunction in patients with DM, diabetic nephropathy is a likely diagnosis. In contrast, fever and lower back pain in middle-aged women readily suggest acute pyelonephritis. Acute pyelonephritis is also complicated with acute renal dysfunction in cases of DM, as well as impaired baseline renal dysfunction [2]. By contrast, anti-glomerular basement membrane (GBM) glomerulonephritis, an autoimmune disease, is one of the causes of rapidly progressive glomerulonephritis, which is often accompanied by gross hematuria, anuria or oliguria, edema, and high blood pressure. Furthermore, systemic symptoms such as fever, malaise, joint pain, and muscle pain also appear in anti-GBM glomerulonephritis [3]. Notably, there has been a prior report on anti-GBM glomerulonephritis complicated by another autoimmune disease, i.e., IgA nephropathy [4]. Here, we report the case of a 44-year-old woman with type 1 DM, who was initially diagnosed with diabetic nephropathy and acute pyelonephritis based on her fever and renal dysfunction. She was later found to have anti-GBM glomerulonephritis.

Case Report

A 44-year-old Japanese woman with type 1 DM was admitted to our hospital, with a 10-day history of malaise and anorexia, a 5-day fever, and 1 day of left low back pain with nausea. Three days prior, at a nearby hospital, a computed tomography (CT) scan showed enlargement of the right kidney and left kidney stones. This led to the diagnosis of acute pyelonephritis and administration of ceftriaxone (CTRX). On the day of admission, she visited our emergency department because of the persistent fever, left low back pain, and exacerbation of nausea. We could not get any information on the results of the initial urine analysis and Gram staining.

Five years prior to this admission, the patient had been diagnosed with type 1 DM, due to weight loss, hemoglobin (Hb) A1c 18.2%, anti-glutamic acid decarboxylase (GAD) antibody positivity, and almost complete absence of endogenous insulin secretion. She was then started on insulin therapy. Diabetic retinopathy and nephropathy had not been observed, nor had hypertension or dyslipidemia. The patient had no family history of DM or kidney disease. One year prior, she had developed obstructive pyelonephritis due to right ureteral stones and had undergone nephrostomy and lithotripsy.

On admission, she appeared weak, but her consciousness was clear. Her body temperature was 37.2°C, pulse was 76 beats per minute, respiration rate was 16 breaths per minute, oxygen saturation of peripheral artery was 99%, and blood pressure was 99/66 mmHg. Physical examination revealed tenderness of the epigastric area and left costovertebral angle, but no other significant findings. Laboratory results were as follows: C-reactive protein (CRP), 23.59 mg/dL; white blood cell count (WBC), 12 900/μL with 89.4% neutrophils; Hb, 11.8 g/dL; platelets, 358 000/μL; alanine aminotransferase (ALT), 9 IU/L; aspartate aminotransferase (AST), 10 IU/L; urea nitrogen (BUN), 31 mg/dL; creatinine (Cre), 2.90 mg/dL; sodium, 132 mmol/L; potassium, 4.7 mmol/L; total protein, 6.7 g/dL; albumin, 2.4 g/dL; bicarbonate ion (HCO_3^-), 22.7 mmol/L; glucose, 261 mg/dL; and HbA1c, 9.2%. Although urine examination showed proteinuria, hematuria, and glycosuria, it did not show nitrite or pyuria. We did not check 24-h urinary protein, but the urine albumin-to-creatinine ratio (UACR) was 1.27 mg/gCr. No significant bacterial growth was found in the blood or urine cultures. Chest radiograph and electrocardiogram showed no abnormal findings. Abdominal and pelvic CT showed bilateral enlargement of the kidneys, which was apparent on the right side, and left renal pelvic calculi. Diffusion-weighted magnetic

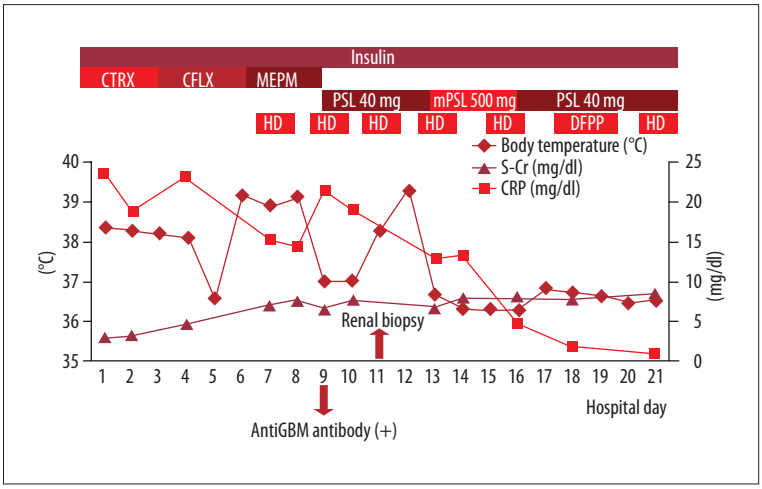

Figure 1. Clinical course of the patient. CTRX – ceftraxione; CFLX – ciprofloxacin; MEPM – meropenem, PSL – prednisolone; mPSL – methylprednisolone; HD – hemodialysis; DFPP – double filtration plasma exchange; GBM – glomerular basement membrane.

Table 1. Laboratory data of the patient.

Variable	Reference range	On hospital day 1	On hospital day 2	On hospital day 4	On hospital day 7	On hospital day 9	On hospital day 13	On hospital day 18
White blood cell count, 10^3 cells/μL	3.3–8.6	12.9	13	12.4	13	15	14.6	12.7
Differential,%								
Neutrophils	38.3–74.7	89.4	90.1	90.3	90.7	89.8	89.4	91.8
Hemoglobin, g/dL	11–14.8	11.8	10.4	10.7	8.9	9.6	8.8	8
Hematocrit,%	34.7–44.4	36.1	31.1	31.8	26.1	28.2	26.7	24
Mean Corpuscular Volume, fl	81–98	91	90	90	89	89	90	87
Platelet count, 103 cells/μL	158–353	358	348	344	336	333	302	283
C-reactive protein, mg/dl	<0.15	23.59	18.82	23.37	15.15	21.48	12.95	1.92
Alanine aminotransferase, U/L	7–28	10	8	7	11	13	19	16
Aspartate aminotransferase, U/L	13–30	9	14	12	18	20	29	36
Urea nitrogen, mg/dL	8–20	31	24	28	42	33	46	83
Creatinine, mg/dl	0.35–0.58	2.9	3.13	4.83	7.15	6.67	6.87	7.88
Sodium, mmol/L	137–144	132	132	125	120	129	133	137
Potassium, mmol/L	3.6–4.8	4.7	3.6	4.6	5.1	4.7	4.3	4.5
Chloride, mmol/L	101–108	97	101	96	92	98	103	105
Albumin, g/dL	4.1–5.1	2.4	1.8	1.5	1.6	1.6	1.9	2.7
Globulin, g/dL.	1.5–3.9	4.3	3.8	3.7	3.5	3.8	3.6	2.4
Immunoglobulin G, mg/dL	870–1700				1146			
Immunoglobulin A, mg/dL	110–410				263			
Immunoglobulin M, mg/dL	46–260				49			
Complement 3, mg/dL	86–160				98			
Complement 4, mg/dL	17–45				21			
Antinuclear antibody	Negative				Negative			
PR3-ANCA, U/mL	<3.5				1.1			
MPO-ANCA, U/mL	<3.5				<1.0			
Anti-GBM antibody, U/mL	<3				36.5			
C-peptide, ng/mL	0.61–2.09				0.15			
Anti-insulin antibody, U/mL	<0.4				<0.4			
Anti-GAD antibody, U/mL	<1.5				8.2			

PR3-ANCA – proteinase 3 anti-neutrophil cytoplasmic antibody; MPO-ANCA – myeloperoxidase anti-neutrophil cytoplasmic antibody; GBM – glomerular basement membrane; GAD – glutamic acid decarboxylase.

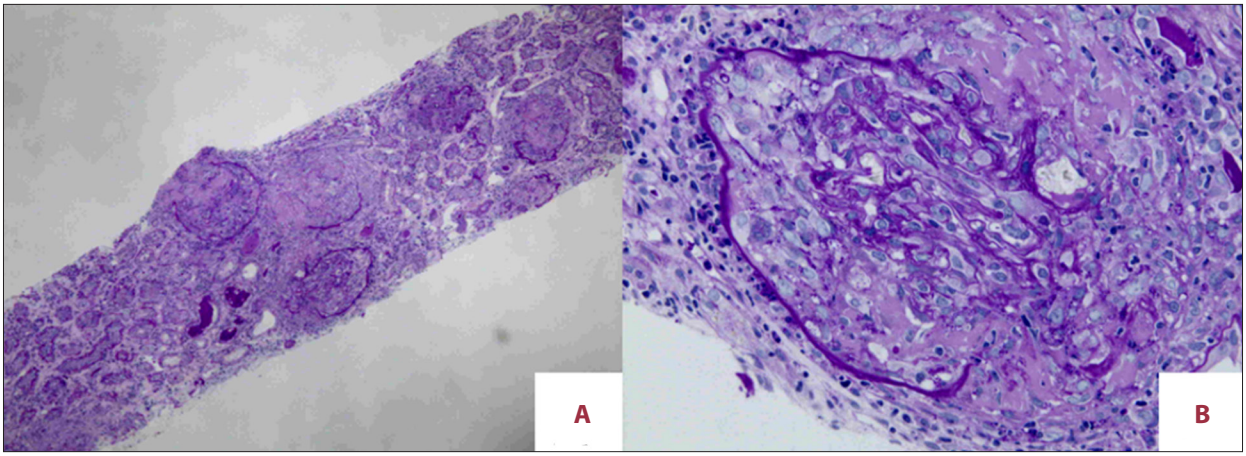

Figure 2. Renal biopsy specimens. (**A, B**) All glomeruli show cellular crescent formation or necrosis, with deposition of fibrin and neutrophil infiltration (Periodic acid-Schiff stain).

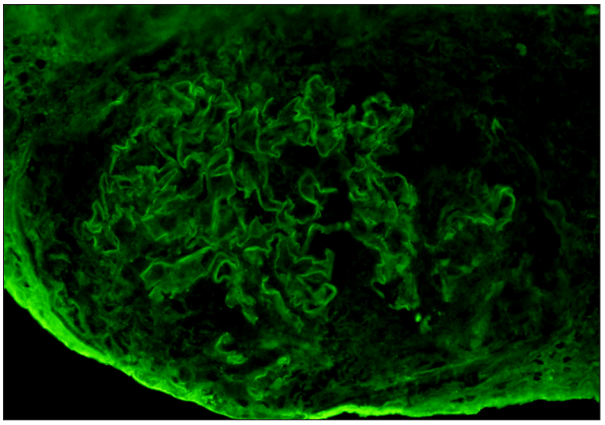

Figure 3. Renal biopsy specimens. The remaining glomerular capillary wall is linearly positive for immunoglobulin G (fluorescent antibody method).

resonance imaging (MRI) showed mild signal elevation of the bilateral whole kidneys, but no obvious abscess formation. Considering the prior use of antibiotics and suspecting acute pyelonephritis, acute focal bacterial nephritis (AFBN), and renal abscess, CTRX was initiated.

Figure 1 and Table 1 show the patient's clinical course and laboratory data. Fever did not abate even after more than 3 days. Furthermore, glycemic control was difficult, so continuous infusion of rapid-acting insulin was maintained. Considering diseases other than infections, tests to screen for nephropathy or nephrotic syndrome other than diabetic nephropathy were ordered. Gradually, urine output reduced and renal dysfunction deteriorated, with BUN 42 mg/dL and Cre 7.15 mg/dL. On day 7, hemodialysis was initiated. The next day, testing for anti-GBM antibody showed a positive result, which led us to suspect anti-GBM glomerulonephritis. Upon administration of prednisolone, after day 9, her body temperature decreased and her clinical condition rapidly improved. Renal biopsy examination revealed a typical linear pattern around the glomerular basement membrane (Figures 2, 3). No nodular lesion, which is typical for diabetic nephropathy, was recognized. The inflammatory reaction also improved, but urine was not produced, so the patient required maintenance hemodialysis. Although double-filtration plasma exchange (DFPP) should have been started as soon as possible after the detection of anti-GBM antibody, in some points, the course and presentation of this case were not characteristic of anti-GBM disease. Therefore, we had to confirm the diagnosis using the results of renal biopsy before deciding on a course of action. Thus, we had to delay the start of treatment. Both methylprednisolone pulse therapy and DFPP were performed, but renal function did not improve. During the hospitalization, a chest CT scan showed no evidence of alveolar hemorrhage.

Discussion

In this case, we found it difficult to distinguish rapidly progressive glomerulonephritis from a complicated urinary tract infection at an early stage. This patient presented with a fever, chills, nausea, low back pain, and malaise, without accurate information about initial bacterial data before starting antibiotics. This led to an initial diagnosis of acute pyelonephritis. At first, the moderate renal dysfunction was considered an exacerbation of diabetic nephropathy, and hematuria was considered due to kidney stones or urinary tract infection. However, the symptoms and signs resulted from the onset of anti-GBM glomerulonephritis. Believing the initial diagnosis by a prior physician and considering the patient's past medical history of complicated urinary tract infection, she had been readily diagnosed with complicated acute pyelonephritis, which led to delays in the proper diagnosis.

In DM patients with renal dysfunction, it is important to consider diseases other than diabetic nephropathy. Diabetic nephropathy results in nephrotic syndrome and renal dysfunction, which may be exacerbated by causes such as infection. However, in patients with DM, there have been many reports of other confounding diseases causing renal dysfunction. For example, membranous glomerulonephritis, IgA nephropathy, membranoproliferative glomerulonephritis, lupus nephritis, and post-infectious glomerulonephritis [5–8] are all possible confounding diseases.

To the best of our knowledge, thus far, only 1 case report of type 1 DM complicated with anti-GBM glomerulonephritis has been reported [9]. In that case, the patient was a 35-year-old man whose pathological findings showed complications of diabetic nephropathy and anti-GBM antibody type nephritis. His clinical course was poor; despite plasmapheresis, corticosteroids, and cyclophosphamide therapy, he began hemodialysis after a follow-up of 3 months. Type 1 DM is an autoantibody disease; therefore, in the present case, anti-GAD antibody was present. Among autoantibody diseases, autoimmune thyroid disease, celiac disease, pernicious anemia, and Addison's disease tend to complicate type 1 DM [10]. Although the most common autoantibody disease co-occurring with type 1 DM is autoimmune thyroid disease, this case suggests that we should also be vigilant for other autoimmune diseases. This case suggests that the approach of considering autoimmune polyglandular syndrome in patients with type 1 DM could be useful for early diagnosis and treatment of some rare autoimmune diseases.

It might have been possible to improve the patient's prognosis through earlier initiation of the treatment. Generally, the prognosis of anti-GBM antibody nephritis is thought to depend on the patient's condition at the time of initial examination. Patients who presented with a creatinine concentration less than 500 mmol/L (5.7 mg/dL) had 100% patient survival and 95% renal survival at 1 year [11]. In the present case, although the patient had been consulted at a relatively early stage, when Cre was 2.9 mg/dL, the start of treatment was delayed by the time needed to establish the diagnosis. Eight days passed before the start of corticosteroids, by which time the Cre concentration had increased to 7.15 mg/dL. This case also highlights the difficulty of early diagnosis in actual clinical practice.

Conclusions

The present case provides evidence that upon observation of progressive renal dysfunction accompanied by fever, regardless of the underlying disease, rapidly progressive glomerulonephritis, including anti-GBM glomerulonephritis, should be considered as an early differential diagnosis.

Acknowledgment

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Conflict of interest

The authors have no conflicts of interest relevant to this article to disclose.

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