Repeated acute kidney injury associated with *Mycobacterium gordonae* infection

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Abstract *Mycobacterium gordonae* is a nontuberculous mycobacterium widely distributed in the environment. Although *M. gordonae* is not usually pathogenic and glomerular lesions due to *M. gordonae* are very rare, infection has been reported in both immunocompromised patients and healthy persons. We report a case of acute kidney injury (AKI) in which *M. gordonae* was ultimately identified as the cause. A 70-year-old man was admitted to our hospital because of fever, polyarthritides, and AKI. He was a hepatitis B virus carrier, suffered from diabetes, and had a past history of erysipelas. No causative bacteria were identified, but coexisting infection was suspected. The patient experienced remission with antibiotic therapy, but the same symptoms recurred eight times. Blood polymerase chain reaction was performed during the 7th recurrence, and *M. gordonae* was detected. Clarithromycin was initiated, but 2 years after initial hospitalization, the patient died due to *M. gordonae* infection. In this case, acute kidney injury was a consequence of infection-related glomerulonephritis due to *M. gordonae*. Mycobacterium is

difficult to detect by routine culture methods; therefore, diagnosis remains challenging.

Keywords Acute kidney injury · *Mycobacterium gordonae* · Polymerase chain reaction (PCR) · Infection-related glomerulonephritis

Introduction

Mycobacterium gordonae is a nontuberculous mycobacterium widely distributed in the environment that is typically not pathogenic. Infection has been reported in immunocompromised patients [1] as well as in otherwise healthy persons [2, 3]. Routine culture methods alone are usually insufficient to diagnose mycobacterial infections. The present patient was ultimately diagnosed with a systemic infection due to *M. gordonae*, detected by blood polymerase chain reaction (PCR). The occurrence of *M. gordonae* with kidney involvement is very rare. We herein report this case and review the literature.

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Case report

A 70-year-old man was admitted to our hospital because of acute onset arthritis, fever, and acute kidney injury (AKI). He was a hepatitis B virus carrier, suffered from diabetes, and had a past history of erysipelas. Examination revealed palpebral edema, temporomandibular joint tenderness with restricted mouth opening, and bilateral symmetrical tenderness accompanied by swelling of the fingers, wrist, elbow, shoulder, knee and ankle joints. Laboratory test results were as follows: white blood cell (WBC) count, $7.85 \times 10^9/L$ (stab 42 %, seg 45 %); blood urea nitrogen

Fig. 1 Initial renal biopsy. Glomeruli showing diffuse hypercellularity and endocapillary proliferative changes with neutrophilic infiltration. Immunofluorescence is positive for C3 and weakly positive for IgG. Electron microscopy shows hump-like electron-dense deposits beneath the epithelium

(BUN), 75 mg/dL (26.78 mmol/L); creatinine (Cr), 5.44 mg/dL (415 µmol/L); and C-reactive protein (CRP), 54.3 mg/dL. Hemoglobin A1c (HbA1c) was 7.9 %, with the patient on diet therapy alone. Serum myeloperoxidase (MPO), proteinase 3 (PR3), antineutrophil cytoplasmic antibody (ANCA) and anti-glomerular basement membrane (GBM) antibody were all negative. Antinuclear antibody (ANA) was positive 1:80, no hypocomplementemia was detected, and no rise in antistreptolysin O (ASLO) titers was seen. Hepatitis B virus (HBV) DNA was positive, but serum HBV DNA was less than 2.1 log copies/ml. Urinalysis revealed hematuria of 5–9 dysmorphic red blood cells (RBCs)/high power field (HPF), proteinuria (0.63 g/gCr), and granular casts. Chest X-ray and whole body computed tomography (CT) revealed no abnormal findings. All blood cultures and cultures of arthrocentesis fluid were negative. Testing for viruses (Epstein-Barr virus, cytomegalovirus, rubeola, rubella, mumps, and parvovirus) showed a previous infection pattern or were negative.

In addition to AKI, the proteinuria reached nephrotic levels (10 g/day) without changing in complement or ASLO titers after admission. Diagnostic renal biopsy revealed endocapillary proliferative glomerulonephritis (Fig. 1). Tubulointerstitial damage was not seen. No causative bacteria were identified, but coexisting infection was suspected. With antibiotic administration for 10 days, the arthritis and fever

Fig. 2 Clinical course after admission. Fever and acute kidney injury were observed eight times over 2 years, and remission was achieved shortly after antibiotic administration, except for the final attack. Horizontal axis shows the number of days after initial hospital admission. (Upper) Left vertical axis: solid line shows changes in creatinine. Right vertical axis: dotted line shows changes in CRP. (Lower) Solid line shows urinary protein. Small triangles show the presence of casts (granular casts or red blood cell casts) in urinary sediment. Conversion factors for units: serum creatinine in mg/dL to µmol/L, $\times 88.4$. CTRX ceftriaxone, MEPM meropenem; LVFX levofloxacin; CAM clarithromycin; CRP C-reactive protein

improved in 3 days, and the creatinine decreased to 1.13 mg/dL (86 µmol/L) and the CRP decreased to 0.69 mg/dL after 10 days.

Subsequently, the patient had recurring fever, polyarthritis, and AKI (oliguria and creatinine elevation with transient proteinuria, granular casts and RBC casts) requiring dialysis a total of eight times over a 2-year period, with the patient achieving remission with antibiotic treatment each time (Fig. 2). During the 7th recurrence, approximately 14 months after initial onset, polymerase chain reaction (PCR) analysis of bacteria from the blood was performed [4, 5]. Broad-range PCR for bacteria was positive. On a more detailed analysis, *M. gordonae* was confirmed from the *16S rRNA* and *hsp65* base sequences. By the PCR method, *M. gordonae* was also detected in a previous kidney sample. The fever, arthritis, and AKI were induced by *M. gordonae* infection. Treatment with clarithromycin was started, and there was no recurrence for 8 months; however, 2 years after the initial hospitalization, the patient experienced septic shock and died. *M. gordonae* was isolated from acid-fast blood cultures collected at that time. The results of genetic analysis (which was specially performed in Tuberculosis Surveillance Center) were consistent for cluster D with the *rpoB* sequence. No focal infection was detected in autopsy.

Discussion

This patient, in whom the etiology of his illness was unable to be identified by routine blood cultures and whose diagnosis had been elusive, was ultimately diagnosed with *M. gordonae* infection by blood PCR. Detection of mycobacterium requires the use of acid-fast cultures as opposed to routine cultures, and suspicion of mycobacterial infection is important. *M. gordonae* is a nontuberculous mycobacterium that exists not only in nature, but also in medical facilities. It has been found in bronchoscopes [6], tap water [7], and refrigerated water [8], all of which are in frequent contact with patients. Therefore, *M. gordonae* is often handled as ordinary contamination. When a nontuberculous mycobacterium is isolated from a clinical specimen, denying the contamination is very important.

For blood PCR performed in the present case, nuclease-free water was used instead of purified water from within the hospital facility. In addition, in a manner similar to blood cultures, contamination was carefully avoided by skin disinfection. The usefulness of PCR has already been reported [9, 10]. In our hospital microbiology laboratory, blood PCR in bacteremic situation has a sensitivity of 85.9–97.5 %, specificity of 84.5–91.7 %, positive predictive value of 47.0–93.2 %, and negative predictive value of 83.0–99.6 % [4, 11]. As a test procedure, blood PCR is at least as effective as blood cultures. Moreover, when this patient had his last “attack,” *M. gordonae* was isolated on blood cultures using a dedicated mycobacterial culture

medium. *M. gordonae* was detected by blood PCR, PCR of kidney sample at first attack, and acid-fast blood culture at last admission. And the genetic analysis revealed the existence of *M. gordonae*. However, his kidney function has deteriorated gradually and the clinical course was very similar in each attack. So *M. gordonae* was thought to be one cause of his repeated fever elevation, arthritis, and AKI.

M. gordonae infection has often been reported in immunocompromised patients, including those with HIV infection, those with malignant tumors, and organ transplant recipients [1, 3]. However, *M. gordonae* infection is also occasionally reported in patients with normal immune function [2]. For cluster D, which was identified on genetic analysis using an *rpoB* sequence, high virulence based on its strong urease activity has also been reported [12]. *M. gordonae* most often causes infection of the lungs, but intraperitoneal, soft tissue, corneal, urinary tract, and disseminated infections have also been described [3]. Kidney involvement is very rare. On admission, infection and hemodynamic change were thought to be the cause of the present patient's AKI; however, diagnostic biopsy was performed due to the appearance of nephrotic-range proteinuria, granular casts, and RBC casts. Renal histopathology revealed endocapillary proliferative glomerulonephritis with a “hump” beneath the epithelium, without lobulation or duplication of glomerular basement membrane. Electron-dense deposits were seen in neither the intramembrane nor the subendothelium. Immunofluorescent testing showed intense, coarsely granular staining for C3 with only minor staining for IgG, which looks like the garland pattern in acute glomerulonephritis (AGN). Nasr et al. reported the following five characteristic criteria of infection-related glomerulonephritis: (1) clinical or laboratory evidence of infection preceding or at the onset of glomerulonephritis; (2) depressed serum complement; (3) endocapillary proliferative and exudative glomerulonephritis; (4) C3-dominant or co-dominant glomerular immunofluorescence staining; and (5) hump-shaped subepithelial deposits on electron microscopy. Of 86 patients with infection-related glomerulonephritis, 37 % fulfilled all five criteria, 41 % fulfilled 4 of the 5 criteria, and 22 % fulfilled 3 of the 5 criteria [13]. In the present patient, as shown in Fig. 2, proteinuria and/or casts (granular casts or red blood cell casts) were detected in each attack. And in pathologically, endocapillary proliferation, C3-dominant deposition, and hump were documented prior to infection. The patient's AKI was probably a result of infection-related glomerulonephritis. In our review of the literature, two cases of glomerular lesions due to *M. gordonae* have been reported. In one patient, glomerulonephritis was suspected based on the presence of occult blood, proteinuria, and granular casts on urinalysis [3]. The other patient was the

only case of *M. gordonae* with nephritis confirmed by renal biopsy, which showed diffuse mild glomerular hypercellularity with subendothelial and mesangial deposits [14].

Definitive treatment for *M. gordonae* infection has not been established. Guidelines proposed by the British Thoracic Society for mycobacterial opportunistic infections in immunosuppressed patients who are HIV-negative recommend a combination of clarithromycin plus rifampicin plus ethambutol [15]. According to an American Thoracic Society/Infectious Diseases Society of America statement [16], ethambutol, rifabutin, clarithromycin, linezolid, and new quinolones are active in vitro as antibiotics against *M. gordonae*, but useful data are limited. Clarithromycin has occasionally been reported in Japan to be effective in lung infections due to *M. gordonae* [17]. Our patient was treated with cephem or carbapenem antibiotics for 2 weeks and achieved remission within a short time. This was compatible with the PCR result that the production of beta-lactamase was not identified. However, he continued to have recurrences, suggesting repeated infection from the external environment, or reactivation from a persistent infection site. One recurrence occurred in hospital, suggesting the latter form. The patient was treated with clarithromycin, and there was no recurrence for 8 months, but he eventually died due to *M. gordonae* infection. Continued treatment consisting of rifampicin or ethambutol should possibly have been considered.

We have presented a case of repeated acute kidney injury that was a consequence of infection-related glomerulonephritis due to *M. gordonae*. *Mycobacterium* is difficult to detect by routine culture methods; therefore, diagnosis remains challenging.

Conflict of interest None of the authors have any conflicts of interest to declare.

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