Glomerulonephritis Caused by CV Catheter-related Blood Stream Infection

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Abstract

A 45-year-old woman under home parenteral nutrition was admitted with recurrent fever and a worsening renal function. A diagnosis of central venous catheter-related blood stream infection (CVCRBSI) was made according to the identification of coagulase-negative Staphylococcus from both the peripheral blood and the removed CV catheter, along with an improvement of the symptoms following the removal of the catheter. Renal impairment with hypocomplementemia was thought to be secondary to the immune complex formation and deposition in the kidneys in response to prolonged bacteremia. This was confirmed by the pathological findings. Clinicians should therefore be aware that glomerulonephritis may be induced by long-term CVCRBSI.

Key words: CV catheter-related blood stream infection (CVCRBSI), glomerulonephritis, coagulase-negative Staphylococcus (CNS)

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Introduction

Since the widespread use of intravenous catheterization in hospitals, catheter-related blood stream infections have been recognized as one of most critical complications. Totally implantable central venous catheters have also been frequently used in many patients who require long-term venous access, including those undergoing total parenteral nutrition or chemotherapy. For many clinicians, however, it is not a well-known fact that long-term central venous catheter-related blood stream infection (CVCRBSI) may cause glomerulonephritis because there have been few reports. We herein report a patient who developed glomerulonephritis in association with totally implantable CVCRBSI.

Case Report

A 45-year-old woman with a four-year history of eating disorders was admitted for the evaluation of a fever of unknown origin and a worsening renal function.

One and a half years prior to this admission, the patient had had a subcutaneous central venous port implanted to initiate home parenteral nutrition because of her insufficient oral intake and repetitive hypoglycemia. Three months after implantation of the catheter, she had had recurrent episodes of low-grade fever. Five months after implantation of the catheter, hematuria and proteinuria were detected accompanied by a worsened serum creatinine level. Although her creatinine level spontaneously recovered, hematuria and intermittent low-grade fever persisted for approximately a year. Two weeks prior to this admission, the patient had had a high-grade fever accompanied by a rapidly worsening renal function.

On examination, her height was 165 cm, weight 32 kg, and BMI 11.8. The patient’s body temperature was 37.1°C, the blood pressure 94/61 mmHg, the pulse 64 beats per minute, and the respiratory rate 16 breaths per minute. Although she was very skinny and her conjunctivae were noted to be slightly pale, the other examination findings were normal. There was no erythema or tenderness on the subclavicular CV port. According to the laboratory data (Table), a urinalysis showed hematuria, proteinuria (1.5 g/day), erythrocytes, and red blood cell casts. The blood biochemi-
Table. Laboratory Data at the Time of Admission.

| Blood count          | Serology       |
|----------------------|----------------|
| White blood cells    | IgG 1264 mg/dL |
| Neutrophils          | IgA 250 mg/dL  |
| Lymphocytes          | IgM 233 mg/dL  |
| Monocytes            | C3 48 mg/dL    |
| Eosinophils          | C4 10 mg/dL    |
| Basophils            | CH50 11 CH50/mL|
| Red blood cells      | CRP 3.26 mg/dL |
| Hemoglobin           | RF 56 IU/mL    |
| Hematocrit           | ANA x40        |
| Platelets            | MPO-ANCA (-)   |
|                      | PR3-ANCA (-)   |
|                      | Cryoglobulin (+) |
| Blood chemistry      | Protein (3+) 1.5 g/day |
| Sodium               | Uriaanalysis   |
| Potassium            | Albumin (3+)   |
| Chloride             | Glucose (-)    |
| Urea nitrogen        | AST 56 IU/L    |
| Total protein        | ALT 58 IU/L    |
| Albumin              | LDH 266 IU/L   |
| AST                   | ALP 316 IU/L   |
| Total bilirubin      | GGT 53 IU/L    |
| HDL-cholesterol      | a1MG 11.4 µg/L |
| LDL-cholesterol      | β2MG 50 µg/L   |

AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, ALP: alkaline phosphatase, GGT: γ-glutamyltransferase, CH50: 50% hemolytic unit of complement, CRP: C-reactive protein, RF: rheumatoid factor, ANA: anti-nuclear antibody, MPO-ANCA: myeloperoxidase-anti-neutrophil cytoplasmic antibody, PR3-ANCA: serineproteinase 3-ANCA, ASO: anti-streptolysin O antibody, HBs-Ag: hepatitis B surface antigen, HCV-Ab: hepatitis C antibody, a1MG: α1-microglobulin β2MG: beta-2-microglobulin, NAG: N-acetylβ-D-glucosaminidase.

cal findings revealed an impaired renal function, decreased levels of total protein and albumin, and hypocomplementemia. Additionally, cryoglobulins were detected and renal ultrasound revealed bilateral enlargement of the kidneys.

The patient was formally an office worker without any past medical history until the eating disorder emerged. There was no relevant family history. She drank 2 glasses of beer 4 times a week and never smoked. She consumed small meals (approximately 200-300 kcal each) 3 times a day without bulimia or vomiting. She was on 500 kcal parenteral nutrition per day without any other medication. She had no known allergies.

After admission, the patient was persistently febrile and complained of a generalized feeling of fatigue. Because methicillin-resistant coagulate-negative *Staphylococcus* (CNS) was detected in two sets of blood cultures, CVCRBSI was highly suspected. Thus, the CV catheter port was removed along with the administration of intravenous vancomycin; subsequently, the fever immediately remitted. CNS was cultured from the removed CV catheter and showed the same drug susceptibility profile as the isolates from the blood cultures. Furthermore, her serum creatinine level and proteinuria gradually improved after the removal of the catheter (Fig. 1).

We suspected immune complex glomerulonephritis induced by CVCRBSI for the following reasons: a recurrent fever emerged after the implantation of the CV catheter, her laboratory findings suggested glomerulonephritis with hypocomplementemia and cryoglobulinemia (which improved after the removal of the CV catheter), and other causes of glomerulonephritis, such as lupus nephritis, were unlikely since she had no suggestive manifestations. To confirm the diagnosis and predict the prognosis, a percutaneous renal needle biopsy was performed. The specimen was prepared for light microscopy, electron microscopy and immunofluorescent studies. On light microscopy (Fig. 2), the glomeruli showed lobulation with a marked mesangial expansion due to the increased proliferation of mesangial cells and many capillary loops were occluded. Crescent formation was not apparent, however, interstitial and tubular fibrosis was partly present. On electron microscopy (Fig. 3), the thickened capillary walls appeared to be composed of dense deposits on the subendothelial aspect of the lamina densa of the basement membrane. The mesangial interposition was observed on some of the thickened capillary walls. Immunofluorescent studies (Fig. 4) showed C1q, C3 and IgM dominant staining with a granular pattern on the capillary loops. These findings were in agreement with a diagnosis of immune complex-mediated membranoproliferative glomerulonephritis (MGN) caused by chronic infection.
Figure 1. Clinical course. Cre: serum creatinine, U-pro: urinary protein, g/g Cre: urinary protein to urinary creatinine ratio, U-O.B: urinary occult blood.

Figure 2. A light micrograph shows increased lobulation, hypercellularity in the mesangium, and thickening of the capillary walls. In addition, interstitial and tubular fibrosis is partly present (A: Hematoxylin and Eosin staining, 200×; B: PAS stain, 400×).

Discussion

The association of glomerulonephritis with infection of CNS was first described by Black and colleagues (1), which has also been referred to as shunt nephritis. Shunt nephritis is an immune complex-mediated nephritis which occurs with a chronically infected ventriculoatrial-shunt (VA shunt) placed for hydrocephalus. Low virulent bacteria, such as CNS, are the responsible pathogens because a prolonged infection is essential for immune complex-mediated nephritis (2, 3). While the overall incidence of VA shunt infection is estimated to be between 3 and 11%, shunt nephritis accounts for only 0.7-2.25% of patients with an infected shunt (4). Although many cases of shunt nephritis were reported from 1970-1990s, its incidence has continued to decline over the last decade because ventriculoperitoneal shunts are now used as an alternative for VA shunts (5).

In contrast, central venous catheters are increasingly used in both inpatient and outpatient settings to provide long-term venous access. Similarly, implantable CV port devices have become widespread and have improved the quality of life in those receiving home parenteral nutrition or regular chemotherapy. CVCRBSI is broadly recognized as one of the most
common complications. It is estimated that approximately 90% of CRBSI occur in association with CV catheters (6).

CVC-RBSI-induced glomerulonephritis, however, is not well-recognized by many clinicians. There have been only eight reported cases, including three published cases, according to a search in the PubMed database prior to December 2014 (7-9). There may have been more cases in which the diagnosis of glomerulonephritis associated with CVC-RBSI was overlooked because it may be difficult to suspect that a low-grade fever in patients with chronic disease is caused by CVC-RBSI. Moreover, most clinicians may hesitate to remove a totally implantable CV port device unlike a non-tunneled CV catheter.

In the present case, we diagnosed the patient with glomerulonephritis caused by CVC-RBSI one and a half years after the implantation of the CV port. In retrospect, the disease onset appeared to be approximately 5 months after the implantation of the CV port because there were some suggestive manifestations, such as hematuria, proteinuria and hypocomplementemia accompanied with two-month episodes of recurrent fever. Considering that the disease onset was relatively early, we speculate that direct contamination of the catheter occurred during the implant operation. Her creatinine level, proteinuria, and hypocomplementemia improved after the removal of the catheter; however, the renal impairment could not be fully recovered, which was likely due to the renal parenchymal scarring consequent to the delayed recognition of CVC-RBSI.

Although the clinical spectrum of glomerulonephritis caused by CVC-RBSI is not well known, it supposedly resembles that of shunt nephritis. According to Haffner and colleagues who reviewed the clinical findings in 148 patients with shunt nephritis, the median time from the last shunt operation to diagnosis of shunt nephritis was 4 years.

Figure 3. An electron micrograph in which thickening of the basement membrane with mesangial interposition (arrows) is shown and electron dense aggregations are shown on the subendothelial aspect of the basement membrane (original magnification, 8,000×).

Figure 4. An immunofluorescent micrograph demonstrating C1q, C3 and IgM dominant staining with a granular pattern on the capillary loops (400×) is shown.
The initial event of infection is the colonization of bacteria, mostly coagulase-negative *Staphylococcus*, on the surface of the catheter. Bacterial growth induces intermittent bacteremia followed by the production of immunoglobulin and circulating immune complexes which are attracted by the kidney. Serologically, the complement level was shown to be decreased and cryoglobulins were detected in many patients. The predominant finding on the renal biopsies was MPGN, and the immunofluorescent studies indicated granular staining of immunoglobulin and complement, in particular IgM, C1q, and C3, on the basement membrane, thus suggesting an activation of the classical complement pathway. The immunofluorescent findings in the present case were consistent with the results of the previously reported case. Moreover, the less intense staining of IgG implied that lupus nephritis was unlikely since glomerular immune deposits attributable to lupus nephritis almost always contain dominant polyclonal IgG (10). The prognosis of renal function is typically favorable provided that the infected shunt is removed within a few weeks after the first signs of infection. Nevertheless, some cases in which the infected shunts or catheters were belatedly removed experienced a rapidly deteriorating course with crescent formation on the glomeruli (4, 7). One of possible reasons for this may be that prolonged bacteremia due to the delayed recognition of CRBSI may lead to excessive immunological responses.

In conclusion, we herein reported a 45-year-old woman with glomerulonephritis caused by CVCRBSI. Clinicians must be aware that CVCRBSI may cause glomerulonephritis, and the early detection of this complication followed by the prompt removal of the infected catheter is indispensable for achieving a favorable renal prognosis.

The authors state that they have no Conflict of Interest (COI).

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