Infective Endocarditis-induced Crescentic Glomerulonephritis Dramatically Improved after Removal of Vegetations and Valve Replacement

Min Yang, Guo-Qin Wang, Yi-Pu Chen, Hong Cheng

Division of Nephrology, Beijing Anzhen Hospital, Capital Medical University, Beijing 100029, China

Key words: Infective Endocarditis; Crescentic Glomerulonephritis; Heart Valve Replacement Surgery

Infective endocarditis (IE) is associated with poor prognosis and higher mortality. IE-induced glomerulonephritis, especially crescentic glomerulonephritis (IE-CGN) with renal dysfunction, is an independent risk factor for mortality.[1] For the treatment of IE-CGN, many therapeutic strategies including antibiotics alone, antibiotics combined with corticosteroid, immunosuppressive agents, plasmapheresis, or cardiac surgery have been applied and obtained various results.[2] Here, we reported a case of CGN with progressive renal failure secondary to IE in which the renal function was dramatically improved by the treatment of surgical valve replacement and antibiotics.

A 68-year-old woman was admitted to the Beijing Anzhen Hospital on July 28, 2011 with lower extremity edema and pink urine over 1 month. Four months ago, she had a fever about 38°C about 2 weeks, and then her body temperature gradually came back to normal after antibiotics therapy. She has been diagnosed having "rheumatic heart disease with mitral regurgitation" about 50 years, but her heart function was relatively good. On physical examination, her temperature was 36.8°C, blood pressure was 110/70 mmHg, and pulse rate was 80 beats/min. A Grade IV/VI systolic murmur at the cardiac apex with radiation to left armpit, a Grade IV/VI systolic murmur in the second right intercostal space with radiation to carotid artery, and a diastolic murmur in the third left intercostal space was heard. The patient had clubbed fingers.

Laboratory tests showed that the white cell count (WBC) count was 11,330 /μl with 85% neutrophils, and the hemoglobin level was 81 g/L in the peripheral blood. Urinalysis found >100 red blood cells (RBCs)/hpf and 15–25 WBCs/hpf. Urinary protein excretion was 2.0 g/d. The serum creatinine level was 263 μmol/L, which was 62 μmol/L one month ago. Urine osmolality after 12 hours of water deprivation was 275 mOsm/kg·H_2O. Serum IgG level was 27.4 g/L, IgM 3.2 g/L, C3 0.27 g/L. Serum ASO level was 88 U. RF was negative. Erythrocyte sedimentation rate was 32 mm/h. Blood culture of 3 times showed no bacterial growth. Echocardiogram revealed two very large vegetations (both 16 mm) on aortic valve and two small vegetations (both 8.9 mm) on mitral valve, with moderate mitral regurgitation, moderate aortic stenosis, and regurgitation [Figure 1]. The vegetations on aortic valve moved back and forth between aorta and left ventricle accompanied heartbeat. Hence, infection endocarditis associated with renal lesion was diagnosed. Since the blood culture was negative, according to the literature,[3] it maybe culture-negative endocarditis.

On hospital day 6, the patient's serum creatinine level was increased to 365.4 μmol/L. In order to understand the nature of renal lesion, thereby more accurately evaluate the possible risks of deterioration of renal function after cardiac surgery, a renal biopsy was performed. Immunofluorescent examination showed IgM (3+), C3 (3+) and C1q (3+) deposition in the mesangial area and peripheral capillary wall. Under light microscope, the specimen contained 18 glomeruli, in which there were 11 glomeruli with large cellular crescents, one with large fibrocellular crescent, three with small cellular crescents, and two with global sclerosis. Fibrin deposits were found in some large cellular crescents. Focal interstitial infiltration of mononuclear cells was observed. Hence, the renal pathological diagnosis was crescent glomerulonephritis type 2 [Figure 2a and 2b].

Treatment with intravenous piperacillin sulbactam and linezolid was initiated soon after admission. According to the guidelines for treatment of IE[4] the patient had

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.150118

Address for correspondence: Dr. Hong Cheng, Division of Nephrology, Beijing Anzhen Hospital, Capital Medical University, Beijing 100029, China
E-Mail: chenghong65@medmail.com.cn

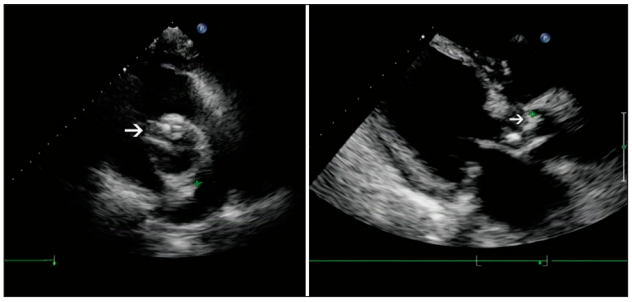

Figure 1: Vegetation on aortic valve by echocardiography. Arrow denotes the vegetation.

definite indicators for cardiac surgery, so she received valve replacement operation of aortic valve and mitral valve on August 10, 2011. Pathological examination showed mitral and aortic valvular fibrosis with hyaline degeneration and calcification, multifocal fibrinoid necrosis, bacterial colonies, tissue infiltration of many neutrophils, lymphocytes, and plasma cells as well as granulation tissue formation [Figure 2c and 2d]. The pathological diagnosis was IE, which further confirmed the clinical diagnosis, but the bacterial culture of vegetations was still negative.

After cardiac surgery, the patient continuously accepted antibacterial therapy with meropenem and vancomycin hydrochloride for 3 weeks and continuous renal replacement treatment for 1 week. To our surprise, the patient's renal function was dramatically improved and discharged from hospital on September 10, 2011.

At discharge, her urinalysis showed 10–20 RBCs/hpf and 0–1 WBCs/hpf. Urinary protein excretion was 1.59 g/d. The serum creatinine level was 87 μmol/L and the urine osmolality after 12 hours of water deprivation was 488 mOsm/kg·H_2O.

Six months later, the patient was readmitted to our hospital for a second renal biopsy to assess the recovery state of renal tissue. Pathological examination found 34 glomeruli in the specimen. There were 11 glomeruli with large fibrous crescent, three with large fibrocellular crescent and six with global sclerosis. The rest glomeruli only displayed mild mesangial cell proliferation and matrix increase. However, multifocal mononuclear cell infiltration still existed in the interstitium besides focal interstitial fibrosis and tubular atrophy. Because of the active inflammatory reaction in interstitium, the patient was given oral prednisone and cyclophosphamide for 3 months.

The patient has been followed-up by us for 2 years. At present, her general state and heart function were quite good. Urinalysis showed trace or negative protein, 0–3 or 3–8 RBCs/hpf and 0–1 WBCs/hpf. The serum creatinine levels fluctuated in 113–127 μmol/L and the urine osmolality after 12 hours of water deprivation was in the range of 316–430 mOsm/kg·H_2O.

Up to now, effective therapeutic strategies for IE-CGN have not been established.[2,5] IE-CGN is considered as an immune complex-mediated disease, so theoretically it should

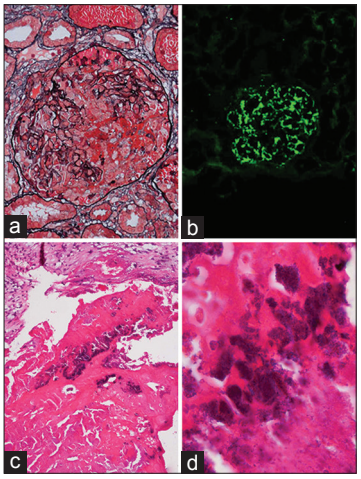

Figure 2: Pathological findings of renal tissue and infected vegetations on aortic valve. (a) Large cellular crescent with fibrin deposition in glomerulus (PASM and Masson staining, ×400); (b) IgM deposition in mesangial area and peripheral capillary wall (Immunofluorescence, ×200); (c and d) Many scattered colonies of bacteria which were stained blue, can be observed in the vegetation (H and E staining, [c] ×100; [d] ×1000).

be reasonable to apply corticosteroid, immunosuppressive agents and/or plasmapheresis treatment in combination with antibiotics.[2] In clinical practice, however, these therapeutic strategies are controversial because of the possible risk of the aggravating the infection responsible for the IE.[2,5]

Another therapeutic choice that might block the pathogenic immune reaction is eradication of immunogen, that is, infection foci. Although there were a few reports in which the resolution of IE-CGN was achieved by antibiotics therapy alone, many reports considered that the antibiotics alone might not be enough for IE-CGN treatment.[2,5] The favorable outcome of our case suggests that the early surgical valve replacement with antibiotics therapy is a satisfactory therapeutic strategy that can eradicate immunogen and therefore induces IE-CGN resolution. In 1996, Gao *et al*.[6] reported a similar case in which clinical resolution of IE-CGN was successfully achieved after valve replacement and antibiotic therapy. To confirm the efficiency of this therapeutic strategy, more clinical observations are necessary for the future.

Second renal biopsy was performed 6 months later. Besides obsolescent glomeruli, there was still active inflammatory reaction in the interstitium. The residual interstitial inflammation is often observed in the recovery process of crescent glomerulonephritis and may exert adverse effects on the disease outcome. Therefore, the patient was given oral prednisone and cyclophosphamide treatment for a short course, which might be helpful in strengthening the previous therapeutic efficacy.

In conclusion, we suggest that patients with rapidly progressive glomerulonephritis associated with IE might be treated with early surgical valve replacement and antibiotics treatment and therefore induce IE-CGN resolution, although in the case of immune-mediated pathogenesis.

Acknowledgment

We acknowledge Dr. Hong-rui Dong and Li-jun Sun by making substantial contributions to staining of the tissue section. Written consent was obtained from the patient for publication of the study in the BMC nephrology.

References

1. Buchholtz K, Larsen CT, Hassager C, Bruun NE. In infectious endocarditis patients mortality is highly related to kidney function at time of diagnosis: a prospective observational cohort study of 231 cases. Eur J Intern Med 2009;20:407-10.
2. Kannan S, Mattoo TK. Diffuse crescentic glomerulonephritis in bacterial endocarditis. Pediatr Nephrol 2001;16:423-8.
3. Naber CK, Erbel R. Infective endocarditis with negative blood cultures. Int J Antimicrob Agents 2007;30 Suppl 1:S32-6.
4. Gould FK, Denning DW, Elliott TS, Foweraker J, Perry JD, Prendergast BD, *et al.* Guidelines for the diagnosis and antibiotic treatment of endocarditis in adults: a report of the Working Party of the British Society for Antimicrobial Chemotherapy. J Antimicrob Chemother 2012;67:269-89.
5. Manzoor K, Khan S, Ahmed E, Akhter F, Mubarak M, Naqvi SA, *et al.* Crescentic glomerulonephritis associated with bacterial endocarditis – Antibiotics alone may be sufficient. A case report. J Pak Med Assoc 2005;55:352-4.
6. Gao GW, Lin SH, Lin YF, Diang LK, Lu KC, Yu FC, *et al.* Infective endocarditis complicated with rapidly progressive glomerulonephritis: a case report. JCMA 1996;57:438-42.

Received: 14-09-2014 **Edited by:** Yi Cui
How to cite this article: Yang M, Wang GQ, Chen YP, Cheng H. Infective Endocarditis-induced Crescentic Glomerulonephritis Dramatically Improved after Removal of Vegetations and Valve Replacement. Chin Med J 2015;128:404-6.

Source of Support: Nil. **Conflict of Interest:** None declared.