A rare case of spontaneous renal cholesterol crystallization embolism

Ling-Yun Chen[1], Yan-Ping Huang[1], Shao-Jun Liu[2], Pei-Jyu Mao[1]

[1]Department of Nephrology, Tongren Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200336, China;
[2]Department of Nephrology, Huashan Hospital, Fudan University, Shanghai 200040, China.

To the Editor: Cholesterol crystal embolism (CCE) is a systemic disease caused by cholesterol crystal embolization leading to the occlusion of small arteries in a variety of organs. It may occur spontaneously, or more often, after intravascular procedures such as coronary angiography and carotid artery stenting, cardiovascular surgery such as coronary artery bypass grafting or aortic aneurysm surgery.[1] The kidneys were previously reported to be the most frequent target organ for CCE, and renal CCE was found during the course of clinical illness in approximately 50% of patients with CCE.[2]

We reported a case of spontaneous renal CCE in a 78-year-old man. Most cases could be linked to signs of peripheral emboli, a precipitating event or histologic confirmation, intravascular procedures, and cardiovascular surgery were precipitating events. In our case, the patient was reportedly diagnosed only when renal biopsy indicated cholesterol clefts without precipitating events. After more than 3 years of treatment, he took a return and showed a better renal function.

This 78-year-old man presented with a spontaneous proteinuria was treated by simple low protein diet at 2 months before admission, resulting in a reduced renal function with serum creatinine of 2.26 mg/dL. He had to be hospitalized for acute renal injury in May 2014. He had a history of diabetes for 10 years with oral agents and hypertension with amlodipine and valsartan for 5 years. He had no signs of blue toes, livedo reticularis, or digital gangrene. He had no precipitating event or histologic confirmation. He had no intravascular procedures or cardiovascular surgery precipitating events. We had no abnormal findings on the physical examination. He had a proteinuria with 0.44 g and reduced renal function with 2.19 mg/dL of serum creatinine accompanied by an increased eosinophilic granulocyte of 8.3%. He had anemia of 103 g/L in hemoglobin. He had normal lipid with triglyceride of 1.06 mmol/L and cholesterol of 3.85 mmol/L. The erythrocyte sedimentation rate (ESR) was 21 mm/h. The anaphylactogen was negative. He had not been found abnormal in echocardiographic measurement. With color Doppler imaging, the arterial plaque was found in his carotid and lower extremity artery. There were no abnormalities in the urography of computed tomography examination. Senile cataract was found by fundus examination.

Since the suspicion of acute kidney injury, the patient was received an examination of kidney biopsy [Figure 1]. About two of the larger arterial lumens were almost completely occluded and needle-like fissures were visible. Immunofluorescence showed that IgM(+) had a small amount of deposition in a few segments of the arteries, and the rest were negative. He was diagnosed with a rare case of spontaneous CCE nephropathy. Then, he was turned to insulin and clonidine 75 μg bid, arotinolol 10 mg bid, benidipine 8 mg qd with his blood sugar, and blood pressure in control. His blood sugar and blood pressure were well controlled (At diagnosis: blood sugar, 8.9 mmol/L; blood pressure 160/95 mm Hg *vs.* Day 135: blood sugar, 5.6 mmol/L; blood pressure 110/70 mm Hg). He also had lipitor 20 mg qn, aiming to stabilize the artery plaque and prevent heart attack, stroke and CCE for carotid plaque and lower extremity arterial plaque. The combined therapy was based on high-quality low-protein diet and ketosteril. Corbrin based on traditional medications was also used by 1.0 tid po for the supportive functions of the kidney. He continued to have follow-up examinations in our out-patient clinic after discharge. However, renal function continued to deteriorate. As shown in Figure 1, the highest value of the serum creatinine was 3.50 mg/dL in Sept. 2014 without any inducement. Then the value of the serum creatinine was returned to normal in the next 3 years. The most recent value of serum creatinine was 0.90 mg/dL in September 2017. Now he has enjoyed a good quality and happy life.

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.1097/CM9.0000000000000078

Ling-Yun Chen is now working at Department of Nephrology, Shanghai Electric Power Hospital.

Correspondence to: Prof. Pei-Jyu Mao, Department of Nephrology, Tongren Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200336, China
E-Mail: pjmaotr@163.com

Chinese Medical Journal 2019;132(3)

Received: 03-12-2018 **Edited by:** Ning-Ning Wang

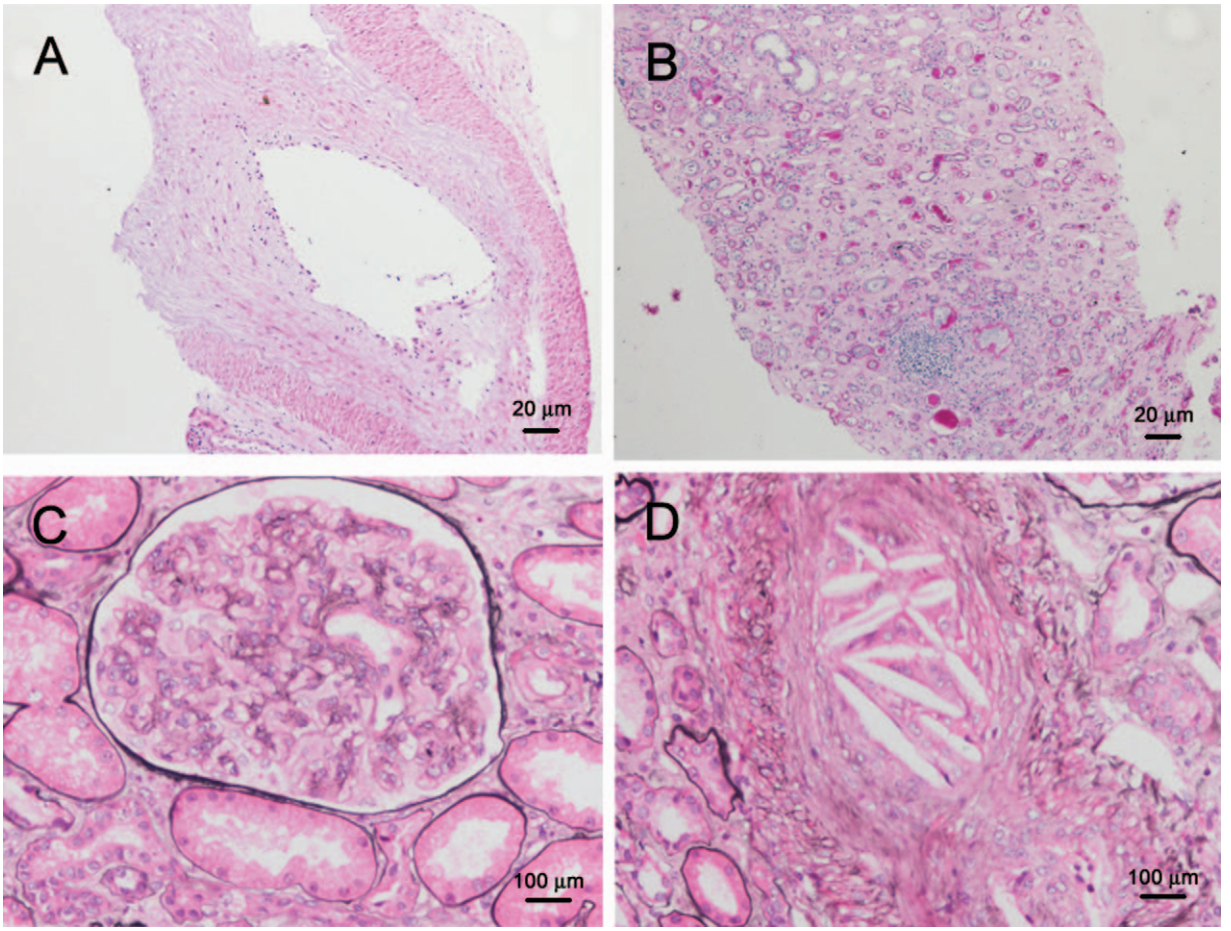

Figure 1: Renal biopsy indicated cholesterol crystallization embolism. (A) Hematoxylin and eosin staining. (B) Periodic acid-Schiff staining. (C and D) Periodic acid-silver methenamine staining. A total of about 7 glomeruli were observed, including 2 glomerular glass-like changes. Other glomerular segments had mild mesangial cell proliferation or slightly increased matrix, and occasionally the capillary wall irregularly thickened. We also observed a small number of renal tubule atrophied, a small amount of inflammatory cell infiltration in the medulla, mild interstitial fibrosis, a number of larger arteries, some thickening arterial intima, and two large arterial lumens which were almost occluded.

Renal CCE was diagnosed according to the following criteria: (1) Acute or subacute renal failure. Serum creatinine elevation of more than 50% after the precipitating event; (2) Symptoms of peripheral emboli such as blue toes, livedo reticularis, and digital gangrene; (3) A precipitating event or histologic diagnosis. Intravascular procedures and cardiovascular surgery were precipitating events.[3] Based on these criteria, a diagnosis of renal CCE could be made even in the absence of histologic confirmation. In addition, the spontaneous form of renal CCE was reportedly diagnosed only in skin, gastrointestinal, or renal biopsy documented cholesterol clefts without precipitating events.[3,4] In this study, the patient presented a spectrum of clinical symptoms, including proteinuria, elevated serum creatinine, rapid ESR, high eosinophil blood counts, and hypocomplementemia. The diagnostic marker of this disease is the histologic detection of intravascular cholesterol crystals in biopsy specimens, whereas symptoms in other organs may be regarded as compensatory ways for the diagnosis for renal CCE.[5,6] As clinical symptoms of the patient in our case was not classical, the patient had a renal biopsy for further diagnosis. He had a renal cholesterol crystallization embolism, as the intravascular cholesterol crystals were found in his kidney. In addition, he had the spontaneous form of renal CCE in view of his medical history.

The onset of renal CCE cannot be precisely diagnosed since renal CCE sometimes has a smoldering course with renal function declining over a long period lasting for several months. CCE frequently results in the deterioration of renal function, which sometimes could lead to end-stage renal failure. There has been no established therapy for CCE except symptomatic and supportive play chemotherapy. At the initiation of chronic kidney disease (CKD) integration therapy, his creatinine significantly decreased to 1.62 mg/dL after 1 year.

The aim of treatment was to prevent the progression of tissue ischemia and further showering of cholesterol crystals or provide supportive care in case of renal failure. The purpose of corticosteroid use was to reduce the reactive inflammatory response along with atheroembolization. However, the effects of steroids remain controversial. Statins may have a beneficial effect in CCE by reducing the cholesterol and anti-inflammation, thus contributing to plaque stabilization and renal regression.[7] Although the patient had no hyperlipidemia, we continued

to provide patient with Statins because of his atherosclerotic plaques. Belenfant *et al*[8] recommended heparin-free dialysis to avoid anticoagulation and thereby prevent further embolization. Surgical therapies, such as endarterectomy, vessel ligation, or bypass, may decrease the probability of further embolism.[9] The recovery rate of renal function has been reported in only 21% to 28% of such cases.[10] Pre-existing CKD is associated with the increased risk of progressing to end stage renal disease (ESRD) in CCE. Age, diabetes, history of heart failure, baseline renal function, time course of decline in renal function, and extra-renal manifestations are found to be the risk factors for both ESRD and death.[3]

Prevention is important for CCE to a larger part because no effective treatment is available at present. Prophylaxis against further episodes of cholesterol embolization is beneficial. However, diagnosis of CCE remains a clinical challenge since its symptoms are non-specific. For the current case, we conclude that CKD integration therapy may have beneficial effect on renal outcome of CCE.

Conflicts of interest

None.

Compliance with ethical standards

All procedures in this study were performed in accordance with ethical standards of our institutional accordance to ethical standard of *Declaration of Helsinki* 1964. Informed consent was obtained from the individual participant included in study (see attached supplementary material).

Author contributions

Chen LY, Huang YP and Mao PJ designed the study and drafted the manuscript. Chen LY, Huang YP and Mao PJ developed a treatment plan for the patient and followed up to conceive the study. Liu SJ performed the renal biopsy. All authors have read and approved the final manuscript.

References

1. Scolari F, Ravani P. Atheroembolic renal disease. Lancet 2010;375:1650–1660. doi: 10.1016/S0140-6736(09)62073-0.
2. Scolari F, Tardanico R, Zani R, Pola A, Viola BF, Movilli E, *et al*. Cholesterol crystal embolism: a recognizable cause of renal disease. Am J Kidney Dis 2000;36:1089–1109.
3. Scolari F, Ravani P, Gaggi R, Santostefano M, Rollino C, Stabellini N, *et al*. The challenge of diagnosing atheroembolic renal disease: clinical features and prognostic factors. Circulation 2007;116:298–304. doi: 10.1161/CIRCULATIONAHA.106.680991.
4. Yang XL, Yu HJ, Zhu HY, Zheng Y, Han QX, Cai GY, *et al*. Potential value of datura stramonium agglutinin-recognized glycopatterns in urinary protein on differential diagnosis of diabetic nephropathy and nondiabetic renal disease. Chin Med J (Engl) 2018;131:180–187. doi: 10.4103/0366-6999.222328.
5. Kronzon I, Saric M. Cholesterol embolization syndrome. Circulation 2010;122:631–641. doi: 10.1161/CIRCULATIONAHA.109.886465.
6. Quinones A, Saric M. The cholesterol emboli syndrome in atherosclerosis. Curr Atheroscler Rep 2013;15:315. doi: 10.1007/s11883-013-0315-y.
7. Abela GS, Vedre A, Janoudi A, Huang R, Durga S, Tamhane U. Effect of statins on cholesterol crystallization and atherosclerotic plaque stabilization. Am J Cardiol 2011;107:1710–1717. doi: 10.1016/j.amjcard.2011.02.336.
8. Belenfant X, Meyrier A, Jacquot C. Supportive treatment improves survival in multivisceral cholesterol crystal embolism. Am J Kidney Dis 1999;33:840–850.
9. Shames ML, Rubin BG, Sanchez LA, Thompson RW, Sicard GA. Treatment of embolizing arterial lesions with endoluminally placed stent grafts. Ann Vasc Surg 2002;16:608–612. doi: 10.1007/s10016-001-0278-2.
10. Theriault J, Agharazzi M, Dumont M, Pichette V, Ouimet D, Leblanc M. Atheroembolic renal failure requiring dialysis: potential for renal recovery? A review of 43 cases. Nephron Clin Pract 2003;94:c11–c18. doi: 10.1159/000070819.

How to cite this article: Chen LY, Huang YP, Liu SJ, Mao PJ. A rare case of spontaneous renal cholesterol crystallization embolism. Chin Med J 2019;132:367–369. doi: 10.1097/CM9.0000000000000078