Idiopathic cholesterol crystal embolism with atheroembolic renal disease and blue toes syndrome: A case report

De-Jin Cheng, Lin Li, Xiang-Yue Zheng, Shui-Fu Tang

Abstract

BACKGROUND
Cholesterol crystal embolization (CCE) is a multisystemic and fatal disease with multiple clinical manifestations; however, there are few cases of idiopathic CCE. Here we report a patient with idiopathic CCE accompanied by atheroembolic renal disease and blue toes who had a relatively good prognosis in the short-term due to early treatment with corticosteroids and statins.

CASE SUMMARY
A 76-year-old man complained of coldness, numbness and purple color change in his left foot for 7 days. He had a feeling of fatigue, constipation, foamy urine, poor appetite and sleep. He had a lacunar infarction for 5 years and hypertension for 9 mo. Laboratory results showed elevated eosinophils, cholesterol, uric acid, serum creatinine, urea and 24-h urine analysis revealed proteinuria. A renal biopsy revealed atheroembolic renal disease. Taken together, these findings strongly supported the diagnosis of idiopathic CCE and atheroembolic renal disease.

CONCLUSION
Atheroembolic renal disease and blue toes syndrome can be caused by idiopathic CCE, and early treatment with corticosteroids is effective but requires further investigation.
**Key Words:** Idiopathic cholesterol crystal embolism; Atheroembolic renal disease; Blue toes syndrome; Corticosteroids; Case report; Prognosis


**Core Tip:** Idiopathic cholesterol crystal embolization can induce atheroembolic renal disease and blue toes syndrome, and the early corticosteroids treatment is effective.

**INTRODUCTION**

Cholesterol crystal embolization (CCE) is caused by diffusion of cholesterol atheroma debris and can be triggered by intraarterial interventions and anticoagulant therapy, leading to both ischemic and inflammatory damage to the target organ[1]. However, there are only a few reports of patients with idiopathic CCE who did not receive medication or arterial intervention[2-3]. As cholesterol atheroma can occlude all types of small arteries, the disease has various clinical manifestations involving organs such as the brain, eye, kidney, gastrointestinal system and skin, which makes CCE a fatal disease with poor prognosis[4]. In a review of 221 cases of histologically proven CCE, the mortality rate was as high as 80%[5]. Here we report a patient with idiopathic CCE accompanied by atheroembolic renal disease and blue toes who had a relatively good prognosis in the short-term due to early treatment with corticosteroids and statins.

**CASE PRESENTATION**

*Chief complaints*

A 76-year-old man complained of coldness, numbness and purple color change (Figure 1A) in his left foot for 7 days. He had a feeling of fatigue, constipation, foamy urine,
poor appetite and sleep, but no fever, headache or abdominal pain. His urine output was normal.

**History of present illness**

A 76-year-old man complained of coldness, numbness and purple color change in his left foot for 7 days. And he came to our hospital for treatments.

**History of past illness**

The patient had a lacunar infarction for five years and took three Fufang Xueshuantong capsules three times daily. He also had hypertension (maximum blood pressure: 189/102 mmHg) for 9 mo and took one tablet of amlodipine, atorvastatin calcium and fosinopril sodium tablets 10 mg once daily. There was no history of surgery.

**Personal and family history**

None

**Physical examination**

Physical examination upon admission showed no abnormalities.

**Laboratory examinations**

Laboratory findings (Table 1) showed elevated eosinophils, triglycerides, serum creatinine and urea. 24-h urine analysis showed increased proteinuria.

**Imaging examinations**

Doppler ultrasonography showed carotid atherosclerosis with carotid plaque formation (Figure 2A) and both kidneys were of normal size; however, kidney parenchymal thickness (approximately 13 mm) was slightly thinner (Figure 2b). Liver, spleen and pancreas were normal. A renal biopsy (Figure 3) showed glomerulus ischemic globular sclerosis in all 41 glomerulus; and mesangial cells and stroma showed slight
hyperplasia in the rest of the glomerulus, one small cell fibrous crescent, and some of the glomerular capillaries were ischemic and wrinkled. With regard to the renal tubules, epithelial cells showed cavitation and granular degeneration, crystal nucleation within some renal tubules, a few renal tubules demonstrated cavity expansion, disappearance of brush border, multifocal and atrophy (shrinkage area of approximately 60%); diffuse and patchy infiltration of the kidney interstitium by lymphocytes, plasma cells and a few eosinophils; small artery wall thickening with a narrow lumen, endometrial hyperplasia, and cholesterol embolism filling several small arteries. Congo and oxidized Congo red were negative. Immunofluorescence showed no deposition of immune complexes.

**FINAL DIAGNOSIS**

The patient was diagnosed with idiopathic cholesterol crystal embolization and atheroembolic renal disease.

**TREATMENT**

He was treated with 30 mg of prednisone acetate tablets once daily during hospitalization and the dosage was gradually tapered after discharge. The patient also received a 20 mg tablet of atorvastatin calcium, 50 mg tablet of clopidogrel bisulfate, 10 mg tablet of fosinopril sodium and 10 mg of amlodipine once a day, respectively.

**OUTCOME AND FOLLOW-UP**

During the 12-mo follow-up period, the color of his left foot gradually returned to normal (Figure 1b). The gradual reduction in prednisone acetate is shown in Figure 4. Following treatment with prednisone, eosinophils and serum creatine gradually decreased after discharge (Figure 4).

**DISCUSSION**
CCE is a multisystemic disease with various clinical manifestations induced by atherosclerotic plaques, and these plaques are composed of platelets, fibrin, necrotic cell debris, and cholesterol crystals (CCs)[6]. Hemodynamic changes, intraplaque hemorrhage, and inflammation, which may occur spontaneously (namely idiopathic CCE) or due to invasive procedures, can induce plaque erosion and rupture that expose the plaque components to the systemic circulation. Initially, CCs only cause ischemic injury; but the subsequent inflammatory reaction aggravates end-organ injury. Endothelial injury, oxidative stress, activation of the renin-angiotensin-aldosterone system (RAAS), leukocyte aggregation, complement activation, and release of leukocyte enzymes are all considered responsible for end-organ injury[7,8]. Approximately 80% of cases of CCE have been reported to be due to anticoagulation therapy and catheter manipulation, and there are few cases of idiopathic CCE[8]. The patient with definite pathological findings in this report had no history of surgery or anticoagulation therapy, which supported the diagnosis of idiopathic CCE. Male and older patients with atherosclerotic cardiovascular risk factors are more susceptible to CCE than other patients, and the overall in-hospital mortality among patients with CCE was 11%,[9]. Older age, hypertension and lacunar infarction in this patient were high risk factors.

With regard to treatment, secondary prevention of cardiovascular disease is of utmost importance in these patients, such as statins, antiplatelet therapy, cessation of smoking, and control of blood pressure, weight, and glycemia. Furthermore, anti-inflammatory treatment such as corticosteroids and cyclophosphamide are alternative choices but these drugs have not been evaluated in randomized controlled trials[7]. Some studies demonstrated improved renal function with high-dose corticosteroid treatment in patients with CCE[10,11]. One patient with leg ulceration caused by CCE was reported to improve with colchicine and corticosteroids[12]. However, several studies have shown that corticosteroid therapy results in good renal outcome in CCE patients in the short-term, but does not have a favorable effect on long-term renal outcome[13]. Statins, prednisone, clopidogrel and antihypertensive agents were administered to our patient. In the 12-mo follow-up period, his renal function gradually improved and the
level of eosinophils gradually decreased, which demonstrated that prednisone treatment was effective. However, the long-term effect of corticosteroid treatment and the dose reduction regimen require further investigation in randomized controlled trials.

**CONCLUSION**

Atheroembolic renal disease and blue toes syndrome can be caused by idiopathic CCE, and early treatment with corticosteroids is effective but requires further study.
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