CASE REPORT

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# Rare Cause of Acute Kidney Injury Following Coronary Angiography: Cholesterol Crystal Embolus

## Koroner Anjiyografi Sonrası Gelişen Akut Böbrek Hasarının Nadir Bir Nedeni: Kolesterol Kristal Embolisi

Sümeyye Memiş[1], Rukiye Saka Tuna[1], Hakan Çalış[1], Elif Itır Şen[1], Chaki Raşit[2], Numan Görgülü[1], Ahmet Engin Atay[1]

[1]University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital, Department of Internal Medicine, İstanbul, Turkey
[2]University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital, Department of Family Medicine, İstanbul, Turkey

**Abstract**

Cholesterol crystal embolus (CCE) is characterized by atheroembolization of the small vessels of the kidney, skin, brain, eye, gastrointestinal system, and extremities with crystal emboli originating from atherosclerotic plaques. It may develop spontaneously or after a cardiovascular intervention, other invasive procedures or subsequent to anticoagulant or thrombolytic therapy. Subacute renal injury is the most common clinical presentation. Skin involvement is the most frequent extrarenal manifestation associated with this condition. We present a case of CCE presented with subacute kidney injury following coronary angiography.

**Keywords:** Acute renal injury, cholesterol crystal embolus, coronary angiography

**Öz**

Kolesterol kristal embolisi (KKE), aterosklerotik plaklardan kaynaklanan kristal emboliler ile böbrek, deri, beyin, göz, gastrointestinal sistem ve ekstremitelerdeki küçük damarların ateroembolizasyonu ile karakterizedir. Kendiliğinden gelişebileceği gibi bir kardiyovasküler girişim, diğer invaziv işlemler ve antikoagülan veya trombolitik tedavi sonrasında da gelişebilir. Subaküt böbrek hasarı en sık görülen klinik tablodur. Bu tabloya eşlik eden böbrek dışı bulgular arasında en sık karşılaşılan bulgu deri tutulumudur. Biz koroner anjiyografi sonrası gelişen ve subaküt böbrek yetmezliği ile prezente olan bir KKE olgusunu sunuyoruz

**Anahtar kelimeler:** Akut böbrek hasarı, kolesterol kristal embolisi, koroner anjiyografi

## Introduction

Acute kidney injury (AKI) is characterized by a sudden deterioration of renal function, indicated by elevated serum creatinine levels and decreased urine output, especially oliguria. This condition typically lasts up to 7 days. Additionally, renal dysfunction may persist beyond the acute phase and can lead to the development of both acute and chronic kidney disease (1,2).

**Address for Correspondence:** Ahmet Engin Atay, University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital, Department of Internal Medicine, İstanbul, Turkey
**E-mail:** aeatay@hotmail.com **ORCID:** orcid.org/0000-0002-3711-5157
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Among three types of AKI, prerenal AKI is the most common subgroup, which accounts for 60% of all AKI, and is mainly associated with hypovolemia and develops as a result of the adaptation of structurally normal kidneys to reduced blood flow. Secondly, intrarenal AKI results from structural damage to the renal tubules, glomeruli, interstitium, or vasculature, and accounts for up to 40% of cases. Finally, less frequently, postrenal AKI occurs due to obstruction of the urinary outflow tract and constitutes 5% of all cases (3).

Cholesterol crystal embolization (CCE) is a multisystemic disease that occurs due to the rupture of atherosclerotic plaques, leading to the release of cholesterol crystals (CCs) and atheromatous material into the circulation. While it is most commonly induced iatrogenically by invasive procedures, it can also occur spontaneously. Embolized CCs become lodged in smaller arterioles, causing varying degrees of ischemia and triggering an inflammatory response in target organs. This process primarily affects the kidneys, skin, gastrointestinal system, and central nervous system (4).Despite significant variability among studies, the incidence of clinically apparent CCE has been reported to range from 0.09% to 2.9%. Autopsy studies have reported CCE in 0.31-2.4% of cases, though its prevalence is significantly higher (12-77%) in selected populations, particularly elderly patients who died following aortic surgery or aortography. CCE is frequently missed in many cases, and the actual incidence is probably much higher than what has been reported (5).

A case of CCE that develops after cardiovascular intervention is presented in this report. Written informed consent was received from the patient.

## Case Report

A 59-year-old male patient presented to our emergency department with a complaint of dyspnea. He had a known history of smoking, along with diagnoses of diabetes mellitus, coronary artery disease, and hypertension. Three weeks before his admission, he underwent two consecutive coronary angiographies which were performed 2 days apart; the first for diagnostic purposes and the second for stent placement.

On physical examination, decreased breath sounds in the lower pulmonary segments and bilateral pretibial edema were noted. Laboratory tests revealed AKI and hyponatremia (urea: 165 mg/dL, creatinine: 5.6 mg/dL, sodium: 126 mmol/L). Thoracic tomography showed bilateral pleural effusion. The patient was hospitalized for evaluation and treatment with a preliminary diagnosis of acute kidney failure.

On the third day of hospitalization, the patient developed a blue discoloration on his fingernails and foot soles (Figure 1). Considering the patient's history of an angiographic intervention three weeks prior to hospital admission and subsequent initiation of antiplatelet therapy, the observed finding was deemed suggestive of blue toe syndrome (BTS) and potentially attributable to CCE. However, due to the history of acute coronary stent placement and ongoing clopidogrel therapy, renal biopsy was contraindicated for confirming the presence of CCE.

Since Hollenhorst plaques (HP) are specific for CCE and their diagnosis does not require an invasive procedure, an ophthalmology consultation was requested. Fundoscopic examination revealed three HP in the right eye (Figure 2).

The patient who required intermittent dialysis and whose renal function did not improve was discharged with the recommendation of dialysis maintenance therapy and outpatient follow-up. Four days post-discharge, the patient developed Coronavirus disease-2019 (COVID-19) pneumonia and required hospitalization. The patient

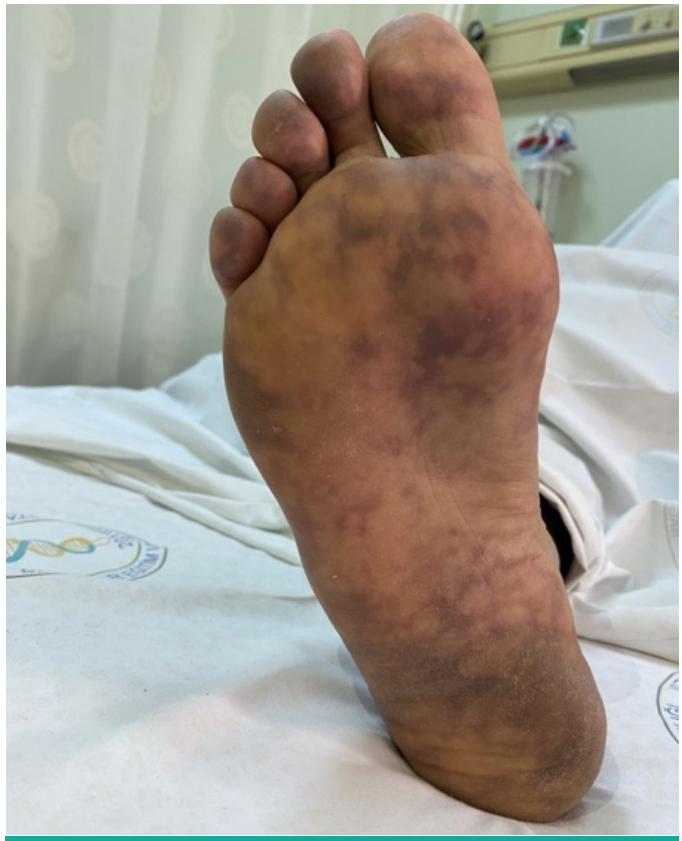

**Figure 1.** Cyanotic appearance with blue-purple discoloration on the toes and sole of the right foot

passed away due to respiratory failure from COVID-19 on the fifth day of hospitalization. Consequently, long-term follow-up could not be performed.

## Discussion

Antemortem diagnosis of CCE is difficult and requires a high degree of suspicion. Identification of risk factors, recognition of clinical findings and consideration of CCE in the differential diagnosis of AKI in patients that underwent certain cardiovascular interventions is of vital importance. A triad consists of a triggering factor including history of coronary angiography, the presence of acute or subacute AKI and the occurrence peripheral crystal embolization in especially male, white and older than 60 years of age patients strongly suggestive of the diagnosis. Contrast nephropathy, small vessel vasculitis, drug-induced interstitial nephritis, and subacute bacterial endocarditis are among the differential diagnoses (6). Our patient, similar to cases reported in the literature, was a 60-year-old male who developed CCE following coronary angiography. However, the presence of HP in our patient was a significant finding supporting the diagnosis.

Histopathologic identification of atheroembolic renal injury is crucial to confirm antemortem diagnosis; however, in case of contraindications for biopsy and when the diagnostic procedures are properly conducted, only 20% of cases require kidney biopsy (7). Moreover, tissue samples taken from the retina, skin, or the muscle may provide clues (8). In patients for whom a biopsy cannot be performed, fundoscopy can be used to confirm the diagnosis if HP are detected.

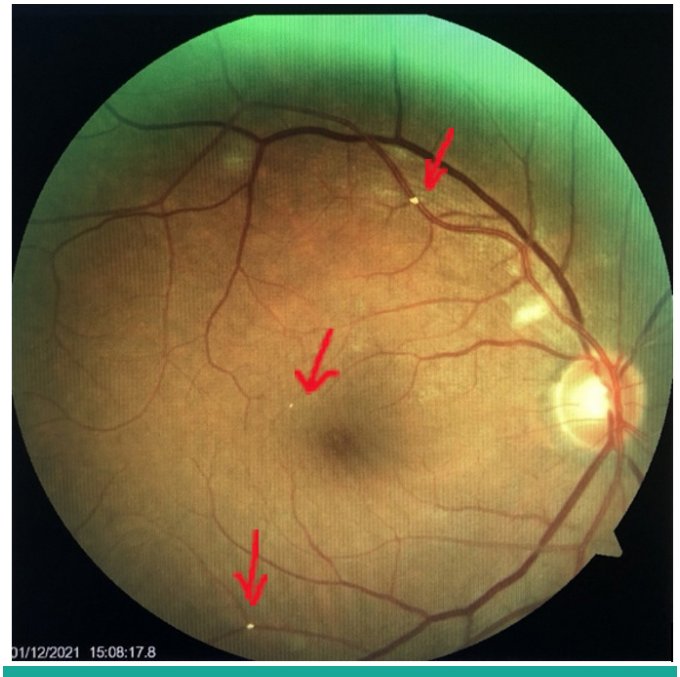


**Figure 2.** Fundoscopic examination showing 3 Hollenhorst plaques which are arterioler deposition of cholesterol embolus

In this case, CCE must be differentiated from contrast-induced nephropathy (CIN) and vasculitis. CIN is defined as a ≥0.5 mg/dL or >25% increase in the level of creatinine, which sustains for at least 2 to 5 days, in the absence of other identifiable factors, and it is usually initiated within 48 to 72 hours of the administration of an iodinated contrast agent. On the other hand, atheroembolic renal injury has a late onset and long duration and has a poor prognosis, compared to CIN (9). The timing of the AKI, which occurred three weeks after the coronary angiography procedure, combined with the lack of improvement in renal function, led to the exclusion of CIN as a potential diagnosis.Vasculitis may mimic CCE due to overlapping features such as eosinophilia, elevated sedimentation rate, and multiorgan involvement. However, urine sediment analysis can help differentiate between the two (10). In our case, the absence of nephritic-type urine sediment findings and the presence of non-specific urine sediment led to the exclusion of vasculitis in the differential diagnosis.

In CCE, the skin is the most commonly affected organ outside the kidneys. The most frequent cutaneous findings are BTS and livedo reticularis (11). The main pathophysiologic mechanism inBTS (Figure 1) is embolism of small vessels, sluggish blood flow to nail-bed, and red cell extravasation that cause non-blanchable discolouration (12). In the present case, the development of BTS findings raised the suspicion of CCE, leading to further diagnostic investigations and treatment planning.

Cholesterol emboli originate from the carotid arteries, and because the ophthalmic artery is the first branch of the internal carotid artery, CCE may cause HP, which can be observed by fundoscopic examination (13). In a patient presenting with BTS and a history of coronary angiography, fundoscopic examination was performed to confirm the diagnosis, and HP were detected.

Although there are promising studies with corticosteroids, lipid-lowering agents, and prostacyclin, no curative treatment is available for CCE at present. Thus, treatment approaches are symptomatic and should be aimed at preventing the development of the disorder. However, Belenfant et al. (14) recommended discontinuation of

anticoagulation and avoidance of unncessary surgery or interventions, initiating angiotensin II antagonists or vasodilators the treatment of hypertension, volume control by loop diuretics or hemodialysis, parenteral nutrition and steroid therapy to improve abdominal discomfort. Considering the profit and loss account before starting anticoagulation or performing a surgery or a radiologic intervention is the mainstay of the preventive strategy.

The prognosis of CCE is generally poor, with a renal function recovery rate of 21-28%. The short-term (one-year) survival rate is around 87%; however, it remarkably decreases to 52% by the fourth year. The major cause of death is cardiovascular complications, rather than renal problems. The predictors of mortality are diabetes, advanced age, history of cardiovascular disease, eosinophilia, baseline renal functions and rapid deterioration of renal functions (15,16).

In conclusion, CCE is a rare but serious cause of AKI that should be considered in patients with a history of cardiovascular interventions. Early recognition of clinical findings and imaging techniques such as BTS and HP is essential for timely diagnosis and management. Treatment is largely supportive, and early diagnosis along with preventive measures may reduce mortality.

### Ethics

**Informed Consent:** Written consent was received from the patient.

### Footnotes

### Authorship Contributions

Surgical and Medical Practices: S.M., N.G., A.E.A., Concept: S.M., R.S.T., H.Ç., A.E.A., Design: S.M., N.G., E.I.Ş., C.R., Data Collection or Processing: S.M., A.E.A., H.Ç., R.S.T., Analysis or Interpretation: N.G., A.E.A., R.S.T., Literature Search: A.E.A, C.R., E.I.Ş., H.Ç., Writing: S.M., A.E.A., C.R., E.I.Ş., N.G.

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