Türk Nefroloji Diyaliz ve Transplantasyon Dergisi/Office Journal of the Turkish Nephrology, Association 1998; 3:154-156

KOLESTEROL KRİSTAL EMBOLİZASYONUNA BAĞLI BÖBREK YETMEZLİĞİ VE GANGRENOZ PARMAK LEZYONLARI: İKİ VAKA SUNUSU

RENAL FAILURE AND GANGRENOUS TOE LESIONS DUE TO CHOLESTEROL CRYSTAL EMBOLIZATION: A REPORT OF TWO CASES

Reha Erkoç, Semra Bozfakıoğlu, Süleyman Türk, Tevfık Ecder, Işın Kilıçaslan*, Veli Uysal*, Selçuk Özarmağan, Fatih Ata Genç**, Taner Gören***, Nilgün Aysuna, Rümeyza Kazancıoğlu, Tevfik Kahraman, Ergin Ark**

İstanbul Üniversitesi İstanbul Tıp Fakültesi İç Hastalıkları Anabilim Dalı Nefroloji Bilim Dalı,
*Patoloji Anabilim Dalı, **Genel Cerrahi Anabilim Dalı, ***Kardiyoloji Anabilim Dalı, İSTANBUL

ÖZET

Nadir görülen bir hastalık olan kolesterol kristal embolizasyonu değişik klinik tablolarda karşımıza çıkabilir. Genellikle anjiyografik girişim veya vasküler cerrahi operasyonlardan sonra ileri yaştaki erkeklerde görülür. Yazımızda, koroner damarların anjiyografik incelemelerinden sonra sistemik kolesterol embolisi ve böbrek yetersizliği gelişen iki vaka sunulmaktadır.

Anahtar kelimeler: Kolestrol embolisi, böbrek yetersizliği

SUMMARY

Cholesterol crystal embolization is a rare disease, presenting with a large clinical spectrum, occurding usually in elderly men who undergo an angiographic procedure or vascular surgery. We report two patients who developed systemic cholesterol embolic disease and renal failure after angiographic interventions of the coronaries.

Keywords: Cholesterol emboli, renal failure

INTRODUCTION

The cholesterol crystal embolization (CCE) is a multisystem disorder characterized by cholesterol crystals in the lumina of small arteries and can give rise to a confusing clinical picture. Emboli may affect many organs causing renal failure, acute pancreatitis, gastrointestinal haemorrhage, cerebral infarction, gangrenes of toes and ischemic pain in the lower extremities, pleural effusion, retinal lesions and neuropathy (1, 2). Cholesterol crystal embolization is most commonly seen after invasive procedures that involve manipulation of the aorta with extensive atherosclerosis (1). The embolization can also follow anticoagulant and intravenous thrombolytic therapy (1,3). Cholesterol crysal embolization is infrequently recognised clinically; so here we present two cases, one with o proven biopsy.

CASE 1: A 55-year-old man with heavy smoking and alcohol abuse presented with severe leg pain and purplish mottling of the legs and toes. Two months ago he had a myocardial infarction and coronary angioplasty was performed one moth later. Few days after the procedure gangrenous lesions appeared on his legs and toes with accompanying limb pain. Within one month he became gradually weak and nausated, without any change in urine output. On physical examination, arterial pressure was 160/100 mm Hg, pericardial friction rub was heard and gangrenous lesions were noted bilaterally on his toes with palpable peribheral pulses. Two grams of proteinuria per day was present and urine sediment contained 1 red, 2-3 white cells and amorphous urate crystals per high power field. The blood urea nitrogen (BUN) was 120 mg/dl, serum creatinine 21 mg/dl and the potassium was 7.2 mEq/L. Hemoglobin and hematocrit were 10.8 g/dl and 24.5%, respectively, white cell count was 11860/mm^3 with 8.7 % eosinophils, platelet count was 359000/mm^3 and the erytrocyte sedimentation rate (ESR) was 80 mm per hour. Anti-nuclear antibody, anti-DNA and ANCA tests were negative. Intermittent hemodialysis treatment was

initiated immediately and renal and skin biopsies were performed. Cholesterol crystal clefts, hyperplastic arteriolar changes and endocapillary proliferation in glomeruli were seen in kidney biopsy specimens **(Figure 1).** Skin biopsy specimens also had cholesterol crystal clefts within arteriolar lumen with perivascular lymphocytic and giant cell infiltration **(Figure 2).** Two months later the patients was stable with incomplete healing of toe lesions and persisting renal failure requiring haemodialysis and was discharged from the hospital. One month after discharge he died with sudden obtundation and coma. Autopsy could not be performed.

Figure 1: Cholesterin crystals in the vascular lumen of the kidney (HEx310)

Figure 2: Cholesterin crystals in the vascular lumen of dermis (HEx 125)

CASE 2: A 51-year old heavy smoker man was admitted because of dyspnea, decreased urine output, blue discoloration of his feet and painful lesions on his toes. He had two consecutive myocardial infarctions two months before admission. After his second myocardial infarction coronary arteriography was performed and anticoagulation was started due to the echocardiographically detected left ventricular thrombus. Physical examination revealed a dyspneic man with a blood pressure of 150/95 mm Hg and signs of volume overload. Livedo reticularis was observed on his legs and gangrenous toe lesions were present with normal pedal arterial pulses. A daily urine output was 500 ml, with trace proteinuria. Urine microscopy revealed 1-2 red and 3-4 white cells per high power field. Blood urea nitrogen was 160 mg/dl, serum creatinine was8.8 mg/dl and sodium was 122 mEq/L. Hemoglobin and hematocrit were 9.4 g/dl and 27%, respectively. White blood count was 11460/mm^3 with 0.1% eosinophilia, platelet count 254000/mm^3 and ESR was 130 mm/hour. ANA, anti-DNA and ANCA tests were negative and C3, C4, antiphospholipid antibodies (IgG and IgM) were within normal limits. Ultrasonography of the kidneys revealed normal parenchymal appereance and size. The renal biopsy could not be performed due to ongoing anticoagulation. The skin biopsy of the affected area could not demonstrate the CCE and remained inconclusive. Hemodialysis was performed and there was no improvement in his renal function within the next three months. Livedo reticularis gradually disappeared but mottling of the toes continued without additional problems. Anticoagulant treatment was not discontinued.

DISCUSSION

Cholesterol crystals were found in 77 % of the autopsies after aortic surgery (4). Additionally in one report, the incidence of systemic emboli detected with examination of the fundus oculi five days later cardiac catheterization was found to be 12.8 % (5), These high incidences are in contrast with the rarity of clinical cases reported probably due to a subclinical course of the cholesterol embolization in the majority of the patients.

Acute nonoliguric renal failure after invasive procedures has been the most common presentation of cholesterol embolism to kidneys (1). Usually there is a rise in serum creatinine a few weeks after the procedure accompanied by accelerating hypertension. Acute renal failure with necrotizing glomerulonephritis and crescent formation has also been reported (6). It is suggested that immunologic factors may play a role in the development of renal failure due to CCE. In some cases with renal function impairment necessitating dialysis, partial recovery of renal function is reported (6).

The most common cutaneous manifestation is livedo reticularis; gangrene, cyanosis, ulceration, nodules and purpurae can also be seen (1). The characteristic presentation of renal failure accompanied with livedo reticularis of the lower body and focal digital ischemia of toes with intact peripheral pulses

make the diagnosis on clinical grounds possible (7). In our second case the absence of other factors causing kidney failure suggests that cholesterol crystals could play a role in renal function impairment. Various laboratory tests help to establish the diagnosis, such as eosinophilia, leukocytosis, elevated sedimentation rate and hypocomplementemia. But the definite diagnosis needs biopsy confirmation. The birefringent cholesterol crystals are dissolved in the routine histologic fixation process, consenquently only the imprint is seen as the characteristic biconvex needleshaped cleft as shown in our first cases' biopsy speciment. On the other hand, fundus oculi examination may reveal cholesterol emboli. Serological tests in order to exclude other diagnosis should also be performed such as ANA, ANCA, cryoglobulin, cold agglutinines and antiphospholipid antibodies. Differentiation from radiocontrast induced nephropathy is quite important

In conclusion, cholesterol crystal embolization is most commonly an iatrogenic problem which is frequently underdiagnosed. Patients with generalised atherosclerotic vascular disease are at high risk for developing the CCE after invasive vascular and cardiac procedures or thrombolytic treatment; therepore in patients with multisystem involvement including renal failure and ischemic skin lesions with normal peripheral pulses, the cholesterol embolization syndrome should always be considered.

REFERENCES

1. Van Jaarsveld BC, Bartelink AKM, Erkelens DW: Cholesterol crystal embolization. Netherlands Journal of Medicine 1991;38:86-92.
2. Bendixen BH, Younger DS, Hair LS, and et al. Cholesterol emboli neurophaty. Neurology 1992;42:428-430.
3. Quenn M, Biem J, Moe GW and et al. Development of cholesterol embolisation syndrome after intravenous streptokinase for acute myocardial infarction. Am J Cardiol; 65:1042-1043.
4. Thurlbeck WM, Castleman B. Atheromatous emboli to the kidneys after aortic surgery. N Engl J Med 1957;257:442.
5. Launay J, Baudouy PY, Amortilla A and et al. Incidence of cholesterol embolism in 70 atheromatous patients hospitalised for cardiovascular evaluation. Rev Med Intern 1992;4:268.
6. Mannesse CK, Blankestjin PJ, Veld MI and et al. Renal failure and cholesterol crystal embolization: a report of 4 surviving cases and a review of the literatüre. Clin Nephrol 1991;5:240-245.
7. Rosman HS, Davis TP, Reddy D and et al. Cholesterol embolization: Clinical findings and implication. J Am Coll Cardiol 1990;15:1296-1299.