Cholesterol embolization syndrome: A case report

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ABSTRACT:

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Cholesterol embolization syndrome (CES) is a rare complication following invasive cardiovascular intervention. This systemic disease affects multiple organs including skin, kidney, brain, eye and gastrointestinal tract. We report a case of 71-year-old man with atherosclerotic risk factors who presented with livedo reticularis, progressive renal failure and eosinophilia after cardiac catheterization. Histopathology of the skin confirmed the diagnosis of cholesterol embolization syndrome. He was treated with statins, antiplatelet agent and oral prednisolone; his skin lesions improved however the kidney function reached end-stage renal disease which required hemodialysis within one month.

Key words: Cholesterol embolization syndrome, livedo reticularis, renal failure, eosinophilia

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Introduction

Cholesterol embolization syndrome (CES) is a rare systemic condition which results from distal embolization of cholesterol crystals originated from the aorta as complication of angiography, vascular surgery, anticoagulant or thrombolytic therapy. It is also known as cholesterol crystal embolization, atheromatous embolization syndrome or atheroembolism. CES frequently affects males in their 5^{th}- 6^{th} decade of life.[1,2] The syndrome has a variety of clinical manifestations since it could involve many systemic organs including the skin, kidney, brain, eye and gastrointestinal tract. The definite diagnosis is usually made by skin, muscle or kidney biopsy. It is important to recognize the disease as it has a very high mortality rate and is often associated with adverse outcomes.[2]

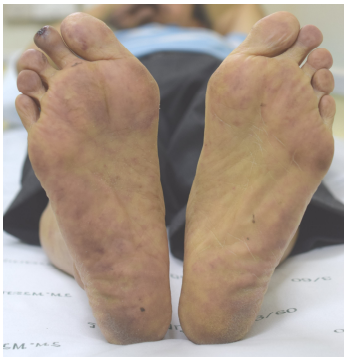

Figure 1 Dermatological findings showed multiple purplish reticulated patches consistent with livedo reticularis on the plantar surface of both feet and some dusky discoloration of the skin with focal sites of necrosis on the distal portion of the right second toes.

Case report

A 71-year-old Thai man with hypertension, dyslipidemia, chronic kidney disease and history of ischemic stroke was admitted to our hospital due to progressive dyspnea, orthopnea and marked edema of both lower legs. He was diagnosed with and treated for congestive heart failure. Coronary angiography was performed which revealed normal coronary artery. Two weeks after the procedure, he noticed diffuse blue mottling with purplish discoloration on the skin on his toes without fever, abdominal pain or myalgia. Physical examination revealed normal vital signs, good consciousness and well-cooperated. Peripheral pulses at all extremities were palpable. Dermatological findings showed dusky discoloration of the skin with focal sites of necrosis on the distal portion of his toes with multiple purplish reticulated patches consistent with livedo reticularis (Figure 1). Funduscopic examination was normal. Laboratory tests revealed leukocytosis with eosinophilia (WBC 11300 cell/mm^3, absolute eosinophils 1096 cell/mm^3) and a progression in renal dysfunction (serum creatinine had increased to 4.86 mg/dl from the baseline level of 2.46 mg/dl). Rheumatological markers including ANA, ANCA, rheumatoid factor and complement were unremarkable. The skin biopsy was performed on his right second toe, suspecting of cholesterol embolization syndrome. Histopathology revealed

an increase of dilated small vascular vessels in the dermis with cholesterol clefts seen in the vascular lumen (Figure 2). The histopathological result confirmed the diagnosis of cholesterol embolization syndrome.

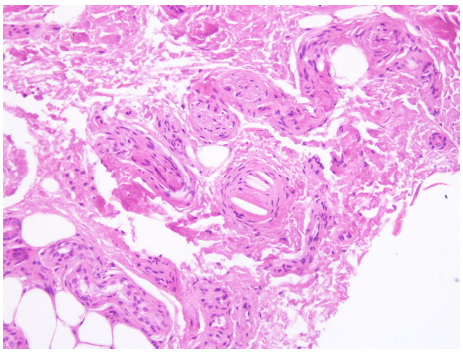

Figure 2 The skin biopsy from the patient's right second toe revealed an increase of dilated small vascular vessels in the dermis with cholesterol clefts in the vascular lumen (H&E, X200)

Discussion

Cholesterol embolization syndrome (CES) is a rare multisystemic disease involving skin, kidney, central nervous system, eye and gastrointestinal tract, first described by Panum in 1862.[1] CES predominantly affects elderly men older than 50 years of age with multiple atherosclerotic risk factors such as hypertension, hypercholesterolemia, diabetes mellitus and smoking.[2,3] Postmortem studies reported cholesterol emboli in 25%-30% of cases following cardiac catheterization, compared with 0.79%-3.4% of spontaneous CES in patients over 60 years.[4-6]

The pathogenesis of CES is explained by the detachment of cholesterol emboli from atherosclerotic plaque at the wall of large-sized arteries which throw towards small or medium-sized arteries at the distal part. As a result of the mechanical obstruction, multiple end-organ damages are noted as consequence after the inflammation. The embolization occurs after invasive vascular procedures such as arteriography, angioplasty or surgery and also after anticoagulation or thrombolytic therapy.[7] The onset of clinical manifestation depends on the mechanism of cholesterol obstruction. Early onset CES begins within hours to days after the direct mechanical dislodgement of the cholesterol plaque from vascular procedures or using thrombolytic agents to disrupt fibrin clots. Late onset CES is observed 1 to 2 months after the anticoagulant therapy as a result of gradual weakening of fibrin clots by inhibition of the normal remodeling system.[8,9]

The wide variety of clinical presentation is associated with the location of the atheromatous plaque and the affected distal sites. Cholesterol emboli from the descending aorta can cause renal failure, mesenteric ischemia and emboli to skin and skeletal muscles, whereas emboli originating in the ascending aorta may cause neurological

complication. The inflammatory response may also lead to non-specific constitutional symptoms including fever, anorexia, myalgia and weight loss.[10]

Reported incidence of cutaneous manifestation ranges from 35% to 96% of patients with CES.[11] The most common skin finding was livedo reticularis, found in 49% of patients, followed by gangrene (35%), cyanosis (28%), ulceration (17%), nodules (10%) and purpura (9%). They are often seen on lower extremities, especially feet and toes, and less frequently on the trunk or upper extremities.[12] The most common visceral manifestation is renal involvement, found in up to 50% of patients with CES. Renal manifestation includes elevation of serum creatinine, proteinuria and accelerated hypertension which can lead to renal failure.[2,13]

Other extra-cutaneous manifestation involving the gastrointestinal (GI) system could result in abdominal pain, diarrhea and GI bleeding. For the central nervous system, it could cause transient ischemic attack, stroke or neurological deficits. Rare manifestation such as pancreatitis, adrenal insufficiency and pulmonary embolization have also been reported.[10,14]

The history of precipitating factor, acute renal failure and cutaneous manifestation may warrant the diagnosis of CES, as in our patient. Retinal cholesterol crystals or Hollenhorst plaques are also strong evidence of the disease. However, confirmation of CES is provided by histopathological findings of cholesterol clefts in small arteries of the biopsy specimen. Peripheral biopsy from skin or muscle is recommended to avoid the more invasive sites.[7,10] Hypereosinophilia may occur in up to 80% of patients with CES who have renal involvement.[15] Other laboratory abnormalities including anemia, thrombocytopenia, leukocytosis, hypocomplementemia, and increased markers of acute inflammation such as erythrocyte sediment rate and C-reactive protein were reported.[10]

Currently, various therapeutic strategies have been proposed including conservative, invasive and surgical treatment. The principle of medical treatment consists of supportive care and aggressive control of risk factors such as using statins, antiplatelet therapy and avoidance of further vascular procedures.[10] A report suggested corticosteroid might have some benefit, as it reduced the inflammation reaction associated with CES. However, cardiovascular side effects of corticosteroids have to be taken into consideration especially in elderly and diabetic patients with vascular compromised.[16]

Our patient was treated with rosuvastatin 10 mg/d, clopidogrel 75 mg/d and oral prednisolone 20 mg/d. After two weeks of the treatment, the livido reticularis lesion on both

feet subsided and there was no further skin necrosis or digital gangrene. However, his kidney function continued to deteriorate and reached end-stage renal disease requiring renal replacement therapy within one month.

The prognosis of CES is poor, with 1-year mortality rate ranging from 64% to 87%.[2,17] The complication includes gangrene of the extremities that may need amputation, progressive renal failure which requires dialysis, or multi-organ failure.

Conclusion

We report a case of cholesterol embolization syndrome after cardiac catheterization. The gradual onset of renal impairment with cutaneous manifestation in an elderly man following invasive cardiovascular intervention, in the presence of eosinophilia, should alert clinicians towards the diagnosis of cholesterol embolization syndrome. Since the disease may have poor prognosis and treatment options are limited and unsatisfactory, close monitoring of renal function and supportive treatment are required.

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