Cholesterol Emboli Syndrome: Acute Renal Insufficiency After a Procedure or a Thrombolytic Therapy or Anticoagulant Therapy

C. Chandra Sekhar · Parveen Jindal · V. Guru Karna ·
Manoj Aggarwala · Soma Sekhar

Received: 6 October 2011 / Accepted: 21 June 2012 / Published online: 7 October 2012
© Association of Surgeons of India 2012

Abstract Cholesterol emboli syndrome is due to dislodgement of cholesterol crystals from the atherosclerotic plaques lining the walls of major arteries resulting in an occlusion of small arteries. We describe a case of severe cutaneous and renal cholesterol emboli syndrome following coronary angiography showing our observation that this syndrome is often unrecognized or misdiagnosed and that a better evaluation of risks factors in patients undergoing invasive procedures could prevent this severe complication.

Keywords Cholesterol emboli syndrome · Blue toe syndrome · Coronary angiography complications

Introduction

Cholesterol crystal emboli syndrome is a clinical entity that is recently being diagnosed more often. It is thought to be a

complication of atherosclerosis and is found in 2–8 % of necropsies. It often follows invasive procedures involving the aorta and major arteries, such as angiography, angioplasty, and cardiovascular surgery [1–3].

Organs most frequently involved are the skin and the kidneys, but any other organ can be affected. Cutaneous manifestations vary from livedo reticularis and acrocyanosis (blue toe syndrome), which are seen most frequently, to nodules, ulcers, purpuric lesions, and gangrene. Renal failure is documented in 50 % of cases and gastrointestinal bleeding in 10 % [3].

Less common features of the syndrome include central nervous system and coronary artery disease manifestations, ischemic pancreatitis, and gastrointestinal ischemia, as well as the fatal multiple cholesterol emboli syndrome. The pathophysiology of the syndrome includes the dislodgement of cholesterol crystals from ulcerated atheromatic plaques, usually lining the walls of the aorta, and residual embolization of periphery arterioles with a diameter of 100–200 μm .

We describe the case of a 55-year-old patient who developed cholesterol embolism following routine coronary angiography.

Undertaking We undertake that the work described here has not been published before; that it is not under consideration for publication anywhere else; that its publication has been approved by all of us.

C. C. Sekhar (✉) · V. G. Karna
Department of Vascular Surgery, Apollo Hospital,
Jubilee Hills, Hyderabad, AP, India
e-mail: chandrasekharchevuturu@yahoo.co.in

P. Jindal
Department of Vascular Surgery, Renal Care & Dialysis Centre,
Dehradun, UK, India

M. Aggarwala
Department of Cardiology, Apollo Hospital,
Jubilee Hills, Hyderabad, AP, India

S. Sekhar
Department of Nephrology, Apollo Hospital,
Jubilee Hills, Hyderabad, India

Case Presentation

A 55-year-old businessman—a known case of type 2 diabetes on insulin therapy, hypertensive on Angiotensin Receptor Blocker (ARB)s and beta-blockers, Coronary Artery Disease (CAD) with double-vessel disease (2007) not amenable for stenting, and chronic smoker—developed acute dyspnea in a party in September 2010 and treated as acute coronary event. He underwent coronary Multi-Dimensional Computed Tomography (MDCT) which revealed Double Vessel Disease (DVD). After 1 month he underwent conventional coronary angiogram.

Two weeks post-Coronary Angiography (CAG), the patient presented with shortness of breath, cough with

expectoration, fever for 1 week and blackish discoloration of the toes and the feet, painful ulcerations, and cramps in the legs at night for 15 days.

His examination showed heart rate 90 per min, all peripheral pulses felt well, blood pressure 160/90 both limbs, Ankle Brachial Index (ABI) 1.0, Cardio Vascular System (CVS)—both heart sounds were normal, no adventitious sounds, lungs—bilateral crackles at the bases, abdomen—soft, no organomegaly, and neurological examination was unremarkable. Nicotinic stains were found on nail beds, livedo reticularis and small vasculitic rashes on thighs (Figs. 1 and 2).

Laboratory results showed Hb 8.5, TLC 11,400, N 88, E 22, platelet 90,000, ESR 82, urine protein 1+, RBCs 2–3/hpf, and pus cells 3–5/hpf. Renal parameters were serum creatinine 5.5, serum potassium 5.7, serum bicarbonate 17.0, serum calcium 8.0, albumin 2.8, proteinuria 1.2 grams/day, GFR 14 ml/min/1.73 m². Sputum was negative for microbes, Gram stain negative, and screening for viral markers was negative.

Imaging Features Color Doppler of lower limbs—diffuse atherosclerotic changes in the popliteal and DPA both limbs, good flow velocities. 2D echo—Grade II diastolic dysfunction and EF55%.

Collagen Profile ANA negative, ANTI-DSDNA negative, C-ANCA and P-ANCA negative, ANTI-BM negative, complement normal, and urine for eosinophilia negative.

The initial course in hospital started on piperacillin + tazobactam therapy, and workup for peripheral vascular disease was done. He had acute pulmonary edema and cardiac markers were negative. He was started on dialysis daily for the first few days. Fever subsided but cough was not improving for which HRCT chest was done. The HRCT showed bilateral pleural effusion along with features suggestive of alveolitis with a reticular pattern usually seen in ILD .i.e Interstitial Lung Disease or Allergic reactions

Dialysis for ongoing azotemia and fluid overload was continued, and pleural tap done insignificant for any infection. No improvement was in the ulcerations. Renal parameters were fluctuating at 3.5–4.5, on dialysis twice weekly with

Fig. 1 Nail bed staining and early skin discoloration [Blue toe syndrome]

Fig. 2 Ulceration of the skin and surrounding skin gangrene

nonoliguric status. Renal biopsy was planned for the unexplained renal failure. Initially the patient was treated with anticoagulant heparin injection and skin lesions exsperated. Renal biopsy revealed cholesterol crystals embedded in glomerular cleft (Fig. 3). After biopsy the patient was started on injection prostaglandin E2 (Alprost), and his condition improved dramatically (Fig. 4).

Discussion

Cholesterol emboli syndrome is due to dislodgement of atheromatic debris and emboli formation from ruptured atherosclerotic plaques, lining the walls of the aorta, and the major arteries. It may occur spontaneously but often follows

Fig. 3 Livedoreticularis with Skin changes with impending gangrene

Fig. 4 Glomerular cleft showing embedded cholesterol crystals with intimal hypertrophy and luminal stenosis

cardiovascular surgery or coronary angiography and angioplasty (0.08 %) [4]. Due to the crystal morphology, occlusion of the vessels is not always complete, giving rise to ischemic atrophy rather than necrosis. Subsequently, a “foreign body” type response occurs, with intima hypertrophy, giant cell sequestration, and further luminal stenosis. This mechanism is responsible for the characteristic gradual decline of renal function, which develops over a period of 3–8 weeks.

Risk factors are old age, peripheral vascular disease, severe atherosclerosis of the ascending aorta, and repeated invasive procedures. The syndrome may appear following the use of coumadin products, heparin or thrombolytics, where the noneffective coating of a ruptured atheromatic plaque by thrombus might be the possible induction mechanism. The use of these agents, high creatinine levels, low platelet count, and the large size of diagnostic catheters are thought to represent minor risk factors for the evolution of this syndrome [4, 5].

Cholesterol embolization is not a common clinical entity: it is rarely diagnosed in life but can have serious consequences. It is characterized by the classic triad of *ischemic skin lesions*, *acute renal failure* and *eosinophilia*, findings which were evident in our patient. Any organ may be affected, but sometimes it may show atypical features such as fever, muscular pain, or manifestations of systemic vasculitis [6]. The interval between intervention and disease onset is typically 1–4 weeks, but occasionally may extend to several months. This specific “time window” and the subsequent and gradual deterioration of renal function may help to distinguish cholesterol embolism from contrast nephropathy. The part of the clinical picture may be the appearance of the so-called blue toe syndrome, which is a completely different entity of varying etiology and is characterized by cyanotic toe skin lesions with no renal failure and where the treatment is purely etiologic (includes the use of coumadin or low-molecular-weight heparin, which is contraindicated in cholesterol embolism) [7].

Knowledge and awareness of the syndrome, as well as a detailed history, are of great importance for correct diagnosis. Blood tests reveal renal dysfunction and the striking eosinophilia, which is encountered in 70–80 % of cases is usually an early finding [3]. Elevated erythrocyte sedimentation rate and hypocomplementemia are common. Complement levels are frequently reduced in cholesterol embolism, limiting the use of this test in the distinction between vasculitis and cholesterol embolism [8]. Urine analysis usually shows modest proteinuria with or without hematuria, while high blood amylase levels, melena, or anemia may be encountered in the multi-organ-type of the syndrome.

The diagnosis can be confirmed by biopsy of the skin, muscle, or kidney, which demonstrates the characteristic appearance of cholesterol crystal clefts, with giant cell perforation into the arteriole lumen. Occasionally, the crystals can be seen as emboli in the retinal microcirculation in patients with ischemic stroke. Transesophageal echocardiography seems to be an invaluable diagnostic tool in the evaluation of the syndrome, demonstrating in detail the anatomy of heart and aorta, as well as mobile atheromata [9]. Angiography should be avoided in view of the possible recurrence of embolism. Finally, two-dimensional echo of the great vessels, computed tomography, and magnetic resonance imaging may appear helpful.

Mortality varies in the literature and is estimated to be between 64 and 81 % [5]. Death is usually of cardiovascular origin and very often these patients develop end-stage renal failure dependent on dialysis. The worst prognosis is encountered in the multiple cholesterol emboli syndrome with mortality reaching 100 % [10].

Treatment options are limited. In recent years, a conservative approach with the avoidance of any further vascular intervention due to the potent embolism recurrence has been considered the best option [11]. The discontinuation of coumadin products and antiplatelet agents, which may limit or inhibit the atherosclerotic plaque coating by thrombus, is of great importance. Statins might stabilize plaques [14], while steroid treatment remains controversial. Our patient was on a high dose of atorvastatin (80 mg/day), but the dosage was modified to 40 mg/day because of gastrointestinal side effects. There are recent reports of beneficial effects from a prostacyclin analogue (Ilomedin) on renal function and cutaneous lesions [12]. As far as treatment options for painful skin lesions are concerned, it seems that intermittent epidural analgesia promotes the best results. Spinal cord stimulation has been recognized as a quite effective method for pain control, and its established ability to improve peripheral microcirculation may allow an efficient resolution of necrotic lesions [13].

In conclusion, the incidence of cholesterol emboli syndrome seems to be increasing following the widespread

growth in the practice of invasive cardiology. Accordingly, patients prone to developing this devastating clinical syndrome should be managed with extreme attention, in order to make the diagnosis promptly and to begin supportive treatment as soon as possible.

References

1. Piriou V, Claudel JP, Bastien O, Ross S, Lehot JJ (1996) Severe systemic cholesterol embolization after open heart surgery. *Br J Anaesth* 77:277–280
2. Scolari F, Bracchi M, Valzorio B, Movilli E, Constantino E, Savoldi S et al (1996) Cholesterol atheromatous embolism: an increasingly recognized cause of acute renal failure. *Nephrol Dial Transplant* 11:1607–1612
3. Fine MJ, Kapoor W, Falanga V (1987) Cholesterol crystal embolization: a review of 221 cases in English literature-angiology. *J Vasc Dis* 7:769–784
4. Johnson LW, Esente P, Gianbartolomei A, Grant WD, Loin M, Reger MJ et al (1994) Peripheral vascular complications of coronary angioplasty by the femoral and brachial techniques. *Cathet Cardiovasc Diagn* 31:165–172
5. Rhodes JM (1996) Cholesterol crystal embolism: an important “new” diagnosis for the general physician. *Lancet* 347:1641
6. Dupont P, Lightstone L, Clutterback E, Gaskin G, Pusey C, Cook T et al (2000) Cholesterol emboli syndrome. *BMJ* 321:1065–1067
7. O’Keefe S, Woods B, Breslin D, Tsapatsaris N (1992) Blue toe syndrome. Causes and management. *Arch Intern Med* 152:2197–2202
8. Cosio FG, Zager RA, Sharma HM (1985) Atheroembolic renal disease causes hypocomplementemia. *Lancet* 2(8447):118–121
9. Arko F, Buckley C, Baisden C, Manning L (1997) Mobile atheroma of the aortic arch is an underestimated source of embolization. *Am J Surg* 174:737–740
10. Fernandez-Samos R, Suarez D, Ortega JM, Zorita A, Vasquez J, Moran CF et al (1995) Multiple cholesterol embolization syndrome: a lethal complication of vascular procedures. Report of two histologically proven cases. *J Cardiovasc Surg* 36:87–91
11. Belenfant X, Meyrier A, Jaquot C (1999) Supportive treatment improves survival in multivisceral cholesterol crystal embolism. *Am J Kidney Dis* 33:840–850
12. Elinav E, Chajek-Shaul T, Stern M (2002) Improvement in cholesterol emboli syndrome after iloprost therapy. *BMJ* 324:268–269
13. Ghilardi G, Massaro F, Gobatti D, Kunkl E, Scorza R (2002) Temporary spinal cord stimulation for peripheral cholesterol embolism. *J Cardiovasc Surg (Torino)* 43:255–258
14. Woolfson RG, Lachmann H (1998) Improvement in renal cholesterol emboli syndrome after simvastatin. *Lancet* 352:1331–1332