Severe systemic cholesterol embolization after open heart surgery

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Summary

Cholesterol crystal embolization (CCE) may be triggered by various factors: intra-arterial angiographic procedures, aortic or vascular surgery, anticoagulant or thrombolytic treatments, or both. There are few previous reports of patients undergoing coronary artery bypass grafting (CABG) experiencing and therefore displaying severe systemic CCE. We describe four patients presenting, shortly after CABG, cutaneous, renal, neurological and hepatic signs related to severe CCE confirmed by skin biopsy. All patients died 11–92 days after surgery. As systemic CCE reveals severe atheromatous disease and is associated with a poor prognosis, it is advisable to avoid CABG in patients who present symptoms of CCE before surgery. (Br. J. Anaesth. 1996; 77: 277–280)

Key words


An eroded atheromatous aorta may be a source of cholesterol crystal embolism (CCE). Embolization of atheromatous material accounts for obstruction of distal arterioles around which a foreign-body giant cell granuloma inflammatory reaction develops. The diagnosis is often delayed or unrecognized because of varying or misleading clinical signs, such as renal insufficiency, digestive or neurological symptoms, or both, or unexplained multiple-system disease [1]. Various triggering factors have been described such as intra-arterial angiographic procedures, aortic or vascular surgery, and in some cases anticoagulant or thrombolytic treatments, or both.

Patients undergoing coronary artery bypass grafting (CABG) often experience a combination of these factors: anticoagulation—before, during and after surgery— intra-arterial angiographic procedures and intraoperative aortic cross-clamping. These multiple factors could account for the acute and severe postoperative clinical and biological findings observed in the four patients described here.

Case report

From September 1992 to January 1994, four patients developed very severe and acute systemic cholesterol embolization immediately after CABG. All were male with a mean age of 67 yr (range 62–71 yr). They presented at least two risk factors for atherosclerosis, and a previous history of atheromatous disease (coronary artery disease $n = 4$, chronic peripheral arterial disease $n = 2$, carotid vascular surgery $n = 1$) (table 1). These four patients were referred to our institution for unstable angina and therefore received i.v. heparin.

A coronary angiogram was performed in all cases, 3–5 days after admission. During catheterization, patient No. 1 complained of chills and myalgias, and patient No. 3 experienced a transient cerebrovascular ischaemic accident. Multiple coronary artery disease was noted in all patients; patient No. 2 also presented severe stenosis of the left main coronary artery. Patient Nos 3 and 4 experienced a blue toe syndrome with normal peripheral pulses and renal insufficiency (serum creatinine concentration 344 $\mu$mol litre$^{-1}$ and 281 $\mu$mol litre$^{-1}$, respectively) shortly after left heart catheterization, before surgery.

All patients underwent CABG 2–55 days after coronary angiogram. The immediate postoperative course was complicated in all cases: patient No. 2 presented an unstable haemodynamic status related to intraoperative myocardial infarction (confirmed by postmortem examination) which required intra-aortic balloon counterpulsation. All patients had postoperative coma, acute renal insufficiency and required haemodialysis, a highly elevated serum creatine kinase activity (patient Nos 2 and 4) and purple toes accompanied by more diffuse cyanotic mottling of the surrounding skin (livedo reticularis); peripheral pulses were normal. In addition, severe abnormalities of hepatic (elevated serum bilirubin concentration) and pancreatic (elevated serum amylase activities of 367 i.u litre$^{-1}$) functions were observed in patient No. 1. Elevated erythrocyte sedimentation rate (ESR), transient peripheral blood eosinophilia (450 eosinophils mm$^{-3}$) and low C3 complement fraction were present in patient Nos 1 and 2 (table 2, fig. 1). Systemic cholesterol embolization was confirmed in all patients by skin biopsy which showed acute inflammation with cholesterol clefs within small arterioles.

Patient management included interruption of heparin, and administration of antiplatelet agents (aspirin) and methylprednisolone 80–120 mg day$^{-1}$.

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With this treatment, clinical and biological improvements occurred in patient Nos 1 and 3: weaning from haemodialysis and neurological improvement (normal consciousness although both had persistent hemiplegia). However, this treatment failed in patient Nos 2 and 4. All patients died within 11–92 days after surgery: patient No. 1 died from mesenteric infarction, patient Nos 2 and 4 from sudden death, and patient No. 3 from a cerebrovascular accident.

**Discussion**

Embolic migration of cholesterol crystals has been commonly accepted after experimental work carried out by Flory [2] and Snyder and Shapiro [3], in addition to pathological studies [4]. Cholesterol crystals obstruct 100–250 μm size arterioles. As their elimination occurs very slowly, a local foreign-body type inflammation develops, completing arteriolar obstruction. Cholesterol crystals may be released into the vascular lumen in response to rupture of the atherosclerotic plaque related to intraplaque haemorrhage or confined dissection.

CCE occurs in patients with diffuse atherosclerosis and multiple vascular risk factors (high cholesterol concentration, diabetes, tobacco abuse, hypertension) exposed to a triggering agent [5]. This diffuse embolization of atheromatous material may therefore be responsible for various clinical manifestations including: “blue toes syndrome” together with normal peripheral pulses associated with livedo reticularis of the lower limbs; renal insufficiency with severe arterial hypertension; digestive or neurological symptoms, or both; or even “fever of an unknown origin”, therefore mimicking diffuse vasculitis [1] or infective endocarditis. Diagnosis may be very difficult [6] and this complications has to be borne in mind by practitioners. The onset of such clinical features is usually insidious, although acute and severe clinical manifestations after cardiac angiography have been reported [7]. Pathological [4] and clinical observations [8] support the existence of such triggering factors. Thus angiographic procedures (aortography, left heart catheterization), aortic and vascular surgery have commonly been related to the occurrence of CCE [9].

In the literature, angiographic procedures accounted for 50% of cases of CCE [10, 11]; the mean delay between the invasive procedure and symptoms was 13.5 ± 21 days (range 1 h to 3 months). Guidewire and catheter manipulations injure the endothelium and therefore dislodge soft cholesterol material.

Aortic surgery was responsible for 9% of CCE cases published until 1988 [10, 11], but this has since reached 18% among published cases. Aortic surgery was always preceded by an angiographic procedure; aortic cross-clamping and also incision of the artery releases the atheromatous material into the bloodstream [12].

Anticoagulant therapy as a triggering factor of
CCE was first suggested in 1961 by Feder and Auerbach [13]. They reported six cases of “purple toes” with normal peripheral pulses occurring 3–8 weeks after introduction of anticoagulant treatment. Anticoagulant treatment (heparin or antivitamin K, or both) was given in 19% of published case reports [10, 11]. These medications are often associated with another triggering factor, in most cases an angiographic procedure [5, 7, 9, 14]. There are several case reports in the literature [1, 5, 13–16] in which anticoagulant therapy was the sole triggering factor. However, postmortem studies [4] failed to show any difference in the atheroembolic rate according to whether or not anticoagulants were given. This complication seems rare in view of the large number of patients treated.

Thrombolytic therapy was suspected to be an atheroembolism triggering factor as early as 1976 by Spangen and colleagues [17], who observed worsening renal function after i.v. streptokinase therapy. The first well documented case was described in 1979 and involved a patient treated with streptokinase for severe pulmonary embolism [18]. Since then, some cases indicating thrombolytic therapy as the triggering factor for CCE have been reported. In several cases, this therapy was associated with an angiographic procedure [19]; thrombolytic therapy was the sole triggering factor in other cases [20–24]. The underlying pathophysiological mechanism by which anticoagulant and thrombolytic therapy induces CCE is uncertain. Most authors [15, 18] agree that these medications lyse the platelet-fibrin protective thrombi covering ulcerated atheromatous plaques which may expose atheromatous material to the circulation.

Patients requiring cardiac surgery are at high risk of developing CCE [25, 26]. These patients with an atheromatous aorta are at risk of the main triggering factors, such as left heart catheterization, aortic cannulation and cross-clamping, and anticoagulant therapy before, during and after surgery. Severe central nervous system complications after cardiac surgery, as described in our patients, have been described widely [27]. These complications are usually related to haemodynamic (e.g. severe intraoperative hypotension) or embolic (left ventricular mural thrombus, atrial fibrillation, air embolism) events.

Severe systemic atheromatous embolization after cardiac catheterization has been described during procedures which are often long and difficult, requiring prolonged manipulations and numerous catheter changes within a severely diseased aorta [7, 28]. The sudden occurrence of clinical features seems to be related to massive embolization of atheromatous fragments dislodged by catheters. Therefore, aortic cross-clamping and cannulation could be responsible for similar findings. By studying embolic signals with transcranial Doppler during cardiopulmonary bypass for coronary artery revascularization, Barbut and colleagues [29] showed that all patients (n = 20) displayed embolic signals. Most have been recorded during removal of aortic cross clamps (34%) and partial occlusion clamps (24%).

In addition to systemic CCE, atheromatous embolization to the distal coronary circulation may complicate CABG, and be responsible for intraoperative myocardial infarction and death, as experienced in patient No. 2. In a series of 4095 CABG, Keon, Heggvteit and Leduc [30] reported nine deaths (0.22%) related to atheromatous embolization into the coronary microcirculation. Moreover, among 175 patients who were re-operated on after a first CABG, four patients (2.29%) died from intraoperative massive myocardial infarction after atheroembolization of the distal coronary circulation. The atheroemboli were deemed to have originated from ulcerative atherosclerotic lesions in the aortic root at the ostia of the coronary arteries or vein grafts, or both, from coronary endarterectomy sites, or from mechanical disruption of plaques in the major epicardial coronary arteries during intraoperative manipulation of the heart. The higher rate of atheromatous embolic complications in patients undergoing repeated CABG is probably related to more severe atherosclerosis with soft mushy atheroma in old vein grafts.

Even though some investigators reported clinical and biological improvements with steroid therapy [1, 8, 31] or pentoxifylline [32], severe systemic CCE has a poor prognosis. The treatment is usually symptomatic, including renal and haemodynamic support.

In patients with severe aortic lesions, transoesophageal echocardiography led surgeons to modify their technique using an alternative cannulation site, hypothermic circulatory arrest [33], exploration and debridement of the aortic arch [34] or resection and graft replacement of the involved aortic segment [35]. Recently, Katz and colleagues [34] studied 130 patients undergoing open heart surgery and examined atherosclerotic lesions in the aortic arch using transoesophageal echocardiography (TOE). The severity of aortic atheromatosis was the only predictor of stroke. Ribakov and colleagues [33] found similar results, demonstrating that intraoperative clinical evaluation of aortic atheromatous disease by surgical palpation alone is not predictive of embolic stroke. Other observations revealed that TOE may demonstrate atheromatous plaques of the aortic arch involved in cholesterol embolization [36, 37] and so detect patients with a high risk of CCE before surgery. Wareing and colleagues [38] have proposed performing ascending aortic replacement or carotid endarterectomy to decrease the stroke rate after cardiac surgery in patients in whom atheromatous plaques were discovered by intraoperative ultrasonic scanning. Other studies [39, 40] have shown that intraoperative echography during cardiac surgery was able to predict patients with a high cerebral complication rate in relation to different stages of atheroma in the ascending aorta.

However, symptoms related to CCE must be sought before CABG: renal insufficiency after left heart catheterization associated with eosinophilia, blue toes syndrome and livedo reticularis. These symptoms indicate the need for a skin or muscular biopsy. Histological confirmation is essential for diagnosis and may help to age the different lesions.
When CCE is confirmed, we believe that CABG is contraindicated because of the poor prognosis of cardiac surgery.

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References


