CASE REPORT

Uncontrolled Systemic Inflammatory Response Syndrome by Cardiopulmonary Bypass

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ABSTRACT

It is known that the use of a cardiopulmonary bypass (CPB) during cardiac surgery leads to leukocyte activation and may, among other causes, induce organ dysfunction due to increased leukocyte recruitment into different organs. In our patients, pathophysiologically severe systemic inflammatory response syndrome, uncontrolled CPB-induced inflammation, chylomicrons and very low density lipoproteins or immune complexes have been shown to develop immune-dependent agglutination by C-reactive proteins in CPB, which could result in vascular occlusion and resultant infarction.

Keywords: Cardiopulmonary bypass, leukocyte, thoracic surgery

INTRODUCTION

Socha *et al* (1) found that during cardiopulmonary bypass (CPB), phospholipase A_2 degrades arachidonic acid, leading to inflammatory mediators such as leukotrienes, prostaglandins and thromboxanes. The action of these substances triggers adhesion and neutrophil activation, vasoconstriction, tissue injury, platelet aggregation and the ischaemic organ change (2). The differential diagnosis can be divided into three categories: emboli from the cardiac and arterial systems, acquired hypercoagulability disorders, and syndromes which lead to peripheral vascular pathology (1).

CASE REPORT

A 45-year-old woman secondary to rheumatic fever and aortic regurgitation was scheduled for aortic valve replacement. Pre-operative echocardiography revealed severe aortic regurgitation. She denied any cerebral symptoms, including headache, dizziness, transient ischaemic attacks or strokes in her medical history; the patient was found to be fully conscious, alert and oriented with stable vital signs. The blood pressure was 110/80 mmHg, and the diastolic murmur was audible over the mitral area. The physical exam revealed intact cranial nerves, motor power and sensation. There was no evidence of vasculitis such as Osler's nodes, Jane way pad, palmer erythema or cyanosis of fingers. The blood investigation showed an erythrocyte sedimentation rate of 4 mm with no leucocytosis (white blood cells = 10 000 cells/mm^3). The electrolytes and kidney and liver function were within normal limits. The chest X-ray was normal. Electrocardiogram showed no change. The patient scheduled for re-operative aortic valve replacement. Intra-operatively, the aortic valve was tricuspid and was not calcified. The wall of the aorta in the sinus area appeared thin, but there was no root dilatation or wall calcification. A standard CPB with bicaval cannulation was initiated, and cold cardioplegia was performed for myocardial protection after aortic cross-clamping. The aortic valve was carefully excised from the aortic annulus. After an appropriate prosthetic valve was selected, it was placed using five 2/0 non-absorbable monofilament polypropylene sutures with 1/2-circle 17-mm needles with continuous sutures. The aortotomy was closed with a double-layer suture of 4–0 polypropylene; the patient was weaned successfully off CPB with inotropic support and transferred to the intensive care unit. After 6 hours, blood pressure reduced and central

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venous pressure elevated and extremity became cool and cyanotic (Figure 1). Inotropic support was started with dobutamine and adrenaline (2 and 1 μg/kg/min) subsequently. After 3 days, inotropic drugs tapered and discontinued, and blood pressure stabilized, but cyanosis changed to dry gangrene (Figure 2). After 2 weeks, the acral part of lower and upper extremities auto-amputated and pecimens were sent to the pathology. The possibility of systemic embolization was ruled out by echocardiography, and carotid Doppler study, coagulation profile and a disseminated intravascular coagulation workup were all normal. The patient was started on aspirin, pentoxifylline and heparin. The parts were kept warm, and undue handling was avoided. In histopathological exam, there was only non-specific vasculitis with thrombosis.

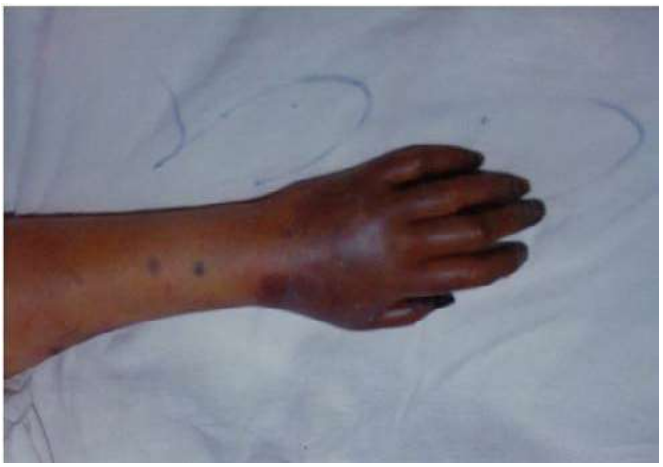

Fig. 1: Shows left-hand ischaemia.

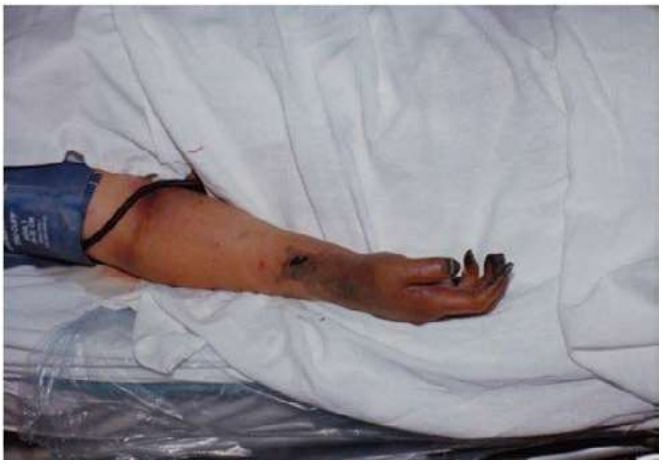

Fig. 2: Shows right-hand ischaemia.

The patient had not regained full consciousness on the following morning; however, she was found to be quadriplegic with non-voluntary movements of the four limbs or face. Both pupils were small and fixed. Magnetic resonance imaging of the brain revealed normal great artery and oedema of the brain cortex (Figure 3). Prolonged ventilatory support was maintained, and eventually a tracheostomy was performed to facilitate tracheobronchial suctioning and weaning. Facility for ultrasonography of the abdomen did not exist in our centre; however, abdominal ascitic fluid amylase was normal. A computed tomography scan of the abdomen was not done as the patient could not be shifted. Acute renal failure with anaemia was managed and kidney was recovered completely. However, the patient remained in a comatose state for 4 weeks with no neurological improvement. Despite all ventilatory, nutritional and nursing support, the patient died eventually of hepatic failure and generalized sepsis. Post-operative laboratories measurements included negative antinuclear antibodies and rheumatoid factor, and the elevation of C4–C3 and tissue necrotic factor alpha (TNF-α) as components of complement, but the Hepatitis B surface antigen (especially in polyarteritis nodosa) was negative. The patient did not have predisposing factors, such as hypertension, arthrosclerosis or diabetes, and the hypercoagulability state was rolled out by the normal serum level of protein C–S, factor of V Leiden and von Willebrand disease. The pathologic exam showed no specific vasculitis as seen in inflammatory response in CPB.

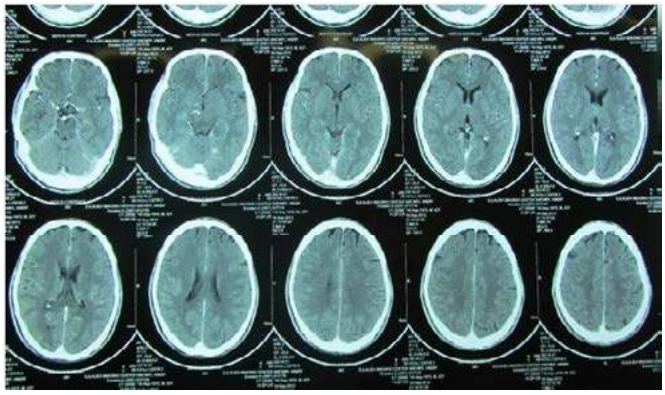

Fig. 3: Shows non-specific brain oedema caused by inflammation.

DISCUSSION

Distal organ ischaemia or acral parts involve arterioles with external diameters of 500–900 nm that may be affected by pathology variables, such as cholesterol emboli, immune complexes produced by CPB, atherosclerotic plaque or vasculitis syndrome (3). The most important differential diagnosis of CPB-induced systemic inflammatory response syndrome (SIRS) is cholesterol crystal emboli (CCE).

The presence of four or more risk factors should be taken as presumptive evidence of CCE. The risk factors that were not found in our patients include atherosclerotic plaque, hypertension, thrombolytic therapy male gender, smoking, hypercholesterolaemia, diabetes and resuscitation (4). The pathognomonic sign of CCE that was not seen in our patient was the needle-shaped cleft in the arteriole wall (5). Some studies found that, however, various treatment strategies have been tested to reduce the severity of the systemic inflammation induced by CPB and to improve the treatment, including anti-inflammatory drugs, novel components of the CPB and new surgical techniques, or anaesthetic drugs or technique but no single strategy has been proven effective; yet some of these drugs were evaluated in presiding studies (6–8). Production of humoral inflammatory mediators and priming of neutrophils by exposure to the CPB apparatus enable a 'post-pump' syndrome characterized by a SIRS and its anti-inflammatory counterpart, termed the compensatory anti-inflammatory response syndrome (9). Interleukin (IL-18) plays a central role in regulating and balancing these responses. IL-18 regulates the expression of the potent pro- and anti-inflammatory mediators, TNF-α (10) and IL-10 (11). In accord with this, Morgan found that the TT genotype was associated with an increased serum IL-18 concentration and also with an increased serum TNF-α and decreased serum IL-10. The increased serum TNF-α and decreased serum IL-10 levels are associated with an increased organ dysfunction (12).

CONCLUSION

The tremendous effect of the inflammatory response to ischaemia reperfusion and the use of CPB indicate the need for measures that might if not inhibit it, at least mitigate it. Thus, the control of risk factors, the reduction of ischaemic cardiovascular events, technical training for off-pump surgery as well as advances in anti-inflammatory therapy are measures to be reinforced while research should be encouraged so that these objectives are achieved.

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