

Acute myocardial infarction following transfusion reaction

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ABSTRACT

Indications for blood transfusion in critically-ill patients in general have become very restrictive. Still, the role for blood transfusion in the setting of acute coronary syndrome is unclear, as evidence regarding outcomes with different blood transfusion strategies has been conflicting. We report a 53-year-old Hispanic woman with acute ST-elevation myocardial infarction (STEMI) following a febrile nonhaemolytic transfusion reaction. Coronary angiogram showed complete occlusion of intracoronary stent in the left anterior descending (LAD) artery. Angiogram done earlier in the day had shown complete patency of the LAD stent with good distal flow. This suggests a possible role for the febrile nonhaemolytic transfusion reaction in triggering the stent occlusion and development of the STEMI.

Keywords: acute coronary syndrome, anaemia, blood transfusion, myocardial infarction, ST elevation myocardial infarction, transfusion reaction

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INTRODUCTION

Acute coronary syndrome is a leading cause of morbidity and mortality. Plaque disruptions and mural thrombosis lead to the development of acute coronary syndromes. Plaque disruptions commonly happen as a result of fracture of the plaque's fibrous cap, and less often, after superficial erosion of the intima overlying the plaque.⁽¹⁾ While the natural history of coronary atherosclerosis and mechanisms of acute coronary occlusion have been extensively studied, the triggering factors for acute coronary occlusion still remain unclear. Proposed triggering or contributing factors include coronary artery spasm, coronary artery embolisation, spontaneous coronary dissection, coronary arteritis, and hypercoagulable states.⁽¹⁾

Blood transfusions have been commonly utilised in the management of critically-ill patients with low haemoglobin levels. While most evidence favour a more restrictive transfusion strategy in general (< 7.0 g/dL),⁽²⁾ evidence is conflicting in patients with acute coronary syndromes. Hebert et al found the restrictive transfusion strategy at least as effective, or possibly superior, in critically-ill patients, with the exception of patients with acute coronary syndromes.⁽²⁾ A haemoglobin threshold

of 10 g/dL has been suggested in patients with acute coronary syndrome.^(3,4) Meanwhile, observational studies of patients with acute coronary syndrome by Rao et al⁽⁵⁾ and Yang et al⁽⁶⁾ showed a higher incidence of death and myocardial infarction in patients receiving blood transfusion. Analysis of adverse events in the study by Hebert et al actually showed a higher incidence of myocardial infarctions in the liberal strategy group (p = 0.02).⁽²⁾ In this light, we present an interesting case of acute ST-elevation myocardial infarction (STEMI) following a febrile blood transfusion reaction.

CASE REPORT

A 53-year-old Hispanic woman with a history of diabetes mellitus, hypertension and hyperlipidaemia was referred to the cardiology clinic for anginal symptoms. The patient underwent elective coronary angiography which demonstrated a 70% stenosis of mid left anterior descending (LAD) artery and 70% stenosis of the obtuse marginal 1 branch (OM1). The LAD lesion was dilated and stented with a drug-eluting stent, with angioplasty of the OM1 lesion planned at a later date. At a follow-up visit one week later, the patient complained of intermittent chest pain at home. She was admitted to the hospital for a repeat coronary angiography. Cardiac enzymes were not elevated and electrocardiogram (ECG) done on admission was unchanged from baseline ECG, showing old inferior wall myocardial infarction (Fig. 1a). Blood chemistries showed haemoglobin of 8.9 g/dL. Coronary angiography showed a patent LAD stent with no new lesion.

Since the patient had intermittent anginal symptoms, the decision was made to transfuse blood before discharge and to plan an elective angioplasty of the OM1 lesion at a later date, if she continued to have anginal symptoms. Two units of packed red blood cells were transfused after typing and cross-matching. Patient was afebrile (36.1°C) and chest-pain free at the beginning of the transfusion. Two hours after initiation of blood transfusion, after receiving approximately 220 ml of blood, the patient developed chills and a generalised burning sensation. Transfusion was stopped. Maximum temperature recorded during the episode was 37.8°C. The patient denied any chest pain or shortness of breath at that time. Symptoms improved after discontinuation of blood transfusion and administration of acetaminophen (paracetamol).

30 minutes later, the patient complained of substernal pressure similar to chest pain, radiating to the left arm, which did not respond to sublingual nitroglycerine. ECG showed diffuse ST elevation in anterolateral leads (Fig.

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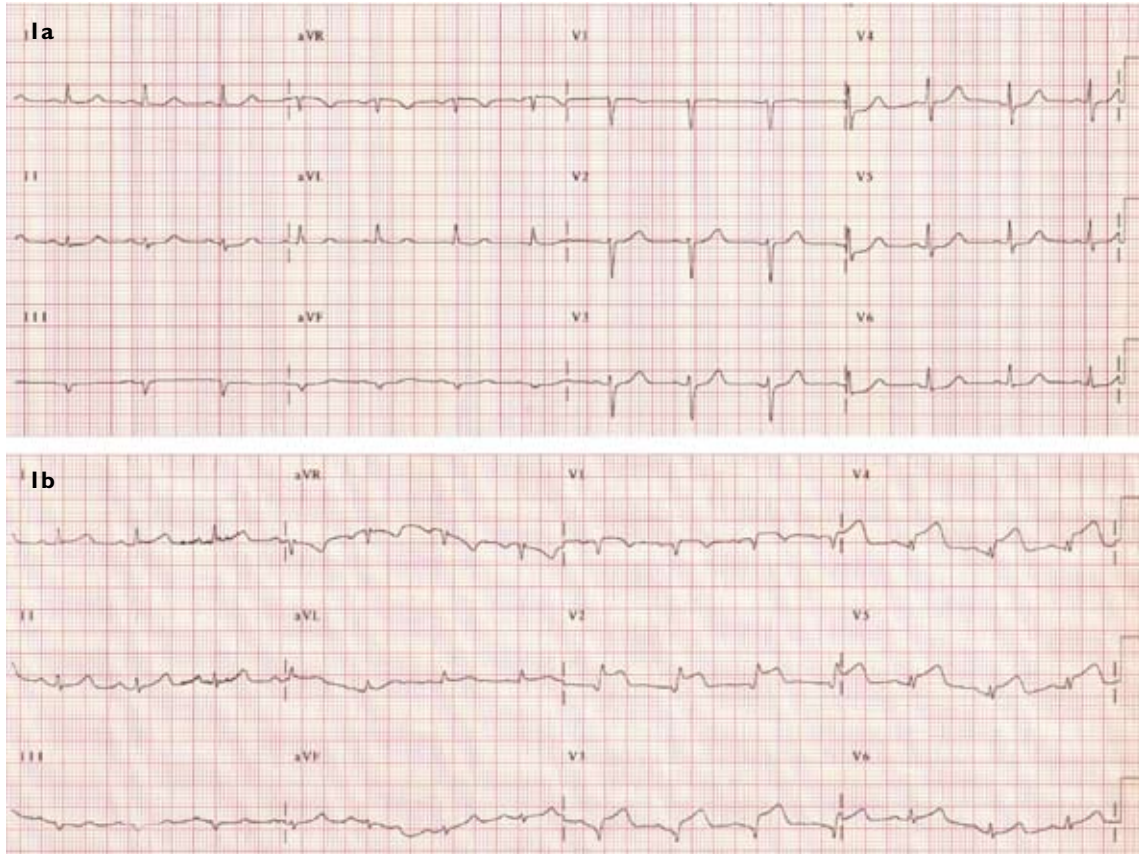


Fig. 1 (a) ECG on admission shows an old inferior myocardial infarction (unchanged from ECG done one week earlier). (b) ECG done one hour after onset of chest pain shows acute ST segment changes (elevations) in the anterolateral leads.

1b). Emergency coronary angiography showed complete occlusion of the LAD stent and stable OM1 lesion (Fig. 2a). The patient underwent successful angioplasty (Fig. 2b) and the subsequent hospital course was uneventful. Blood bank investigation into the apparent transfusion reaction showed no evidence of mismatch or haemolysis, and repeat antibody screen, direct and indirect Coombs tests were negative. The reaction was classified as febrile nonhaemolytic transfusion reaction (FNHTR).

DISCUSSION

Acute coronary syndromes result from plaque rupture and mural thrombus formation. With the advent of widespread use of stents (bare metal and drug eluting), incidence of subacute (< 30 days) and late thrombosis (> 30 days) are well-recognised. A recent two-year follow-up of the SIRIUS trial showed 0.2% incidence of subacute thrombosis in both bare metal and sirolimus eluting stents.⁽⁷⁾ Hence, subacute thrombosis of the LAD stent in this patient is not unanticipated, especially considering the patient's other risk factors, like diabetes mellitus. De-endothelialisation, which occurs during angioplasty and stent placement, leads to platelet activation and fibrin deposition, which in turn result in a cascade of events resulting in a neointima consisting of smooth muscle cells, extracellular matrix and macrophages, leading to stent restenosis.⁽⁸⁾ As discussed earlier, even though the pathogenesis of acute coronary syndromes has been well

studied, the possible triggering factors are unclear.

In this particular patient, the febrile transfusion reaction or the blood transfusion per se, appears to be the triggering factor for the acute coronary syndrome. Coronary angiography done on admission (less than 12 hours before the onset of symptoms) showed patency of the LAD stent with TIMI III (thrombolysis in myocardial infarction) flow. The patient was asymptomatic at the beginning of blood transfusion. The symptoms started 30 minutes after a possible FNHTR. These three facts, when seen together, imply that the FNHTR might have in some manner contributed to or precipitated the acute coronary syndrome.

Blood transfusions, in general, are known to result in a transient hypocoagulable state. However, the effect of transfusion reactions on coagulation is not well understood. Inflammatory responses in general have a tendency for inducing hypercoagulable state as is manifested by disseminated intravascular coagulation (DIC) in severe sepsis. Transfusion reactions are mediated by a release of proinflammatory cytokines, and when severe, can cause DIC requiring heparin therapy.⁽⁹⁾ Also, haemolytic transfusion reactions result in free circulating haemoglobin (haemoglobinaemia) which is known to cause vasoconstriction.^(10,11) Acute inflammatory states are generally associated with hyperdynamic states increasing myocardial oxygen demand. Blood transfusions in critically ill patients have been shown to

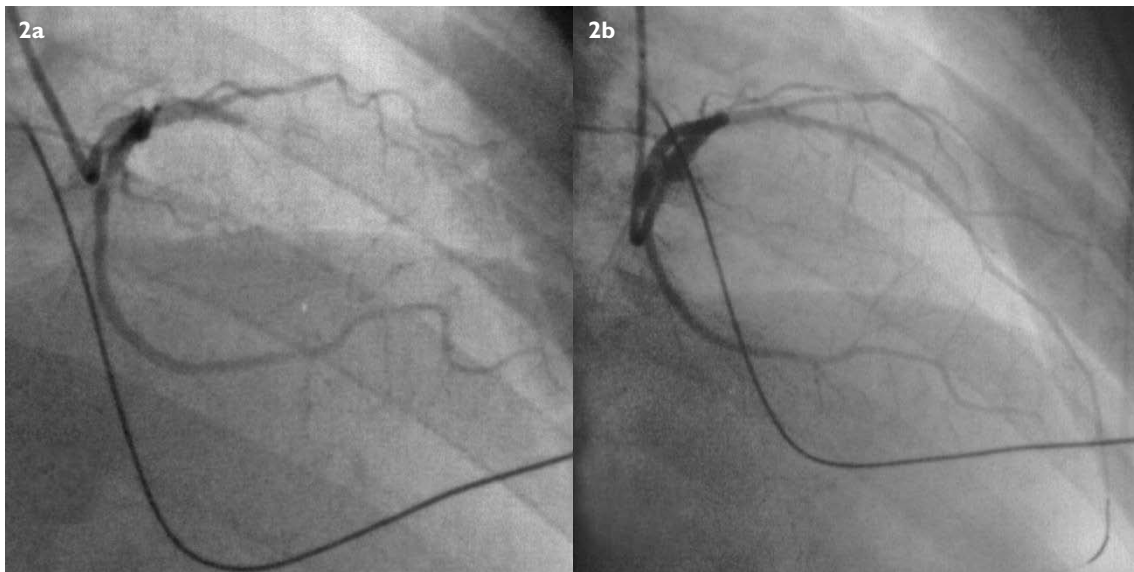


Fig. 2 (a) Coronary angiogram done after onset of acute ST segment myocardial infarction shows complete occlusion of the LAD stent. (b) Angiogram of LAD artery after repeat angioplasty shows restoration of blood flow.

increase myocardial work indices and myocardial oxygen demand.⁽¹²⁾ Thus, a severe transfusion reaction can make the conditions ripe for an acute coronary syndrome: hypercoagulability, vasoconstriction and increased myocardial oxygen demand.

Most transfusion reactions are classified into haemolytic transfusion reaction, FNHTR or allergic transfusion reaction.⁽⁹⁾ Antigen-antibody reactions leading to activation of proinflammatory cytokines and complement cascade, underlie all these reactions even though they differ in the culprit antigen-antibody and in intensity of the inflammatory reaction.^(13,14) The FNHTR in this patient, though not severe as a full-blown acute haemolytic transfusion reaction, is still a proinflammatory state and could have induced a hypercoagulable state leading to occlusion of the LAD stent. The hyperdynamic state resulting from the low grade fever could have worsened the supply demand mismatch resulting from the stent occlusion precipitating the STEMI.

Even though recent target vessel angioplasty and stent placement make this patient a risk for subacute thrombosis, the complete occlusion following a febrile transfusion reaction, of the LAD stent which was patent less than 12 hours earlier, raises the possibility of a role, causative or contributory, for the febrile transfusion reaction in the initiation of the acute coronary syndrome. Patients in acute coronary syndromes are more likely to receive blood transfusion than others. The incidence of FNHTR is roughly 0.5% for every unit of blood transfused.⁽⁹⁾ With roughly 12 million units of blood transfused each year in the United States,⁽⁵⁾ the population at risk is very large. More research needs to be done to clarify the role of FNHTR and transfusion reactions in the acute coronary syndrome.

REFERENCES

- Rosamond TL. Initial appraisal of acute coronary syndrome. Understanding the mechanisms, identifying patient risk. *Postgrad Med* 2002; 112:29-42.
- Hébert PC, Wells G, Blajchman MA, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. *N Engl J Med* 1999; 340:409-17.
- Hébert PC, Yetisir E, Martin C, et al. Is a low transfusion threshold safe in critically ill patients with cardiovascular diseases? *Crit Care Med* 2001; 29:227-34.
- Wu WC, Rathore SS, Wang Y, Radford MJ, Krumholz HM. Blood transfusion in elderly patients with acute myocardial infarction. *N Engl J Med* 2001; 345:1230-6.
- Rao SV, Jollis JG, Harrington RA, et al. Relationship of blood transfusion and clinical outcomes in patients with acute coronary syndromes. *JAMA* 2004; 292:1555-62.
- Yang X, Alexander KP, Chen AY, et al; CRUSADE Investigators. The implications of blood transfusions for patients with non-ST-segment elevation acute coronary syndromes: results from the CRUSADE National Quality Improvement Initiative. *J Am Coll Cardiol* 2005; 46:1490-5.
- Weisz G, Leon MB, Holmes DR Jr, et al. Two-year outcomes after sirolimus-eluting stent implantation: results from the Sirolimus-Eluting Stent in de Novo Native Coronary Lesions (SIRIUS) trial. *J Am Coll Cardiol* 2006; 47:1350-5.
- Bhatia V, Bhatia R, Dhindsa S. Drug-eluting intra-coronary stents: have we got the magic bullet? *J Postgrad Med* 2003; 49:291-6.
- Hoffman R, ed. *Hematology: Basic Principles and Practice*. 4th ed. Philadelphia: Churchill Livingstone, 2005.
- Schmidt PJ, Holland PV. Pathogenesis of the acute renal failure associated with incompatible transfusion. *Lancet* 1967; 2:1169-72.
- Creteur J, Vincent JL. Hemoglobin solutions. *Crit Care Med* 2003; 31(12 Suppl):S698-707.
- Dietrich KA, Conrad SA, Hebert CA, Levy GL, Romero MD. Cardiovascular and metabolic response to red blood cell transfusion in critically ill volume-resuscitated nonsurgical patients. *Crit Care Med* 1990; 18:940-4.
- Capon SM, Goldfinger D. Acute hemolytic transfusion reaction, a paradigm of the systemic inflammatory response: new insights into pathophysiology and treatment. *Transfusion* 1995; 35:513-20.
- de Rie MA, van der Plas-van Dalen CM, Engelfriet CP, von dem Borne AE. The serology of febrile transfusion reactions. *Vox Sang* 1985; 49:126-34.