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Case Report

Perioperative Management of a Patient With CD36 Deficiency Undergoing Urgent Cardiac Surgery

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CD36 (also known as the Nak antigen) is a multi-ligand scavenger receptor expressed on many cell types, such as platelets and monocytes. CD36 deficiency was first reported in 1989 in Japanese patients with platelet transfusion refractoriness (PTR). This condition is classified into the following 2 types: type 1 deficiency involves the loss of CD36 in many cell types, including monocytes, macrophages, and platelets, whereas type 2 deficiency involves the loss of CD36 in only platelets. In the Japanese population, type 1 and type 2 deficiencies are more common than that in Western countries, with a prevalence of 0.56% to 1% and 3% to 11%, respectively.[1] CD36 immunization via blood transfusion or pregnancy is a major concern in patients with type 1 deficiency, and it results in the development of anti-CD36 isoantibody, causing PTR and post-transfusion purpura in subsequent platelet transfusions.[2,3] Furthermore, type 1 deficiency is associated with atherosclerosis,[4] glycolipid metabolism,[5] and cardiomyopathy.[6] As CD36 is involved in free fatty acid uptake, fatty acid oxidation is replaced with glucose uptake in the CD36-deficient myocardium, which affects myocardial remodeling.[7,8] Therefore, type 1 CD36-deficient patients without prior anti-CD36 alloimmunization may require careful attention during perioperative management, especially blood management, when undergoing cardiac surgery. However, there is a paucity of data pertaining to these points. In this report, the authors describe a case of exertional angina requiring urgent coronary artery bypass grafting (CABG), wherein the diagnosis of type 1 CD36 deficiency was confirmed immediately before the cardiac surgery. Written informed consent was obtained from the patient for the publication of this case report.

Case Report

A 60-year-old, non-obese (body mass index: 22.1 kg/m^2) man with a past medical history of hypertension, hyperlipidemia, glucose intolerance, and chronic renal failure (estimated glomerular filtration rate of 42 mL/min and serum creatinine of 1.39 mg/dL) developed dizziness and lightheadedness during a brain magnetic resonance imaging examination for the screening of high adrenocorticotropic hormone levels. Electrocardiography revealed T-wave inversion in leads I, aVL, and V4 to V6. Subsequent coronary angiography revealed three-vessel coronary artery disease (90% stenosis in the distal right and left coronary arteries and 100% stenosis in the middle distal portion of the left circumflex branch), indicating advanced atherosclerosis. After additional investigations via echocardiography and laboratory testing, the patient was diagnosed with non-ST-segment-elevation myocardial infarction.

Accordingly, the patient was scheduled to undergo three-vessel CABG with cardiopulmonary bypass (CPB). Preoperative transthoracic echocardiography revealed left ventricular hypertrophy and left atrial enlargement but with preserved left ventricular contractility (ejection fraction, 60%). As triglyceride deposit cardiomyovasculopathy was suspected,

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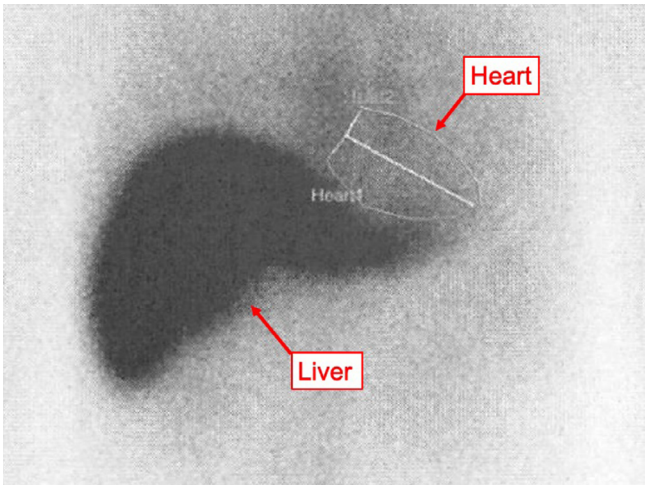

Fig 1. ^{123}I-β-methyl-P-iodophenyl-pentadecanoic acid scintigram showing absence of myocardial ^{123}I-β-methyl-P-iodophenyl-pentadecanoic acid uptake despite normal hepatic accumulation.

^{123}I-β-methyl-P-iodophenyl-pentadecanoic acid scintigraphy was performed, which revealed no uptake in the myocardium (Fig 1), suggesting type 1 CD36 deficiency. The confirmational flow cytometry testing of the peripheral blood was outsourced, and 20 units of CD36-negative ABO-RhD-compatible platelets (containing 4.0×10^{11} platelets[9]) were prepared by the Japanese Red Cross Society. Neither anti-CD36 isoantibody nor anti-human leukocyte antigen and human platelet antigen alloantibody was detected in the patient in antiplatelet antibody testing conducted by the Japanese Red Cross Society, indicating no past immunization. Just 2 days prior to the surgery, the patient was finally diagnosed with type 1 CD36 deficiency (both platelets and monocytes exhibited no CD36 expression). TEG6s platelet mapping revealed 33.6% platelet inhibition of the arachidonic acid channel (Supplementary Fig 1), reflecting the fact that the patient had been ingesting aspirin after the diagnosis of non-ST-segment-elevation myocardial infarction. However, urgent revascularization was prioritized considering the patient's general condition.

On the day of the surgery, the patient underwent autologous normovolemic hemodilution to reduce the need for an allogeneic blood transfusion. Given that myocardial glucose uptake was dominant in this patient with CD36 deficiency, 50% (weight/volume) hypertonic glucose solution and insulin were continuously administered to avoid hypoglycemia. This treatment was discontinued when the blood glucose level was 135 mg/dL at the beginning of the CPB.

Because the CPB duration was long (261 minutes), dobutamine, 3 μg/kg/min, was used only at the beginning of weaning; however, the patient developed systolic anterior movement and hypotension. Accordingly, a continuous infusion of landiolol (an ultra–short-acting β-blocker) and 600 mL of autologous blood transfusion were initiated. The patient was successfully weaned off with additional fluid loading. Although the platelet count was 119,000 cells/μL, the bleeding was difficult to control. As the patient developed coagulopathy after CPB, 480 mL of allogeneic ABO-RhD–compatible fresh frozen plasma (FFP) was transfused; the pre- and post-CPB values of the prothrombin time-international normalized ratio (PT-INR) and activated partial thromboplastin time (APTT) were 1.1 to 1.5 and 31.6 to 38.4 seconds, respectively. Subsequently, the bleeding was successfully stopped without transfusing CD36-negative platelets. The patient was transferred to the intensive care unit with intubation under sedation and was extubated 3 hours later. Perioperatively, the patient neither developed respiratory, circulatory, and neurologic symptoms nor did he require additional blood transfusions.

Discussion

CD36 deficiency has a relatively higher prevalence in East Asia, including Japan, than in Western Europe; this deficiency is observed in fewer than 0.3% of the population in East Asia.[10] However, it is rarely diagnosed, as most CD36-deficient individuals have no apparent clinical symptoms, and there are no standard screening tests. Currently, in addition to the detection of the anti-CD36 isoantibody in PTR patients, the absence of myocardial ^{123}I-β-methyl-P-iodophenyl-pentadecanoic acid uptake is the only reliable indicator of type 1 CD36 deficiency. This situation may stem from a limited number of studies on perioperative blood management in patients with type 1 CD36 deficiency without prior anti-CD36 alloimmunization requiring cardiac surgery.

To avoid alloimmunization with CD36, it is important to reduce allogeneic blood transfusions in CD36-deficient patients. From the perspective of patient blood management, collecting autologous blood by normovolemic hemodilution, as was performed in this case, seems reasonable.

As the patient had been ingesting aspirin, TEG6s platelet mapping on the day before the surgery revealed partial recovery of platelet function (inhibition rate of 33.6%), while the platelet count was 150,000 cells/μL. Nevertheless, CABG was performed as scheduled, along with the preparation of CD36-negative ABO-RhD–compatible platelets.

In a previous case report from Japan, passive anti-CD36 antibody in FFP from a CD36-deficient donor immunized through pregnancy caused severe thrombocytopenia in the recipient.[1] Hence, allogeneic ABO-RhD–compatible FFP transfusion seemed unsuitable in the authors' case. However, post-CPB coagulopathy (prolongations of PT-INR and APTT) prompted them to prioritize plasma transfusion to achieve rapid hemostasis. Additionally, tranexamic acid should have been administered in this case, even though it is not routinely used in the authors' institution as it may lead to tranexamic acid-related seizures.

The authors' patient exhibited no exacerbation of cardiac dysfunction during the surgery; however, the contribution of continuous glucose and insulin infusion until the initiation of the CPB procedure remains unclear. Furthermore, the appropriate blood glucose level for preserving the cardiac function in CD36-deficient patients remains undetermined.

CD36, together with oxidized low-density lipoprotein, forms an inflammatory site, which develops into

atherosclerosis. Previous animal studies have suggested that CD36 deficiency protects against atherosclerosis.[11] However, CD36 deficiency is associated with an increased risk of atherosclerosis in humans.[12] This discrepancy may indicate the existence of compensatory mechanisms for fatty acid metabolism in CD36-deficient individuals. Thus, once a patient is diagnosed with CD36 deficiency, a thorough examination for atherosclerosis should be performed.

Considering the prevalence of CD36 deficiency in East Asia, including Japan, a considerable number of patients with undiagnosed type 1 deficiency may undergo surgery and anesthesia. When a patient presents hypertrophic cardiomyopathy of unknown cause, CD36 deficiency should be suspected and further investigated. The authors' case highlights the importance of perioperative management for type 1 CD36 deficiency in patients with hypertrophic cardiomyopathy undergoing urgent cardiac surgery. Along with a definite diagnosis, preoperative management should include the preparation of CD36-negative platelets for possible transfusions as well as autologous blood collection by normovolemic hemodilution, provided the patient is not anemic. Intraoperative management should include monitoring of bleeding and cardiac movement to ensure timely provision of appropriate fluid loading and blood transfusions. Moreover, careful weaning is required as systolic anterior movement may easily occur in patients with CD36 deficiency-related cardiomyopathy.

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Conflict of Interest

T. T. reports grants from Edwards Life Sciences.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1053/j.jvca.2022.04.038.

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