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Case Report / Olgu Sunumu

DIFFUSE THROMBOSIS DURING PERCUTANEOUS CORONARY INTERVENTION IN A PATIENT WITH GLUCOSE 6 PHOSPHATE DEHYDROGENASE ENZYME DEFICIENCY

GLUKOZ 6 FOSFAT DEHİDROGENAZ ENZİM EKSİKLİĞİ OLAN HASTADA PERKÜTAN KORONER GİRİŞİM SIRASINDA YAYGIN TROMBOZ

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ABSTRACT

Through the pentose monophosphate pathway, glucose-6-phosphate dehydrogenase (G6PD) enzyme protects erythrocytes and hemoglobin molecules against oxidative stress. In G6PD enzyme deficiency, which is seen as the most common enzyme deficiency in the world; clinical conditions such as acute hemolytic anemia, neonatal jaundice, favism and inherited non-spherocytic hemolytic anemia are observed.

During acute coronary syndrome, oxidative agents and medications applied before and coronary angiography may cause hemolytic and thrombotic crisis. In this article, we performed coronary angiography on a 64-year-old female patient with G6PD deficiency with a pre-diagnosis of acute coronary syndrome. We present a widespread case of coronary thrombosis during and after percutaneous coronary intervention (PCI).

Keywords: Acute coronary syndrome, acute thrombosis, glucose-6-phosphate dehydrogenase, percutaneous coronary intervention.

ÖZET

Pentoz monofosfat yolu aracılığı ile glukoz-6-fosfat dehidrogenaz (G6PD) enzimi eritrositleri ve hemoglobin moleküllerini oksidatif strese karşı korur. Dünyadaki en sık enzim eksikliği olarak görülen G6PD enzim eksikliğinde; akut hemolitik anemi, yenidoğan sarılığı, favizm ve kalıtsal sferositik olmayan hemolitik anemi gibi klinik durumlar görülür.

Akut koroner sendrom esnasında genel klinik duruma bağlı oluşan oksidatif ajanlar ve koroner anjiyografi öncesi ve sırasında uygulanan medikasyonlar hemolitik ve trombotik krize neden olabilirler. Bu yazıda G6PD eksikliği bulunan 64 yaşındaki kadın hastaya akut koroner sendrom tanısı ile perkütan koroner girişim (PKG) sırasında ve takibinde gelişen yaygın koroner tromboz vakasını sunduk.

Anahtar kelimeler: Akut koroner sendrom, akut tromboz, glukoz-6-fosfat dehidrogenaz, perkütan koroner girişim.

INTRODUCTION

Glucose-6-phosphate dehydrogenase (G6PD) enzyme deficiency, the most common erythrocyte enzyme defect, is a recessively inherited disease due to X and its incidence is higher in women (1). The G6PD enzyme, which is involved in the pentose phosphate pathway, produces nicotinamide adenine dinucleotide phosphate hydroxylase (NADPH), which acts to prevent oxidative stress. The most important factors that trigger erythrocyte hemolysis in this enzyme deficiency are infections, fava, soybean, broad beans and medicines. The clinic is mostly asymptomatic. Agents that cause hemolysis in G6PD deficiency; analogs such as high-dose acetylsalicylic acid (ASA), acetanilide, niridazole, chloramphenicol, doxorubicin, dapsone, nitrofurantoin, quinidine, furazolidone, phenazopyridine, rasburicase, methylene blue, primaquine, vitamin K analogs, nalidixic acid, sulfamethoxazole (2).

Thrombosis in association with hemolysis is well recognized and has been reported in both hereditary and acquired hemolytic anemia, especially paroxysmal nocturnal hemoglobinuria (PNH), sickle cell disease and thalassemia major/intermedia. Although the mechanisms are not yet clear, circulating free hemoglobin or hemosiderin can cause severe damage to the kidney, causing acute renal failure and triggering disseminated intravascular coagulopathy (DIC) or increasing the risk of thrombosis. Relationship between G6PD and thrombosis is rare. G6PD enzyme deficiency is mainly a clinic that results in hemolysis. Exposure to oxidative agents triggers acute hemolytic attacks. The main diagnosis is made by seeing G6PD enzyme activity (2).

The association of clinical conditions such as ASA hypersensitivity, active gastric bleeding or intracranial hemorrhage with acute coronary syndrome creates difficulty for percutaneous coronary intervention (PCI). The combination of G6PD enzyme deficiency and acute coronary syndrome is one of these special conditions. In this case-report, we present our case with G6PD enzyme deficiency and non-ST elevation myocardial infarction (NSTEMI), where we applied intracoronary tirofiban infusion due to widespread thrombosis during PCI (3).

CASE REPORT

A 69-year-old female patient was admitted to the emergency department with a complaint of chest pain that started 3 hours ago and gradually increased. The

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patient's medical history had G6PD enzyme deficiency, atherosclerotic coronary artery disease and hypothyroidism. The patient's angina persisted. In electrocardiogram (ECG), there was normal sinus rhythm and ST segment depression in V4-V6 and DII-DIII-AVF derivations (Figure 1). Heart rate, blood pressure and body temperature were 69/min, 170/90 mmHg and 36.6℃, respectively. Dynamic T wave changes were detected in the precordial derivations in the control ECGs and early coronary angiography was planned. In laboratory values, troponin I value was 1188 ng / L, hemoglobin (Hb) 10.9 g / dl, urea 64 mg / dl, creatine 1.39 mg / dl, C-reactive protein (CRP) 1.51 mg / dl (Table 1).

Intravenous (IV) nitrate infusion was started to the patient. ASA was not given due to the risk of hemolysis. The patient was taken to the catheter laboratory immediately with a diagnosis of acute coronary syndrome. The procedure was performed by right femoral artery puncture. Coronary imaging revealed lesions in the osteal left anterior descending artery (LAD) and major obtuse marginal (OM) artery (Figure 2). The culprit lesion was accepted as OM lesion (Figure 2). The patient, who also had stenosis in the LAD artery, was considered appropriate to be discussed in the heart team council. But meanwhile, the patient developed hypotension after ventricular fibrillation and had no pulse. Thereupon, cardiopulmonary resuscitation was applied to the patient and PCI was decided for the culprit lesion and cardiopulmonary resuscitation was continued. It was decided to perform PCI for the culprit lesion in the OM artery. 180 mg ticagrelor and 5000 I.U./ml IV heparin were given. Drug-eluting stent (DES) implantation was applied to the culprit lesion at 16 atm (Figure 2). Due to the slow flow and total thrombosed stenosis in the LAD as a reason of thrombosis in the control angiography (Figure 3). The decision of LAD for PCI was made. A stent was implanted in the LAD proximal-middle region. Intracoronary bolus tirofiban (glycoprotein IIb / IIIa inhibitor) infusion was administered. Occlusion was observed as total thrombosis from the proximal (circumflex artery) CX in control images (Figure 4). Non-compliant (NC) balloon was applied to the lesion. CX distal flow was evaluated as TIMI-2 (Figure-5). Tirofiban maintenance infusion was decided and the patient was followed up in the coronary intensive care unit. Ticagrelor (90mg 2x1oral (PO)) and low molecular weight heparin (LMWH) treatment doses (8000 IU 2x1 subcutaneous (SC)), metoprolol 50 mg 1x1 PO, IV nitrate infusion and furosemide 80 mg IV treatment were administered.

Tablo 1. Laboratory values of patient.

Laboratory	Before angiography	After angiography
Troponin I (ng)	1188	5234
Hemoglobin (g/dl)	10.9	10.8
Hematocrit (%)	35	35
Urea (mg/dl)	64	69
Creatine (mg/dl)	1.39	1.40
C-reactive Protein (mg/dl)	1.51	2,9
Platelet (10^3/uL)	511	490

During the coronary intensive care follow-up, the patient was immediately evaluated due to the risk of acute hemolysis. The hematology was consulted and evaluated in terms of ASA use and acute hemolysis. Hemolysis parameters and G6PD enzyme level were seen. Hb 10.8 g / dl, hematocrit (hct) 35%, total bilirubin 0.6 mg / dl, direct bilirubin 0.1 mg / dl, lactate dehydrogenase (LDH) 294 U/L, prothrombin time 13.7 sec, reticulocyte ratio 2.19%, haptoglobin 264 mg/dl was detected. G6PDH enzyme levels were found to be low as G6PDH U/GR HB 5.0 (N:10.01-14.19), G6PDH U/1012 RBC 130.5 (N:290.4-411.6). With the recommendation received by the hematology, ASA 100 1x1 mg PO was started in the patient who had no signs of acute hemolysis. Ejection fraction (EF) 45%, anterolateral segmental wall motion defect was detected on echocardiography. The patient was extubated within 48 hours and his respiratory symptoms were stable. The patient was taken to the cardiology service because his cardiac symptoms regressed and his hemodynamics was stable. The patient was discharged from the cardiology service 11 days later with aspirin 100 mg 1x1, ticagrelor 90 mg 2x1, metoprolol 50 mg 1x1, atorvastatin 40 mg 1x1, pantoprazole 40 1x1 and furosemide 40 mg 1x1.

DISCUSSION

The prevalence of G6PD enzyme deficiency is higher in some regions. It has an incidence of over 1%, especially in the Mediterranean region, North Africa and Middle East countries (3). This distribution has a similar distribution to

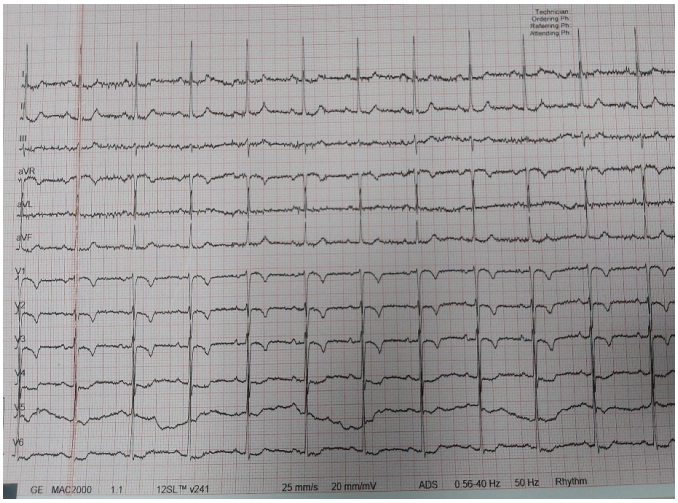

Figure 1. Electrocardiogram showing normal sinus rhythm and ST segment depression in V4-V6 and DII-DIII-AVF derivations.

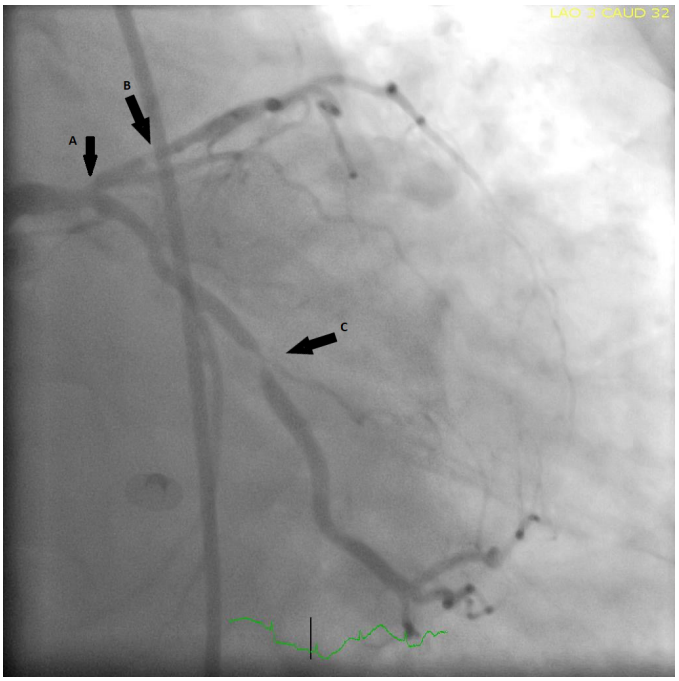

Figure 2. Non-critical stenosis of the distal left main coronary artery (A) and proximal left anterior descending artery (B). Culprit lesion in the obtuse marginal (OM) artery (C).

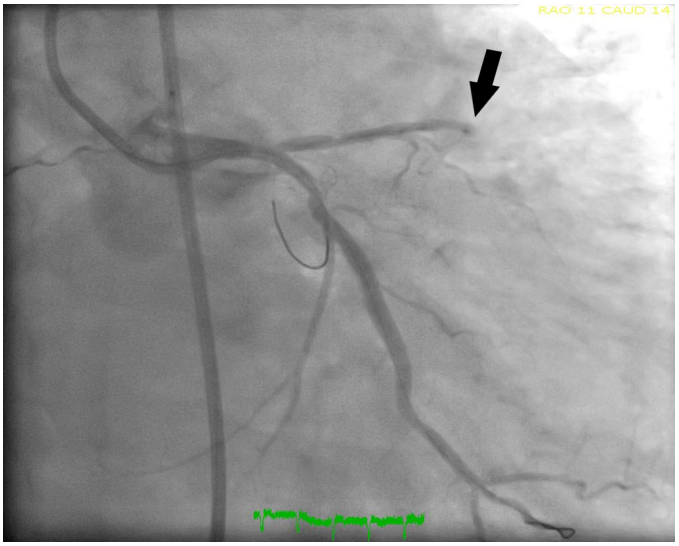

Figure 3. Coronary slow flow and total thrombosed stenosis in the left anterior decending artery.

thalassemia and malaria infection, and these two diseases are correlated in these regions because the treatments used for malaria infection increase hemolysis in favism (4).

There is a well-known relationship between hemolytic anemia and thrombosis, which can be seen with intravascular or extravascular hemolysis. Although the mechanisms are not yet clear, circulating free hemoglobin or hemosiderin can cause severe damage to the kidney, causing acute renal failure and triggering DIC or increasing the risk of thrombosis. Relationship between G6PD and thrombosis is rare. G6PD enzyme deficiency is mainly a clinic that results in hemolysis. What made our case

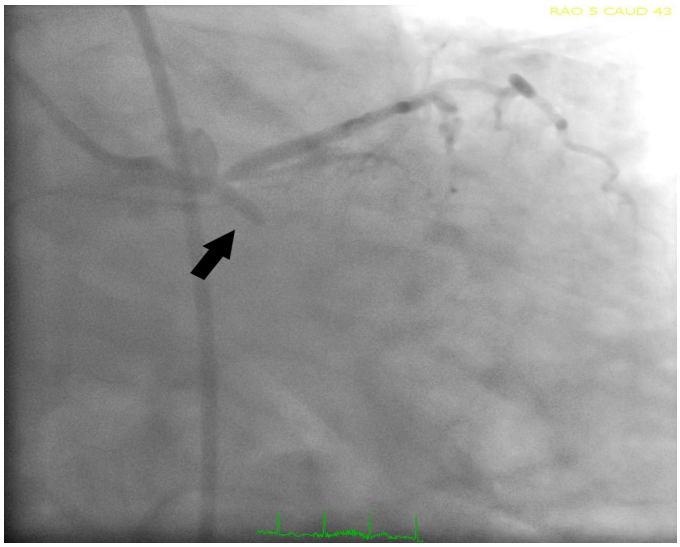

Figure 4. Total thrombosis from the proximal CX in control image.

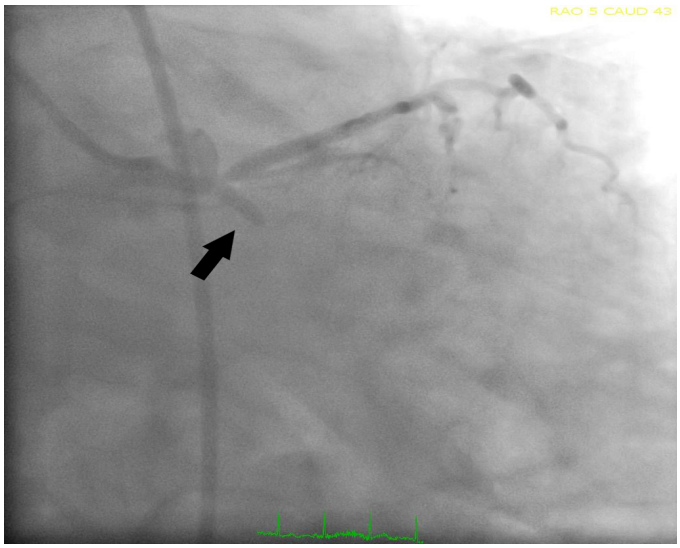

Figure 5. Final angiographic image after bolus infusion of tirofiban and non-compliant balloon.

different was that we encountered widespread coronary thrombosis without hemolysis. Since this situation requires us to use aggressive antiplatelet therapy, we have to be controlled in case of possible hemolysis.

In our case, we avoided ASA loading in the acute period, with the thought that it may cause hemolysis attack. We administered ticagrelor PO before the procedure and unfractionated heparin and GPIIb / IIIA inhibitor IV during the procedure. The relationship between ASA intake and hemolytic attacks in patients with G6PD enzyme deficiency has been reported several times, and a severe hemolytic process occurred after ingestion of small therapeutic doses not exceeding 2 g / day in most patients (5, 6). The use of low-dose aspirin (400 mg) was shown to be responsible for a small series (5%) of 40 hemolytic crisis cases reported in the G6PDdeficiency patient population (6).

Due to the fact that aspirin and its metabolites increase

the formation of hydrogen peroxide radicals, it facilitates hemolysis with oxidative stress on erythrocytes. G6PD, which acts in the pentose phosphate pathway, produces NADPH, which functions to prevent oxidative stress. NADPH is the cofactor of glutathione reductase, which reduces glutathione. Reduced glutathione neutralizes oxidative radicals and protects erythrocytes against oxidant stresses (2). As in our case, it may be considered not to give aspirin until the hematology opinion is obtained and ASA 100mg PO was started on the 24th hour of her hospitalization with the recommendation of hematology after the hemolysis parameters were seen. In one case reported by Rigattieri, there was no clear relationship between ASA use and hemolytic crisis (7). This situation can be considered good for our case, who had to receive dual antiplatelet therapy for 12 months and had 3 DES implanted in total.

We presented a rare case in which high-dose aspirin is contraindicated and extensive thrombosis developed in a patient presenting with NSTEMI. The situation we expected was hemolysis, but in our case, we encountered widespread thrombosis. In this patient, we primarily avoided aspirin by following a 2-step strategy. PCI was primarily considered due to the presence of active angina, dynamic ECG changes, and hemodynamic instability. In more stable cases, thrombectomy or surgery may be a good option to avoid maximal antiplatelet therapy.

CONCLUSION

In patients with G6PD deficiency and acute coronary syndrome coexistence, the risk of thrombosis should be kept in mind as well as hemolysis. GPIIa-IIIb inhibitor drugs can be used in this situation.

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Informed Consent: Informed consent was obtained from individual participant included in the study.

Authorship Contributions: Idea/Concept: MD, GT, Design: MD, ÖFA, Supervision: GT, Data Collection or Processing: MD, Analysis or Interpretation: MD, ÖFA, Literature Search: MD, GT, Writing: MD, Critical Review: GT, References And Fundings: -, Materials: MD, GT.

Conflict of Interest: No conflict of interest was declared by the authors.

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