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Equation with Many Unknowns in a Young Patient with Massive Coronary Thrombus

CASE REPORT

INTRODUCTION

Acute coronary syndrome (ACS) is associated with increased morbidity and mortality all over the world.[1] The most common mechanism of ACS is the rupture or erosion of an atherosclerotic plaque.[2] However, in young patients (<45 years old) presenting with ACS, etiologies other than the atherosclerotic plaque rupture or erosion, including acquired or congenital thrombophilia, illicit substance/drug use, coronary vasospasm, and spontaneous coronary artery dissection should be considered.[3-5] Herein, we presented the management of a 28-year-old male patient who presented with anterolateral ST-segment elevation myocardial infarction (STEMI) after intake of an energy drink and alcohol cocktail in whom detailed investigation unmasked the hereditary thrombophilia.

CASE REPORT

A 28-year-old male patient with unremarkable past medical history and family history except smoking was admitted to the emergency room with complaints of pressure-like chest pain radiating to his left shoulder and upper back for an hour. Physical examination revealed no abnormality. A 12-lead electrocardiography (ECG) on admission demonstrated sinus rhythm and ST-segment elevation at the anterolateral derivations (Figure 1). Bedside transthoracic echocardiography showed a left ventricular ejection fraction (LVEF) of 30%, and severe hypokinesia at the apical, anterior, and lateral segments of the left ventricle. After administration of aspirin 300 mg, ticagrelor 180 mg, atorvastatin 80 mg, and unfractionated heparin 4000 IU, the patient was transferred to the catheterization laboratory for coronary angiography and primary percutaneous coronary intervention (PCI). The right coronary artery was normal, but a giant thrombus was observed extending from the left main coronary artery to the left anterior descending (LAD) and circumflex (Cx) arteries and obstructing the LAD artery (Figure 2, Supplementary Video 1). 0.014-inch floppy guidewire was placed at the distal segments of the LAD and Cx arteries. Since the thrombus load was high, thrombus aspiration was attempted using a thrombus aspiration catheter, and a small amount of thrombus was aspirated. Thereafter, intracoronary tirofiban was administered and balloon-angioplasty was sequentially performed to fragment the thrombus in the LAD proximal segment. After all these interventions, thrombolysis in myocardial infarction (TIMI) grade 2-3 flow was restored at the LAD artery and no stent implantation was planned during the index procedure (Supplementary Video 2). As the procedure was performed on the night shift, intravascular ultrasonography (IVUS) guidance was not available. The patient was transferred to the coronary care unit (CCU). Unfractionated heparin and tirofiban infusion were administered for 48 h. Detailed history taken at the CCU revealed the drinking of 100 cl of beer, 2 bottles of energy drink (each bottle is 250 mL and includes 37.5 mg caffeine per bottle), and smoking weed-containing substance in the form of unknown cigarettes just before his chest pain onset. A toxicology panel was sent to the lab to detect any other drug abuse, including marijuana levels, which all tested negative, and the routine toxicology panel found no abnormal findings. Homocysteine level was 23.2 µmol/L (moderate elevation). Anti-nuclear antibody (ANA), anti-neutrophil cytoplasmic antibodies (ANCA), anti-endomysium IgA, anti-cardiolipin IgM, anti-cardiolipin

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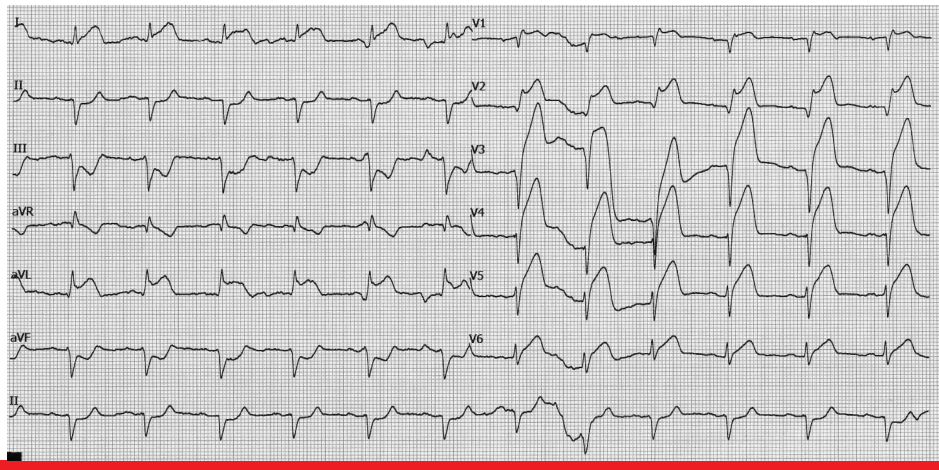

Figure 1. The 12-lead electrocardiography (ECG) on admission showed the ST-segment elevation at the anterolateral derivations.

IgG, anti-Ds-DNA, anti-centromere, anti-cyclic citrullinated peptide (CCP), beta-2-glycoprotein IgM, beta-2-glycoprotein IgG, and rheumatoid factor levels were negative. A computed tomography angiography with vasculitis protocol excluded the large vessel vasculitis, but an incidental multiple contrast filling defects (at the upper lobe of the right lung, the lingular segment, and the segmentary branches of the lower lobe of the left lung) consistent with pulmonary embolism were detected. Transesophageal echocardiography (TEE) was performed to exclude the possible right-to-left shunt and revealed no patent foramen ovale (PFO) or atrial septal defect (ASD). Control transthoracic echocardiography at the 72nd hour of his hospitalization revealed an LVEF of 50%, and the 2D strain showed a mild hypokinetic area at the anterior wall (Figure 3, Supplementary Video 3). Control coronary angiography on the 4th day of hospitalization using IVUS guidance demonstrated a thrombus at the proximal segment of the LAD artery without plaque erosion or rupture and TIMI grade 3 flow at the LAD artery (Supplementary Video 4A and 4B). The genetic panel for congenital thrombophilia revealed the MTHFR (677) homozygous and PAI 4G/5G heterozygous mutations. The remaining hospital stay was uneventful. Thus, he was discharged with warfarin 5 mg/day, ticagrelor 90 mg b.i.d., aspirin 100 mg/day, atorvastatin 80 mg/day, carvedilol 6.25 mg b.i.d., and ramipril 2.5 mg/day. Control coronary angiography was also scheduled for 1 month later to observe the disappearance of the coronary thrombus. There was no adverse clinical event during the 1-month follow-up. Control coronary angiography at the 1st-month visit showed TIMI grade 3 flow at the LMCA, LAD, and Cx arteries without any thrombus (Supplementary Video 5).

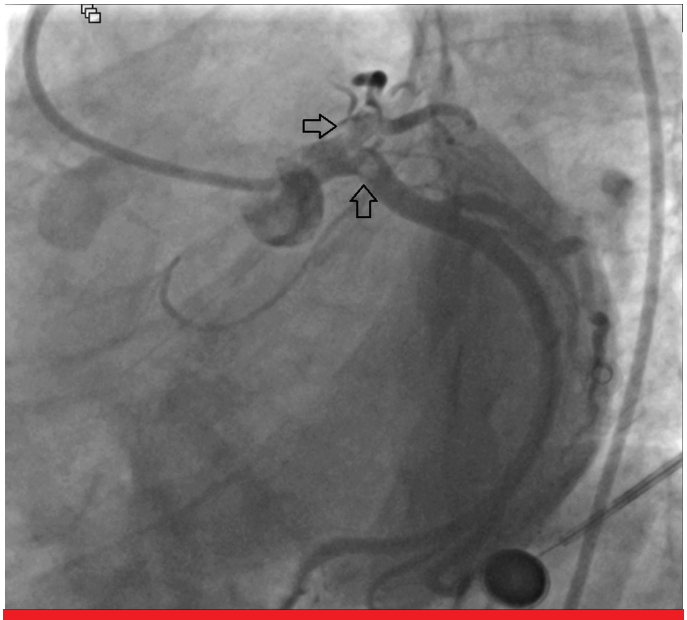

Figure 2. Coronary angiography on admission showed a giant thrombus extending from the left main coronary artery to the left anterior descending (LAD) and circumflex (Cx) arteries and obstructing the LAD artery.

DISCUSSION

Despite a decrease in death rate with an evolving medical service network and technology in ACS, it is still an important cause of morbidity and mortality worldwide and causes serious costs in health care in the long term.[6] Although atherosclerotic plaque rupture or erosion is the main underlying cause in most patients presenting with ACS, spontaneous coronary artery dissection, coronary artery embolism, vasospasm, myocardial bridging, illicit drug/substance use, acquired or congenital thrombophilia, and takotsubo syndrome can also cause ACS.[7] The most important risk factors for ACS in young patients are smoking, male gender, diabetes mellitus, obesity, hyperhomocysteinemia, hypertension, dyslipidemia, family history of coronary artery disease at an early age, hereditary coagulopathies/genetic mutations, illicit/performance-enhancing drugs.[8] We should suspect other causes of ACS, especially in patients with younger age, extreme findings during coronary angiography (e.g. massive coronary thrombosis, aneurysm, etc.), using illicit substances/drugs, and other systemic disease findings (concomitant arterial and venous thrombosis, vasculitis, etc.). Our patient had no previous history of any major cardiovascular risk factor except smoking. As he experienced the ACS event at a very young age, we have suspected other causes as mentioned above. When we detailed the history taking,

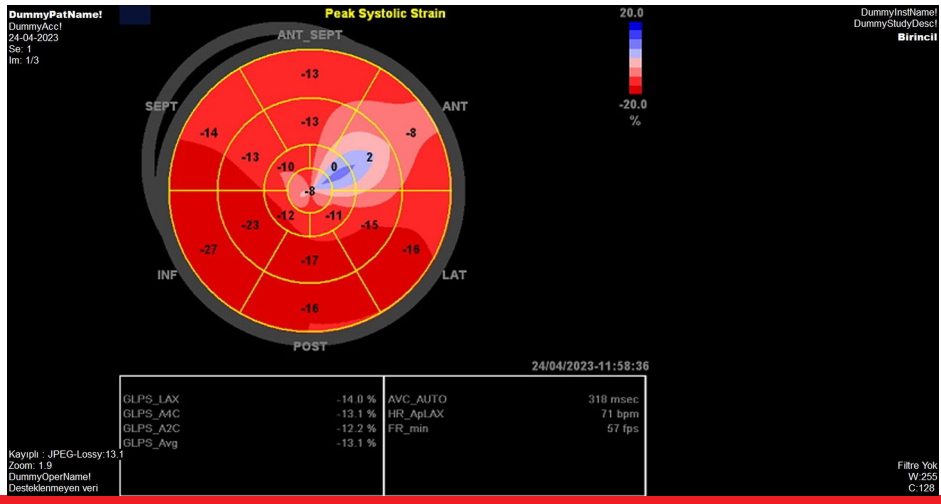

Figure 3. The 2D strain transthoracic echocardiography at the 72nd hour showed an improvement in the left ventricular systolic functions.

he admitted to drinking alcohol and energy drinks and smoking cigarettes containing unknown substances just before symptom onset. Thus, all those substances might have triggered the ACS event in our patient. As there was no atherosclerotic plaque rupture or erosion on IVUS and a fresh thrombus at the coronary arteries and the presence of pulmonary embolism at the same hospitalization, we also further thought about the underlying thrombophilia which has been confirmed by the genetic tests. It was obvious that the illegal drug/substance use was significantly associated with endothelial dysfunction and increased platelet aggregation.[4] Although randomized control studies are insufficient, current evidence and case reports in the literature show that energy drinks can cause ACS by increasing platelet aggregation and causing endothelial dysfunction in healthy young individuals without other risk factors.[9] According to the law in Türkiye, the total amount of caffeine in energy drinks is limited to not exceed 150 mg/L, inositol 100 mg/L, glucoronolactone 20 mg/L, taurine 800 mg/L. Our patient consumed a total of 500 mL of energy drinks, and the amount of caffeine he consumed was limited compared to energy drinks sold in many countries. Studies have shown conflicting results regarding whether energy drinks cause endothelial dysfunction. One study showed that Red Bull and 5-hour Energy drinks improved endothelial function, whereas 1 energy drink (NOS) and coffee did not significantly alter endothelial function.[10] Akhundova et al's[11] study showed that energy drinks with low caffeine content had a neutral effect on endothelial functions. Contrary to the results of this study, it has been shown that endothelial dysfunction develops after consumption of energy drinks and causes an increase in platelet aggregation.[12] Another study found that consumption of a single sugar-free energy drink (250 mL, 140 mg caffeine) was associated with a significant increase in platelet aggregation within 90 minutes in healthy volunteers, although it is not known which substance caused this.[13] In summary, there are various data in the literature about energy drinks. Even if it causes thrombosis, the substance and mechanisms by which this occurs have not been clearly elucidated. In our patient, the underlying MTHFR (677) homozygous and PAI 4G/5G heterozygous mutations along with alcohol use are the leading cause of coronary thrombosis.

Ponomarenko and Sukmanova[14] demonstrated that smoking and the presence of polymorphism in MTHFR were defined as significant risk factors for ACS at an early age. The C677T polymorphism of MTHFR results in elevated plasma homocysteine levels in homozygous mutated individuals and inhibition of the MTHFR enzyme to catalyze the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate[15] Individuals with homozygous mutation have higher homocysteine levels than heterozygous mutation.[16] The homocysteine level in our patient also revealed a moderate elevation. However, in some published reports, it was shown that normal homocysteine levels may also cause hypercoagulability and endothelial damage, which was primarily attributed to the adequate amount of folic acid in the patient's diet.[8]

In young patients presenting with ACS, illicit drug/substance exposure and underlying hypercoagulability should be excluded by detailed history taking and investigations. Our young smoking patient also had C677T homozygous polymorphism of MTHFR. At the same time, our patient had used 2 bottles of energy drinks and an unspecified prohibited substance. Since percutaneous coronary intervention has become easier with advanced methods, one of the most critical points in young patients is analyzing the types of coronary lesions. In our patient, we found the underlying causes of coronary thrombus by taking a detailed anamnesis. In this process, IVUS has been an important tool that guides us when determining the lesion characteristics. We encouraged the patient to abandon energy drinks and illicit substance use, which are known to cause hypercoagulability. To prevent unnecessary stent implantation, especially in young patients, and to prevent the recurrence of possible cardiac events, underlying mechanisms should be highlighted appropriately in such patients. Intracoronary imaging devices such as IVUS should be used if necessary to reveal lesion

characteristics. Treatment of patients should be individualized according to underlying diseases and coronary artery thrombus load at presentation.

Informed Consent: Detailed information was given to the patient regarding the possible contribution of the case report to the literature. The patient gave written and verbal consent for the publication of the case report.

Declaration of Interests: Dr. Canpolat is a proctor for Biotronik & Medtronic, and other authors have nothing to disclose.

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Video 1: Coronary angiography on admission showed a giant thrombus extending from the LMCA to the LAD and Cx arteries and obstructing the LAD artery.

Video 2: After administration of intracoronary tirofiban, balloon angioplasty was sequentially performed to fragment the thrombus in the LAD proximal segment. Finally, a TIMI grade 2-3 flow was restored at the LAD artery.

Video 3: Control transthoracic echocardiography at the 72th hour of hospitalization revealed an LVEF of 50% and mild hypokinesia at the anterior wall.

Video 4: Continuing thrombus at the proximal segment of the LAD artery, no plaque erosion or rupture, TIMI grade 3 flow at the LAD artery (4A: Coronary angiography, 4B: IVUS).

Video 5: The 1st-month visit showed TIMI grade 3 flow at the coronary arteries without any thrombus.

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