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Case Report

Myocardial Infarction with ST Segment Elevation in 19-Year-Old Adult with Multiple Genetic Mutations: A Case Report

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Abstract

Introduction: The clinical manifestations of coronary artery thrombosis are the leading cause of death in developed countries the pathogenesis of arterial thrombotic disease involves multiple complex genetic and environmental factors. It is usually related to atherosclerosis, thrombosis, and their interaction.

Case presentation: We report a 19-year-old male patient who had acute anterior myocardial infarction with ST segment elevation an emergency coronary angiogram was performed revealing a 100% thrombotic occlusion of the proximal portion of Left Anterior Descending (LAD), the lesion was treated by a third-generation drug-eluting stent. In this case, we have a mixture of risk factors predisposing to the occurrence of myocardial infarction at this young age including smoking and a strong positive family history of myocardial infarction, moreover, after investigation, we found eight predisposing genetic mutations to coronary artery thrombosis.

Conclusion: The precipitating factor in the transformation from stable or subclinical atherosclerotic disease to acute myocardial infarction is acute thrombosis at the location of a ruptured and lipid-rich atherosclerotic plaque. In the current era of elucidation of the human genome to improve their understanding of the pathobiology of arterial thrombosis, researchers have focused on the molecular genetics of thrombosis and atherosclerosis, and many genes contributing to increasing the disease risk have been identified. Most of these genes differ from those involved in venous thrombosis, as these entities have essential differences in pathobiology.

Keywords: Myocardial infarction; Percutaneous coronary intervention; Coronary artery thrombosis; Inherited hypercoagulable states; Genetic mutations

Abbreviations

ACE: Angiotensin I Converting Enzyme; ACS: Acute Coronary Syndrome; AMI: Acute Myocardial Infarction; APLS: Anti Phospholipid Syndrome; APO B: Apolipo Protein B; BMI: Body Mass Index; CABG: Coronary Artery Bypass Graft; CAD: Coronary Artery Disease; CCU: Coronary Care Unit; ECG: Electrocardiogram; EF: Ejection Fraction; FGB: Fibrinogen Beta Chain; I/D: Insertion/Deletion; LAD: Left Anterior Descending Artery; MI: Myocardial Infarction; *MTHFR*: Methylenetetrahydrofolate Reductase; PAI-1: Plasminogen Activator Inhibitor-1; PCI: Percutaneous Coronary; RBBB: Right Bundle Branch Block; STEMI: ST Segment Elevation; TIMI: Thrombolysis in Myocardial Infarction

Introduction

Acute Myocardial Infarction (AMI) is a major cause of death worldwide and it is rare in teenagers and young adults, the incidence has increased over years past at younger ages, and the incidence of AMI in young people was as low as 2% to 6% [1,2]. In the Global Registry of Acute Coronary Events (GRACE) study, the prevalence of young Acute Coronary Syndrome (ACS) was 6.3% [3], in the Thai ACS Registry, it was 5.8% [4] and in Spain Registry, it was 7% [5]. AMI has recently begun to rise likely due to the presence of multiple risk factors such as cigarette smoking obesity, diabetes insulin resistance metabolic syndrome, lipid abnormalities positive family history of Coronary Artery Disease (CAD), and cocaine use. CAD is a multifactorial disorder; identifying gene mutations that may account for the development of CAD is fundamental especially in the young who have a highly positive family history that predisposes to Myocardial Infarction (MI).

Infarcts pathophysiology is varied, in people who are genetically predetermined or have familial hyperlipidemia they usually happen due to atherosclerotic plaque rupture. A comprehensive medical history may help to define etiology and guide further management. Diagnostic coronary angiography is important moreover to reduce the incidence of recurrent cardiac attacks, delicate risk factor modification and treatment plan of the underlying cause should be achieved.

We report a 19-year-old male patient who had acute anterior myocardial infarction with ST segment elevation the lesion was treated by a third-generation drug-eluting stent. In this case, we have a mixture of risk factors predisposing to the occurrence of myocardial infarction at this young age including smoking and a strong positive family history of myocardial infarction.

Case Presentation

A-19 years old, male, college student, weight 72 kg, height 170 cm (BMI:24.9), smoker 6 packs/year, occasional alcohol (once a month).

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There is no other medical history and no pharmacological history or drug abuse. Surgical history: Tonsillectomy at the age of 10 years.

Family history: positive family history for CAD in first- and second-degree relatives:

- His father had a myocardial infarction at the age of 38.
- Coronary Artery Bypass Graft (CABG) in the oldest paternal uncle at the age of forty years.
- Myocardial infarction in the second paternal uncle at the age of forty-five.
- CAD in maternal uncle at the age of fifty.

The patient complained of sudden pressured chest pain left behind the sternum, spreading to the left arm, gradually inciting the pain at rest at 4 pm and increasing its intensity (pain intensity 10/10), accompanied by heavy cold sweats and nausea, without other accompaniments, the patient was referred to an external doctor's office 30 minutes after the onset of the pain, and he was diagnosed with acute anterior wide myocardial infarction with ST-segment elevation, he was given a sedative and he was referred to our hospital where the patient arrived to the emergency about 2 hours and 40 minutes after the onset of the pain. The patient was given 300 mg clopidogrel 324 mg aspirin, 5000 unit's heparin, nitroglycerin sublingual, and 80 mg atorvastatin immediately. Twelve lead Electrocardiogram (ECG) revealed: sinus rhythm with ST segment elevation (STEMI) of 5 mm in lead V2-V5 and 2 mm in lead I, Avl V6 (Figure 1 and 2), with reciprocal ST depression in lead II, III, AVF which led to a diagnosis of wide anterior STEMI. The Chest X-Ray showed a normal-sized heart with no abnormality noted in the lungs.

On admission, his heart rate was 110 beats per min and his blood pressure was 70/40 mmHg, his oxygen saturation was 85% on room air. TIMI score was: 9 points: 35%, 30-day risk for mortality. Killip class: 4.

The patient was emergently taken to the cardiac catheterization labina cardiogenic shock state after 17 minutes of arrival (door to balloon 17 min), coronary angiography using the left femoral artery approach with a 6 French sheath showed acute large thrombotic total occlusion (100%) of the ostium of Left Anterior Descending Artery (LAD). The artery was opened using a new generation of drug-eluting stent (RESOLUTE INTEGRITY 3.5 mm diameter/34 mm length), as a result, the normal flow of the anterior descending artery was restored (TIMI score flow grade 3) (Figure 3).

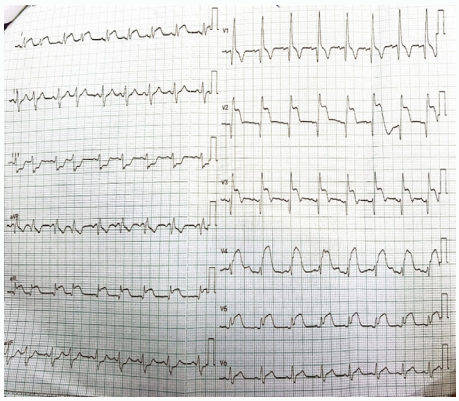

Figure 1: First 12 lead ECG.

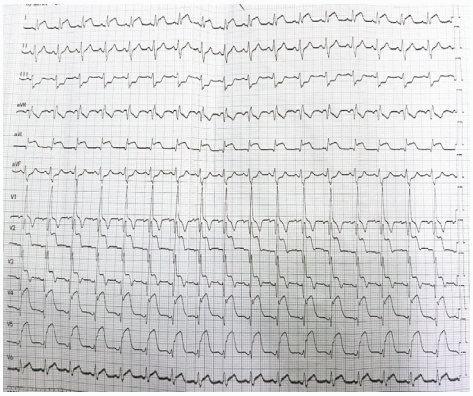

Figure 2: First 12 lead ECG.

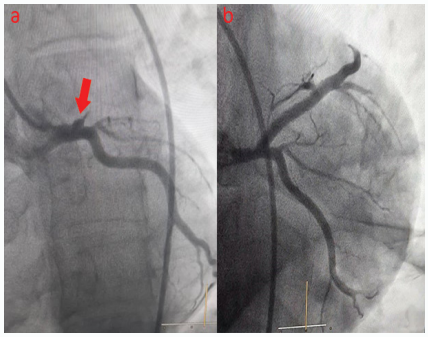

Figure 3: The target artery after and before percutaneous coronary (PCI) intervention.

A Tirofiban bolus of 25 mcg/kg was administered followed by 0.15 mcg/kg/min infusion for 18 hours with the transfer of the patient to the Coronary Care Unit (CCU) for follow-up where the patient remained for 4 days.

On the first day in CCU: The patient was on norepinephrine infusion 8 mcg/min and tirofiban infusion. The patient developed an episode of non-sustained ventricular tachycardia 5 hours later of Percutaneous Coronary (PCI) and was managed by giving amiodarone loading dose 150 mg first then followed by maintenance dose for 24 hours.

Echocardiography: apical anterior septal wall dyskinesia with reduced left ventricular systolic function EF: 30%, normal valves with normal pericardium (stunning heart).

On the second day: The dose of norepinephrine was gradually halved, with the start of giving dapagliflozin 10 m/qd, spironolactone 25 mg/qd with DAPT, and atorvastatin 40 mg/qd. His vital signs were blood pressure 90/50 mmHg, heart rate 112, oxygen saturation 94%.

Twelve lead ECG showed a Right Bundle Branch Block (RBBB) pattern then disappeared on the third day.

On the third day: Norepinephrine was withdrawn, and we started giving Ivabradine 5 mg bid, and furosemide 20 mg qd.

On the fourth day: The patient was discharged to the floor after stabilizing his clinical condition. His vital signs were: Blood pressure 97/51 mmHg, heart rate 95 oxygen saturation 95%.

Echocardiography: apical Anterior septal wall dyskinesia with reduced left ventricular systolic function Ejection Fraction (EF): 37%,

normal valves with normal pericardium.

Chemical lab tests: Cardiac enzymes were gradually elevated and peaked after 24 hours CKMB: 344 - CK: 4600 and then gradually regressed without elevation after that (Table 1).

The patient was discharged on the sixth day of admission, after ensuring that the clinical and vital condition was fully stable and without cardiac mechanical complications, ECG revealed the reverse of electrical changes (Figure 4). Discharge treatment plan: aspirin 100mg qd, clopidogrel 75 mg bid, apixaban 2.5 mg bid, atorvastatin 40 mg /qd, carvedilol 3.125 bid, spironolactone 25 mg qd, dapagliflozin 10 mg qd, perindopril 2 mg qd.

Further genetic investigations on follow-up, for determining the genetic risk factors, in this case, revealed eight mutations that are previously reported to be involved in MI at this young age (Table 2).

Table 1: The patient's chemical lab tests.

	First day	On discharge	After one week	Unit
WBC	19000	11000		
HGB	14.5	13.5		g/dl
PLAT	358	308		
Glucose	148	90		Mg/dl
CREATININE	1.1	1		Mg/dl
UREA	31	32		Mg/dl
CK-TOTAL	1406	270		u/l
CK-MB	108	20		u/l
CHOLESTROL	251		162	Mg/dl
LDL-Chol	201.48	121	80	Mg/dl
HDL- Chol	34	22	34	Mg/dl
Triglyceride	299	156	125	Mg/dl
AST	568	36		u/l
ALT	184	54		u/l
CRP	17.6			Mg/l
INR	1.04	1		
K+	4.3	4.1		mmol/l
Na+	134.5	136		mmol/l

Table 2: Genetic test of CVD-DNA by PCR.

Factor V (G1691A) Leiden	Normal
Factor V(H1299R)	Mutant Heterozygous
Factor II (G20210A)	Normal
Factor XIII (V34L)	Mutant Heterozygous
β -fibrinogen (455G/A)	Mutant Heterozygous
Plasminogen activator inhibitor-1 (PAI-1)	Mutant Heterozygous
Platelets glycoprotein IIIa	Mutant Heterozygous
MTHFR(C677T)	Normal
MTHFR(A1298C)	Mutant Heterozygous
Angiotensin converting Enzyme	Mutant Heterozygous
Apo B (R3500Q)	Mutant Heterozygous

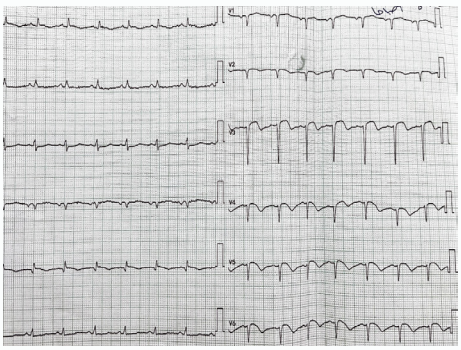

Figure 4: 12 lead ECG for the day of discharge.

Discussion

In this paper, we present the first case reported in Syria of STEMI in a young male with no previous history of angina. A highly positive family history of CAD was reported, and after appropriate management, further genetic investigations revealed eight genetic mutations reported to be positive risk factors for CAD at this young age.

CAD is very unusual at this young age, only a handful of similar cases have been previously reported in the literature [6-8]. The uniqueness of our report is the success in the identification of the known risk mutations. MI in the young is divided into two groups the first group includes patients with coronary artery disease of different etiology and with angiographically normal coronary arteries which can be caused by thrombosis, embolization, spasm, arteritis or myocardial bridging. As in the case of venous thrombosis, coronary thrombosis can be observed in hypercoagulable states, such as Antiphospholipid Syndrome (APLS), protein C and protein S deficiency, factor V Leiden mutation, or nephrotic syndrome [9-12]. MI can also be caused by coronary artery spasm which can be seen in patients with alcohol abuse [13] or cocaine abuse [14]. The second group is CAD with [15,16], angiographically abnormal coronary arteries such as accelerated atherosclerosis, ectasia, aneurysms, anomalous origin of coronary arteries, and spontaneous dissections [17,18].

Proteinuria related to nephrotic syndrome leads to the loss of proteins, which in turn alter the concentration and activity of coagulation factors. Consequently, factors IX, XI, and XII are lost due to urinary excretion [13]. Increased synthesis of factors II, VII, VIII, X, XIII, and fibrinogen leads to raised blood levels while the liver compensates for hypoalbuminemia. In addition, this affects the fibrinolytic system, with decreased concentrations of plasminogen and increased levels of plasminogen activator. Moreover, with hypertriglyceridemia, evidence of decreased fibrinolytic activity has been reported [18,19]. Regarding APLS, the prominent features of this syndrome are arterial and venous thrombosis in addition to antiphospholipid antibodies and recurrent pregnancy loss. The most important antiphospholipid antibodies involved in atherosclerosis and thrombosis are the anticardiolipin antibody, the lupus anticoagulant, prothrombin, and IgG antibodies against plasma phospholipid-binding proteins like β2-glycoprotein I [20]. Factor V Leiden mutation: factor V is a cofactor that allows factor Xa to activate prothrombin, which results in the enzyme thrombin. Fibrin is formed by the cleavage of fibrinogen by thrombin, which polymerizes to form most of the clot. In the presence of this mutation, the hypercoagulable state happens as the anticoagulant protein C which normally inhibits the pro-clotting activity of factor V is not capable of binding normally to factor V. Protein C and protein S are glycoprotein's which are essential components of the anticoagulant cascade, and both are Vitamin K dependent. Protein C and protein S deficiency lead to the loss of anticoagulant activity, thereby leading to unchecked thrombin generation, resulting in thromboembolism [9-12].

Genetic Determinants of Arterial Thrombosis: Thrombosis cases occur within the arteries and are not only limited to the veins. Arterial thrombosis is a multifactorial disorder multiple genetic and environmental factors have been reported to be involved. Hundreds of different thrombotic gene mutations have been identified, the most common are in coagulation factors (β-Fibrinogen, prothrombin G20210A, Factor V Leiden, FVII, and FXIII); Methylenetetrahydrofolate Reductase (*MTHFR*) A1298C

and *MTHFR C677T* mutations fibrinolytic factors (tissue-type plasminogen activator, plasminogen activator inhibitor-1, and thrombin-activatable fibrinolysis inhibitor), platelet surface receptors, Angiotensin I Converting Enzyme (ACE), Apo lipoprotein B (APOB) and APO E mutations.

MTHFR A1298C and *MTHFR C677T* mutations the *MTHFR* gene produces an enzyme that aids in homo cysteine level regulation. The most studied inherited risk factors for elevated homo cysteine levels are genetic mutations in *MTHFR*, elevated homo cysteine levels increasing the risk of CAD, arterial and venous thrombosis, and developing atherosclerosis. *MTHFR C677T* or "thermolabile" mutation is the most common *MTHFR* mutation, *MTHFR A1298C* is also a common mutation [21-23].

β-fibrinogen (455G/A): the fibrinogen beta chain (FGB, β-fibrinogen) gene is related to the increased severity of CAD. The mutation "-455G>A" increases the risk of ischemic stroke and MI in the young population. Many studies showed that patients carrying the allele "-455A" have higher plasma fibrinogen levels, resulting in an increased risk of arterial thrombosis [24-26]. Plasminogen activator inhibitor-1 (PAI-1): high levels of plasma PAI-1 affect the fibrinolytic system which leads to permanent fibrin clot formation thus this mutation may help in the diagnosis of CAD by aiding in the evaluation of the performance of the fibrinolytic system [27]. Angiotensin I Converting Enzyme (ACE): ACE converts angiotensin I into angiotensin II, which is a vasoconstrictor, this results in the destruction of vasodilator bradykinin. Insertion/Deletion (I/D) mutation in the ACE gene affect ACE levels, I/D mutation has been reported to be a risk factor for MI in smokers and older population; elevated ACE activity and plasma levels are also associated with the D allele [28,29].

APO B mutations: Familial defective APOB is a cause of autosomal dominant hypercholesterolemia. An increased risk of CAD has been reported to be associated with various variations of APO B. R3500Q is a rare dominant mutation, that is related to an increased risk of atherosclerosis and severe hypercholesterolemia [30].

Conclusion

The precipitating factor in the transformation from stable or subclinical atherosclerotic disease to acute myocardial infarction is acute thrombosis at the location of a ruptured and lipid-rich atherosclerotic plaque. In the current era of elucidation of the human genome, to improve their understanding of the pathobiology of arterial thrombosis, researchers have focused on the molecular genetics of thrombosis and atherosclerosis, and many genes contributing to increasing the disease risk have been identified. Most of these genes differ from those involved in venous thrombosis, as these entities have essential differences in pathobiology.

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