Acute ST-Segment ElevationMyocardial Infarction in a Patient with Beta Thalassemia / Hemoglobin E

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Abstract: Acute myocardial infarction (AMI) has been very rare in beta thalassemia and has never been seen in the patients with beta-thalassemia/hemoglobin E. Herein we report acase of 38-year-old Thai man with underlying transfusion-dependent beta-thalassemia/Hb E disease which is proved by the genotype study. Other concurrent morbidities arethe low LDL, low HDL, secondary hemosiderosis and hypogonadism. He presents with acute chest tightness and heaviness during watching the television. He is definitely diagnosed as acute ST segment elevation MI of infero-lateral wall based on the history of the acute chest discomfort, the elevation of ST segment on ECG and increased cardiac enzymes.The immediate cardiac catheterization demonstrates the white thrombus completely occluding the LAD and the LCX. He completely recovers from acute MI after the immediate treatment with the percutaneous coronary intervention (PCI) withsimultaneousthrombolytic therapy. The established riskfactors for CAD cannot be identified in our case except for the low HDL while the attributing factors such as high platelet countafter splenectomy, high serum ferritin and low serum testosterone are proposed.

Key words: Myocardial Infarction, Beta thalassemia/hemoglobin E, Hemosiderosis, Low HDL, Hypogonadism

บทคัดย่อ: กล้ามเนื้อหัวใจตายเฉียบพลันแบบ ST-segment ยกตัวในผู้ป่วยโรค BetaThalassemia / Hemoglobin E

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ภาวะกล้ามเนื้อหัวใจตายเฉียบพลันพบได้น้อยมากในผู้ป่วย beta thalassemia และไม่ยังเคยพบเลยในผู้ป่วย beta-thalassemia/hemoglobin E เราจึงเสนอรายงานผู้ป่วย 1 รายซึ่งเป็นชายไทยอายุ 38 ปีที่มีโรคประจำตัวคือโรค beta-thalassemia/Hb E ซึ่งยืนยันการวินิจฉัยด้วยวิธี PCR ต้องได้รับเลือดประจำโรคประจำตัวอื่นได้แก่ LDL ต่ำ, HDL ต่ำ, ภาวะเหล็กเกินทุติยภูมิและฮอร์โมนเพศชายต่ำมีอาการจุกแน่นอกกะทันหันระหว่างนั่งดูโทรทัศน์ผู้ป่วยได้รับการวินิจฉัย ว่าเป็น ภาวะกล้ามเนื้อหัวใจตายเฉียบพลันที่ผนังด้านหลังและด้านข้างแบบ ST ยกตัวเพราะมีอาการเจ็บแน่นอก, ตรวจคลื่นหัวใจพบการยกตัว ST segment และมีเอนไซม์ของหัวใจเพิ่มขึ้นผู้ป่วยได้รับการตรวจสวนหัวใจทันทีพบว่ามีการอุดตันเต็มที่ของเส้นเลือด LAD และ LCX ด้วยก้อนลิ่มเลือดสีขาวแต่ผู้ป่วยฟื้นตัวเป็นปกติทันทีที่ผ่านการทำ percutaneous coronary intervention (PCI) ร่วมกับการให้ยาละลายลิ่มเลือดปัจจัยเสี่ยงที่ชัดเจนในผู้ป่วยรายนี้ไม่มี มีก็เพียงภาวะ HDL ต่ำร่วมกับปัจจัยเสริมอื่น ๆ ได้แก่เกล็ดเลือดเพิ่มสูงหลังตัดม้ามภาวะเหล็กเกินและฮอร์โมนเพศชายต่ำ

คำสำคัญ: ภาวะกล้ามเนื้อหัวใจตายเฉียบพลัน, beta thalassemia/hemoglobin E, ภาวะเหล็กเกิน, ไขมันดีในเลือดต่ำ, ฮอร์โมนเพศชายต่ำ

Introduction

Beta-thalassemia / hemoglobin (Hb) E is a common genetic disease in Thailand[1]. And its clinicalcharacteris-tics mainlyinclude anemia withvaried severity from asymptomatic to transfusion-dependent, jaundice, hepato-splenomegaly[2] and various cardiac manifesta-tionswhich may becongestive heart failure, acute pericarditis or pericardial thickening with or without effusion, leaflet thickening,endocardial calcification, aortic or mitral regurgitation, pulmonary hypertension and high cardiac output in thalassemia intermedia[3], left ventricular dysfunction[4] and cardiac failure mainly attributed bythe iron overload and cardiogenic death, the major cause of death, in thalassemia major[5,6]. Some experts claim that heart disease in beta thalassemia is mainly cardiomyopathy characterized by 2 types: a dilated type, with left ventricular dilatation and impaired contractility and a restrictive type, with restrictive left ventricular filling, pulmonary hypertension and right side failure. And its pathophysiology is multifactorial, mainly the myocardial iron overload and the immunoinflammation[7].

Myocardial infarction (MI) has not been mentioned as the cardiac manifestationinthalas-semiasdue to theproposed hypothesis that they are protected by the reduced blood viscosity from anemia, the hypolipidemia and the microcytosisof RBC[8-10]. Until the first case of acute ST elevation MI (STEMI) in beta-thalassemia major was reported from the USA in 2004. Her diag-nosisdepended onthe chest pain, increased cardiac enzymes and ST elevation, but no coronary artery occlusion[11]. Then, one case of acute STEMI in beta thalassemia intermediawas reported in 2009 from Lebanon whose 2 plaques were demonstrated[12]. Hereinwe report a case of acuteSTEMI in beta-thalas-semia / Hb E,of whomthe occlusion of coronary arterie-sisdocumented.

Case Report

A 38-year-old Thai mansuddenly felt chest tightness and heavinessduringwatching the television for 3 hours. The symptom originated from the precordium and radiated to the left shoulder and isnot relieved by the peptic ulcer disease regimen. He also had dyspnea

and sweating but no orthopnea, palpitation, fever or cough. The symptom was not aggravated by exertion. He denied hypertension, diabetes, smoking, drinking or family history of coronary artery disease (CAD). Since childhood, he was diagnosed as beta-thalassemia / Hb E based on the thalassemicfacy, pallor, mild jaundice, hepatosplenomegaly, Hb typing: Hb F 10.6%, Hb E 70.6% and positive β thalassemia, IVS1#5, no alpha-thalassemia-1 genes (SEA and Thai types). Blood tests: Hb 5.3 g%, WBC 13,350/mm3, NRBC 20/100 WBC, platelet 584,000/mm^3, MCV 63.0 fL, MCH 18.6 pg, RDW 30.4 % and he wasmonthly transfused with RBC to keep Hb close to 7 g%. His spleen was cut at the age of 7 years dueto too frequent transfusion. Hypogona-dism was additionally diagnosed at the age of 32 years because of the delayed secondary sex characteristics and the testosterone of <0.10-0.11 ng/mL (Normal 3.0-10.6). Other tests: ferritin 2,040 ng/mL, serum iron 61.0 mcg%, transferrin 213 mcg%, erythropoietin 82.7mU/mL (Normal 2.6-34.0), triglyceride 129 mg%, LDL61 mg%, HDL 18 mg%, fibrinogen 72 mg%, homocysteine 9.5 micromole/L (Normal 5.9-15.3), protein S 85.2%, protein C 71.8%, antithrombin III 88.4%, normal kidney, liver function testsandcoagulogram, factor VIII activity 234%. HBsAg, anti-HCV and anti-HIV were negative. He was regularly treated with sublingual methyl testosterone and deferiprone.

On admission, BP 107/70 mmHg, PR 105/min, BW 37 Kg, Height 1.55 m, BMI 15.4 kg/m^2, he hadthalassemicfacy withgeneralized hyperpig-men-tation, moderate pallor, mild jaundice, heart apex at the 6th intercostal space, MCL, hepatomegaly 3 FB and no leg edema.

Bloodtests: Hb 8.6 g%, WBC 33,000/mm^3, NRBC 77/100 WBC, platelet 512,000/mm^3, FBS 100 mg%, Hb A1c 4.4%, creatinine 1.3 mg%, direct bili-rubin1.7 mg%, total bilirubin 6.0 mg%, AST 61, ALT 57, AP 64 U/L, albumin 4.3 g%, ferritin 1,465.5 ng/mL, CK-MB mass 3.8ng/mL (Normal 0-3), troponin-I 0.13ng/mL (Normal 0-0.1).

The ECG showed the ST elevation at leads II, III, aVF, V_5-V_6 and ST depression in V_1-V_3. Chest film showed cardiomegaly. The immediate percutaneous cardiac catheterization revealed the complete occlusion of the distal LAD and distal LCX due to the white thrombi. The thrombus was aspirated from LAD for the pathological analysis.

He was diagnosed as acute STEMI of the infero-lateral wallin a case of beta-thalassemia/Hb E. Other morbidities were hemosiderosisand hypogonadism. He was treated with percutaneous coronary intervention with stenting andstreptoki-nase, heparin, eptifibatide, clopidogrel and aspirin. The TIMI flow completely recovered andallelevated ST segmentsbecame normal. The ejection fraction is normal.He was discharged home in a few days with aspirin,clopidogrel, simvastatin, folic acidand ranitidine.

Discussion

Our case is definitely diagnosedas acute STEMI based on the combination of the acute chest symptom, increased cardiac enzymeand the ST elevationin infero-lateral wall on ECG[13] and confirmed to have coronary artery occlusion with the cardiac catheterization.

Among established risk factors for CAD such as smoking, dyslipidemia, DM, hypertension, abdominal obesity, or family history[14-15], the only one our patient has,is dyslipidemia. Before the heart attack, he has low LDL and low HDL, the common findings in beta-thalassemia / Hb E[16]. In fact, high LDL (> 95 mg%)[17] or low HDL (<40 mg%)[18] or low HDL with low LDL[19] is well known as the risk factor for CAD.

Severe thalassemia has thrombophilia particularly aftersplenectomy, ie., platelet activation, enhanced RBC adherence to endothelium, reduced protein C[120] and S, increased thrombin generation[21], plateletsor beta-thromboglobulin[22] butthethromboses havebeen rarely recognized,such ascerebral venous thrombosis in beta-thalassemia/Hb E[23,24], venous thrombo-embolism[25], portal vein thrombosis in thalassemia major or intermedia[26], pulmonary hypertension in splenecto-mized beta thalassemia[27]. Whereas AMIin beta thalas-semia major[11,12] are rare, MI in beta-thalassemia /Hb E has never been reported.

When patients have been transfused with 75 units of blood or more, it can lead to markedly increased serum ferritin,and 50% of recipients can accumulate the excess iron in myocardium[28]. Butthe higher serum ferritin is not associated with the extent of coronary ather-osclerosis[29], so far MI is still rare in thalassemia major, and their major cause of death is cardiomyopathy, not AMI. Our casehashigh serum ferritin from transfusions, hemochro-matosisof the myocardium should have been expected but hisejection fraction is still normal.

Thrombophilia after splenectomyespecially thrombocytosis (platelet >500,000/mm^3) can be the cause of AMI[30,31], two cases of MI after splenectomyoc-cur within 8-12 days. Although our case has persistent thrombocytosis (platelet 512,000-593,000/mm^3) but the splenectomy was performed since his seven years of age.

The risk of MI in our case may beattributed by the male hypogonadism (testosterone <0.1 ng/mL) becausehypogonadismincreases risk of death in cardio-vascular disease[32], furthermorethe low serum dehydro-epiandrosteronecan predict death from all causes and from ischemic heart disease in older men[33].

In conclusion, the acute MI can happen in the patient with beta-thalassemia / Hb E because of low HDL, one of modifiable risk factors, as well as other factors that may possibly attribute risks of MI, including secondary hemochromatosis, thrombophilia after splenectomy and hypogonadism,the common compli-cations in cases of severe thalassemia.

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