Pericarditis in Beta-Thalassemia / Hemoglobin E: A Case Report

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Abstract

The serious and common cardiac complication in cases with severe beta-thalassemia/hemoglobin E is cardiomyopathy due to the iron overload whereas pericarditis with or without pericardial effusion has been rarely reported. Herein we reported a Thai woman of 45 years of age who was proved to have beta-thalassemia/Hb E disease since childhood, presenting with fatigue and dyspnea without fever for one week. She was examined to have the typical thalassemic facy with anemia, distant heart sound without pericardial rub, huge hepatomegaly, tense ascites and leg edema. The chest film showed cardiomegaly without lung infiltration, the ultrasonography of the abdomen additionally revealed a 6.2 cm homogeneous mass at the left kidney supposed to be the extramedullary hematopoiesis, and the echocardiography suspected hemochromatosis with cardiomyopathy and massive pericardial effusion. Her blood tests included Hb 4.6 g%, WBC 7,340/mm^3, ESR 92 mm/hour, ferritin 5,214 ng/mL, AST 80 U/L, ALT 70 U/L, albumin 3.3 g%, normal ASO titer, LDH 1,247 U/L. And anti-dS DNA was not found for two times. The pericardial window yielded the straw-colored fluid of 1,000 ml, WBC 7,800/mm^3, N 81 % and its pathological diagnosis was acute and chronic pericarditis. The common causes of pericarditis such as tuberculosis, rheumatic fever, SLE, were tested negative. She was presumably diagnosed as having pericarditis in severe beta-thalassemia/Hb E disease and mild transaminitis from the iron overload. She was treated with the pericardial window and drainage, red blood cell transfusion, diuretics, antibiotics, deferiprone and anti-tuberculous drugs. She could be discharged but re-admitted again within one month because of the recurrent pericardial effusion. She did not respond to treatments again and passed away on the second day of re-admission. The autopsy was not allowed.

Key Words: Pericarditis, Severe beta thalassemia / hemoglobin E disease

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บทคัดย่อ: เยื่อหุ้มหัวใจอักเสบในผู้ป่วยเบต้าธาลัสซีเมีย/ฮีโมโกลบิน อี: รายงานผู้ป่วย 1 ราย

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ภาวะแทรกซ้อนทางหัวใจในโรค beta-thalassemia/hemoglobin E ชนิดรุนแรง ที่สำคัญและพบบ่อย ได้แก่ cardiomyopathy จากการที่มีเหล็กสะสมมากเกินไป ส่วนภาวะเยื่อหุ้มหัวใจอักเสบ ไม่ว่าจะมีน้ำขังด้วยหรือไม่ก็ตาม ยังพบรายงานน้อยจึงเขียนรายงานนี้ เป็นผู้ป่วยหญิงไทยอายุ 45 ปี ได้รับการยืนยันว่าเป็น เบต้าธาลัสซีเมีย/ฮีโมโกลบิน อี ตั้งแต่เด็ก มาตรวจด้วยอาการอ่อนเพลีย และหายใจไม่สะดวก ไม่มีไข้ 1 สัปดาห์ ตรวจร่างกายผู้ป่วยมีหน้าตาแบบลักษณะจำเพาะที่เรียกว่า thalassemic facy โลหิตจาง เสียงหัวใจไม่ดัง แต่ไม่มี pericardial rub ตับโตมาก ท้องมาน และขาบวมทั้ง 2 ข้าง ภาพเอกซเรย์ทรวงอกพบหัวใจโต ปอดปกติ ภาพจากเครื่องสะท้อนคลื่นเสียงความถี่สูงที่ช่องท้องพบก้อนเนื้อขนาด 6.2 เซนติเมตร ที่ไตซ้ายสงสัยว่าจะเป็น extramedullary hematopoiesis เพิ่มเติมอีกด้วย, ตรวจ echocardiography สงสัยว่าจะมี hemochromatosis, cardiomyopathy และน้ำจำนวนมากในช่องเยื่อหุ้มหัวใจ ผลตรวจเลือด Hb 4.6 กรัม%, WBC 7,340/มม^3, ESR 92 มม/ชั่วโมง, ferritin 5,214 นาโนกรัม/มล, AST 80 U/L, ALT 70 U/L, albumin 3.3 กรัม%, ไม่พบ anti-dS DNA 2 ครั้ง ASO ปกติ LDH 1,247 U/L เจาะช่องเยื่อหุ้มหัวใจ ได้น้ำสีฟางข้าวประมาณ 1,000 มล, เม็ดเลือดขาว 7,800/มม^3, N 81 % ผลตรวจจุลพยาธิเยื่อหุ้มหัวใจเป็น acute และ chronic pericarditis ไม่พบสาเหตุของภาวะเยื่อหุ้มหัวใจอักเสบที่แน่ชัด เช่น วัณโรค ไข้รูมาติด หรือ SLE วินิจฉัยว่าเป็นเยื่อหุ้มหัวใจอักเสบ จากโรคเบต้าธาลัสซีเมีย/ฮีโมโกลบิน อี ชนิดรุนแรงเอง และตับอักเสบเล็กน้อยจากภาวะเหล็กสะสมมากกว่าปกติ รักษาด้วยการเจาะช่องเยื่อหุ้มหัวใจให้เลือด ยาขับปัสสาวะ ยาปฏิชีวนะ ยาขับเหล็ก deferiprone และยาต้านวัณโรค ผู้ป่วยกลับบ้านได้ แต่ต้องรับตัวไว้อีกครั้งภายใน 1 เดือน เพราะน้ำท่วมหัวใจกลับมาอีก ผู้ป่วยไม่ตอบสนองต่อการรักษา และเสียชีวิตภายใน 2 วัน ญาติไม่อนุญาตให้ตรวจชันสูตรศพ

คำสำคัญ: เยื่อหุ้มหัวใจอักเสบ, โรคเบต้าธาลัสซีเมีย/ฮีโมโกลบิน อี รุนแรง

Introduction

One common complication of severe thalassemia disease is the secondary hemosiderosis in multiple organs from the repeated blood transfusion and the increased intestinal iron absorption. The main organs involved are the heart and the liver. Focus on the heart, the common manifestations include biventricular hypertrophy, dilated cardiomyopathy, left ventricular restrictive cardiomyopathy, pulmonary hypertension, myocarditis[1], valvular involvement including leaflet thickening, endocardial calcification, aortic or mitral valve regurgitation[2], ventricular systolic and diastolic dysfunction. In contrast, the pericarditis is far less common[3] in beta thalassemia major[4]. Likewise, the cardiac hypertrophy and dilatation, right ventricular or biventricular hypertrophy are less commonly found in severe beta-thalassemia / hemoglobin E disease[5,6].

Pericarditis with or without pericardial effusion is a rare complication of thalassemia[7]. Besides hemosiderosis, its common causes include infectious agents: viral or mycoplasmal, bacterial or fungal agents[8]. Its clinical manifestation can vary from asymptomatic until severe dyspnea and fatigue which can be easily misunderstood to be the anemic symptom, the most frequent and serious manifestation of thalassemia major. Sometimes the pericarditis can be accidentally found from the echocardiography[9].

Herein we reported one case of severe beta-thalassemia / Hb E disease who presented with massive pericardial effusion.

Case Report

A 45-year-old Thai woman who was proved to have severe beta thalassemia/Hb E disease using the Hb electrophoresis since childhood, was admitted at the medical ward because of the progressive dyspnea and fatigue for a week, without fever. She also noticed that she had both legs swelling without pain. The physical examination revealed BP 145/69 mmHg, pulse 94/min, body temperature 37.0 degree Celsius, slight dyspnea, typical thalassemic facy with marked anemia and jaundice, no murmur, no pericardial rub, no cardiac arrhythmia, distant heart sound, positive pulsus paradoxus, huge hepatomegaly 5 fingers breadth with tense ascites, marked edema of both legs.

She had been transfused every month since the diagnosis of severe beta thalassemia/Hb E disease and the splenectomy was performed four months before this admission. The microscopic pathology of the spleen revealed the congestion with the extra-medullary hematopoiesis.

Investigations: Hb 4.6 g%, Hct 15.9 %, WBC 7,340 /mm^3, nucleated RBC 9/100 WBC, MCV 65.2 fL, MCH 18.9 pg, platelet 220,000/mm^3, severe anisopoikilocytosis, marked hypochromia.

The chest film showed the cardiomegaly with the globular shape and normal lungs.

The ultrasonography of the abdomen revealed the hepatomegaly, one 4.7x6.2 cm homogeneous mass at the left kidney, maybe the accessory spleen or extramedullary hematopoiesis, minimal left pleural effusion, ascites and pericardial effusion.

She was medically treated with oral furosemide 80 mg and spironolactone 75 mg a day, the oxygen and packed red blood cell transfusion.

One week later, no improvement was observed. The echocardiography showed the ejection fraction of 62 %, the hemochromatotic cardiomyopathy and massive pericardial effusion without thrombin, mild thickening of the pericardium, mild mitral regurgitation, early cardiac temponade, and left pleural effusion.

Other laboratory tests: antistreptolysin O titer 101 (normal <125), anti-DNAse B 117 U/ml (normal < 200 U/ml), ESR 92 mm/hour, CRP 4.2 mg/dL, BUN 12 mg%, LDH 1,247 U/L, creatinine 0.44 mg%, ANA positive, diffuse cytoplasmic 1:80, homogeneous nuclear 1:80, ferritin 5,214 ng/mL. FBS 83 mg%, albumin/globulin 3.3/4.7 g%, AST/ALT 80/70 U/L, Anti-dS DNA -negative x 2, TSH 2.1 mIU/mL (normal 0.5-4.7), FT3 2.0 pg/mL (normal 2.3-4.2), FT4 0.7 ng/L (normal 0.8-1.8)

HIV antigen/antibody, HBsAg, anti-HCV and VDRL were all negative.

The EKG showed unremarkable study, no low

voltage, no ST segment elevation and no electrical alternans.

The pericardial window was performed and yielded the straw- colored fluid of 1,000 ml that had WBC 7,800/mm^3, monocyte 8 %, neutrophil 81 %, lymphocyte 11 %, RBC 67,000/mm^3, negative for TB and non-MTB by the PCR method, sugar 114 mg%, protein 5.5 g%, LDH 320 U/L, ADA 19 U/L. The microscopic pathological diagnosis of the pericardium biopsy was acute and chronic pericarditis, no granuloma, no organism, and no malignant cell. The fluid did not contain malignant cell. Tapping of the left pleural effusion yielded the transudate, possibly the hepatic hydrothorax.

The urinalysis was unremarkable and the 24-hour urine protein was 662 mg.

She was diagnosed as having pericarditis with massive pericardial effusion and left pleural effusion and her underlying disease was severe beta-thalassemia/Hb E disease and mild transaminitis from the secondary hemochromatosis and hepatic hydrothorax.

Her management included the pleural tapping, pericardial window, packed blood cell transfusion and drugs: 4-drug anti-tuberculous regimen, antibiotics, spironolactone 75 mg, furosemide 20 mg, and the chelating agent, deferiprone 3 g a day. She seemed promptly responsive to the treatments and could be discharged within 2 weeks with marked clinical improvement. However she was re-admitted because of the severe dyspnea from the recurrence of pericardial effusion in one month. She did not respond to any therapy: the pericardial tapping, antibiotics, anti-tuberculosis, blood transfusion, iron chelation, diuretics and finally she passed away on the second day in this admission. The autopsy or necropsy was not allowed.

Discussion

The common causes of the pericarditis with pericardial effusion such as malignancy, infection, after acute myocardial infarction, uremia or dialysis, hypothyroidism and collagen vascular disease[10] are all proved to be negative in our case hence, it is supposed to be directly associated with the beta-thalassemia / Hb E disease itself. The pathogenesis of pericarditis in thalassemia patients is unclear, a likely cause is the increased susceptibility to viral infection, presumably associated with the anemia, the iron overload, and/or the splenectomy[2].

In tropical countries, the pericarditis with pericardial effusion can be occasionally detected in cases of acute rheumatic fever who have active carditis as one of the major criteria of Jones[11] and acute rheumatic fever in adulthood can still be occasionally found[12] in developing countries including Thailand[13] but our case is proved to be free from the evidence of streptococcal infection, the factor essential for the diagnosis of acute rheumatic fever.

Grossly hemorrhagic pericarditis has been rarely reported in thalassemia patients, one from Taiwan[14] and another case from Europe[15]. But both cases harbor beta-thalassemia major whereas our case has severe beta thalassemia/Hb E disease and has just only microscopic hemorrhage in the pericardial fluid.

If the causes of pericardial effusion in thalassemia major can be identified such as hypothyroidism from secondary hemochromatosis and properly treated, the patient can improve and the pericardial

effusion will disappear within three months[16]. But the definite causes cannot be identified in our patient hence she cannot be offered the definite treatment until she finally passes away on the second day of the second admission.

Conclusion

A 45-year-old Thai woman with severe beta-thalassemia/hemoglobin E disease is proved to have pericarditis with massive pericardial effusion. The pathology of the pericardium is non-specific pericarditis. Because the specific causes could not be identified, the pericarditis is presumed directly relating to beta thalassemia/Hb E disease and the proposed mechanisms is that thalassemia patients may be prone to viral pericarditis due to the severe anemia, the iron overload and splenectomy.

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