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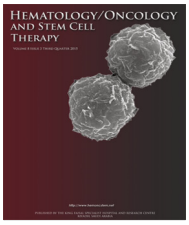

Study of platelet activation, hypercoagulable state, and the association with pulmonary hypertension in children with β-thalassemia

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KEYWORDS
Hypercoagulable state;
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Abstract
Background: The increased survival rate of thalassemic patients has led to unmasking of management related complications which were infrequently encountered.
Objective: Study the increased coagulation and platelet activation in children with β-thalassemia, to analyze the factors that lead to such hypercoagulable state and to study

Abbreviations: BT, blood transfusion; HLPC, high-performance liquid chromatography; MPAP, mean pulmonary artery pressure; MTHFR, methylene tetrahydrofolate reductase; MUCH, Mansoura University Children's Hospital; NTDT, nontransfusion-dependent thalassemia; PASP, pulmonary artery systolic pressure; PH, pulmonary hypertension; RBC, red blood cells; RPAP, right pulmonary artery pressure; RVOT, right ventricular outflow tract; TE, thromboembolic; TM, thalassemia major; TRV, tricuspid regurgitant velocity

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pulmonary hypertension (PH) in conjunction with platelet activation and hypercoagulable state in children with β-thalassemia.

Methods: 36 Egyptian children with β-thalassemia with a mean age of 9.9 years (±4.7 SD). In addition, 20 healthy Egyptian children matched for age and sex were enrolled as a control group. Both were subjected to clinical and laboratory assessments. Echocardiography was done to the patient group and PH was diagnosed based on calculated mean pulmonary artery pressure [MPAP] >25 mmHg.

Results: We found that, mean ± SD serum P-selectin level (platelet activator marker) was significantly higher in thalassemic patients (2337 ± 566 pg/ml) in comparison to controls (1467 ± 247 pg/ml) ($P < 0.001$). Mean serum protein-C and antithrombin-III levels were significantly lower in thalassemic patients (1.2 ± 1.3 μg/ml, 27.3 ± 7.5 mg/dl) in comparison to controls (2.3 ± 1.3 μg/ml, 35.1 ± 4.1 mg/dl) ($P = 0.003$ and <0.001) respectively. PH was detected in 17 (47.2%) patients and it was significantly associated with splenectomy ($P = 0.01$) and non-transfusion dependent thalassemia (NTDT) ($P = 0.04$). PH was positively correlated with serum levels of P-selectin ($r = 0.38$, $P = 0.02$), fibrinogen ($r = 0.41$, $P = 0.01$) and negatively correlated with serum protein-C level ($r = -0.48$, $P = 0.003$).

Conclusion: A chronic hypercoagulable state and platelet activation is present in children with β-thalassemia. Splenectomy and transfusion infrequency are the main risk factors noted to be associated with such hypercoagulable state and platelet activation and consequently the PH among our thalassemic patients.

Introduction

Thalassemia is a common hereditary blood disorder that stems from genetic defects, resulting in deficiency of the hemoglobin polypeptide chain synthesis [1]. The association of the severe forms of the disease with complications of blood transfusion (BT), iron overload, bone deformity, and gall bladder stones is well described. In recent years, there have been increasing reports of hemostatic derangement complications, which significantly influence the morbidity and mortality of this disease. These derangements range from subclinical derangement of hemostatic parameters to various thromboembolic (TE) events such as pulmonary embolism, deep vein thrombosis, and portal vein thrombosis [2]. The mechanism of the TE events in thalassemia has not been fully elucidated. There are diverse factors contributing to its etiopathogenesis. Among the factors that have been actively investigated are increased platelet activation, endothelial activation, red blood cell (RBC) membrane abnormalities leading to activation of the coagulation cascade, and the changes in coagulation protein level [3,4]. Pulmonary hypertension (PH) is increasingly recognized as part of the clinical spectrum for β-thalassemia, and little is understood about the mechanisms and the risk factors for its development. Several studies have suggested that chronic hypoxia and lung injuries due to infections and iron depositions are common causes [5], whereas others suggest a hypercoagulable state causing thrombotic lesions in the lungs as a risk factor [6]. We sought to confirm the hypercoagulability and platelet activation among children with β-thalassemia, and whether such a state of hypercoagulability could be involved in thalassemia-related PH.

Patients and methods

This prospective case control study was conducted at the Mansoura University Children Hospital (MUCH) in compliance with the Clinical Pathology Department (Faculty of Medicine Mansoura University), from September 2013 until March 2015. The study included 36 Egyptian children with β-thalassemia [20 (55.6%) females and 16 (44.4%) males] with a mean age of 9.9 (±4.7 standard deviation) years. In addition, 20 healthy Egyptian children with matched age and sex were enrolled as a control group. Patients were recruited from the hematology outpatient clinic in MUCH. Healthy controls were selected from children attending the MUCH outpatient clinic for routine follow-up care with no known history of blood diseases, chronic systemic illness, or BT.

Diagnosis of patients was by high-performance liquid chromatography electrophoresis [7]. In our study, 25 patients (69.4%) were diagnosed to have beta-thalassemia major (β-TM), whereas 11 patients (30.5%) were diagnosed as nontransfusion-dependent thalassemia (NTDT). Six of our patients (16.7%) were not known to receive any iron chelators through the course of their illness. By contrast, 30 patients (83.3%) were receiving iron chelators [deferazirox 15 (41.7%), deferoxamine 6 (16.7%), and deferiprone 9 (25%)]. Twenty-two (61.1%) of our patients were splenectomized. We excluded patients with congenital heart disease and chronic lung disease. In addition, none of our patients were receiving any antiplatelet or anticoagulant medications. None of our patients had a history of thrombosis including thrombophlebitis due to peripheral angiocatheter insertion. The study was approved by the ethics

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