Editorial

Pulmonary Hypertension in β-thalassemia Diseases: A Common Complication Yet Under-recognized and Poorly Understood

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Pulmonary hypertension (PHT) is a common complication in β-thalassemia diseases, especially in thalassemia intermedia. Previous studies indicated that the prevalence of PHT in thalassemia intermedia and thalassemia major ranged from 23% to 59.1%, and 0% to 24%, respectively.[1-3] It is considered to be the primary cause of congestive heart failure in this patient population. However, the majority of patients with increased pulmonary arterial pressure are asymptomatic. Therefore, this condition is often unrecognized until patients develop heart failure and/or hypoxemia.

Approximately 600,000 Thais suffer from β-thalassemia.[4] A significant number of them develop PHT leading to right-sided heart failure with preserved left ventricular function. The mechanism underlying PHT remains poorly understood due to the lack of well-designed studies on its pathogenesis. Some evidence indicates that chronic hemolysis plays a major role on development of PHT. In fact, most types of chronic hemolytic anemia may develop PHT suggesting a correlation between these two conditions. Several suggested mechanisms include nitric oxide and arginine deficiency resulting in vasoconstriction and increased pulmonary vascular resistance, endothelial dysfunction promoting in situ thrombus formation, oxidative stress and free-radical formation, and pulmonary hemosiderosis.[5] A retrospective studies of PHT in previously splenectomized patients with β-thalassemia diseases showed that female sex, hemoglobin E/β-thalassemia, status many years postsplenectomy, marked anemia, markedly increased nucleated red cell counts, thrombocytosis, and very high serum ferritin levels were associated features of PHT.[6]

Currently, there is very little evidence displaying effective prevention and treatment of PHT in thalassemia patients. Adequate transfusion- iron chelation therapy aiming for suppression of ineffective erythropoiesis and prevention of secondary hemochromatosis is considered a potential strategy to reverse pathological processes. A case report of a splenectomized hemoglobin E/β-thalassemia patient with PHT provided evidence of correction of hypercoagulability and amelioration of pulmonary arterial hypertension by regular blood transfusion.[7] Sildenafil has also been successfully used to decrease pulmonary pressure and improve exercise capacity and functional class of patients with hemoglobinopthy and severe PHT.[8]

In this issue of the journal, Chueamuangphan and colleagues report the prevalence and risk factors of PHT in patients with β-thalassemia diseases in Thailand. Of 88 including 65 splenectomized and 23 non-splenectomized subjects, the prevalence of PHT is 49% comparable with previous studies. Features significantly associated with PHT are post splenectomy status (OR = 2.83 [1.02-7.82]) and nRBC ≥500/100WBC (OR = 3.49 [1.24-9.8]). On the other hand, gender, age,

post-splenectomy duration, hemoglobin concentration, white blood cell counts, platelet counts, and serum ferritin levels are not significantly associated with PHT.

The investigators propose that splenectomy intensifies an increase of anionic phospholipid exposure on red cell membranes, which promotes local clot formation and vasculopathy in the pulmonary vascular bed. Furthermore, elevated nucleated red blood cell counts may impede flow in the microcirculation facilitating local thrombosis. As a result, an increase in pulmonary vascular resistance causes pulmonary hypertension in β-thalassemia diseases. This study suggests that adequate transfusion and iron chelation to avoid complications, as well as splenectomy, are likely to be an effective strategy for prevention of PHT in thalassemia patients. Further studies, especially on pathophysiology and effective managements for this condition, are warranted.

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