Chapter 16

PAROXYSMAL NOCTURNAL HEMOGLOBINURIA; A SINGLE CENTER EXPERIENCE AND REVIEW OF THE LITERATURE

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BACKGROUND

Paroxysmal nocturnal hemoglobinuria (PNH) is an acquired clonal stem cell disorder, leading to a deficient biosynthesis of surface proteins in hematopoietic cells. Clinical symptoms consist of various combinations of intravascular hemolysis, bone marrow failure, and mainly venous thrombotic events. Arterial thrombosis has been described only in a few cases (Heinrich J.Audebert et al., 2005). PNH cells are deficient in cell surface GPI anchored proteins; this deficiency on erythrocytes leads to intravascular hemolysis since certain GPI anchored proteins normally function as complement regulators.

Free hemoglobin released from intravascular hemolysis leads to circulating nitric oxide depletion and is responsible for many of the clinical manifestations of PNH, including fatigue, erectile dysfunction, esophageal spasm, and thrombosis2. Thrombosis is an ominous complication of PNH and the leading cause of death from the disease. It occurs in about 40% of PNH patients with a large percentage of PNH cells and classical symptoms (hemolytic anemia and hemoglobinuria) have a greater propensity for thrombosis than patients with a small percentage of PNH cells (Robert A. Brodsky, 2008). While the mechanism of thrombosis in PNH is not entirely understood, it is almost certainly related to intravascular hemolysis and other consequences of GPI anchor protein deficiency. Indeed, nitric oxide depletion has been associated with increased platelet aggregation, increased platelet adhesion, and accelerated clot formation2.

Classical PNH manifests with overt hemolysis, an elevated reticulocyte count, an elevated LDH and a normocellular to hypercellular bone marrow. Patients

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