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LETTER TO THE EDITOR

Decreased hemolysis following administration of antioxidant—fermented papaya preparation (FPP) to a patient with PNH

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Dear Editor,

Paroxysmal nocturnal hemoglobinuria (PNH) is an acquired clonal hematopoietic stem cell disease (HSC), characterized by intravascular hemolysis [1] due to inactivating mutation of the X-linked PIG-A gene in an HSC; the gene product is essential for the synthesis of glycosylphosphatidylinositol (GPI) anchor molecules [2].

Intravascular hemolysis is a major cause of anemia in PNH. Two surface proteins, CD55 and CD59, which regulate complement activation on the cell surface are GPI-linked [3], and their deficiency explains the hypersusceptibility of PNH red blood cells (RBC) to complement-mediated lysis, intravascular hemolysis, and release of free hemoglobin (Hb). Hb has a vasculotoxic potential, directly impairing endothelial function and generating inflammatory and oxidative stress [4].

Cell-free Hb disintegrates into heme and globin, and the iron from heme catalyzes the formation of reactive oxygen species (ROS) [5] causing damage to various components of the cell.

Flow cytometry analyses of RBC, platelets, and polymorphonuclear cells from patients with PNH disclosed a significant increase in ROS, while reduced glutathione was decreased. Oxidative stress was more profound in cells derived from the pathological clone with a CD55–CD59 phenotype. Increased membrane lipid peroxidation was also documented in PNH RBC [6]. Consequently, there is evidence for increased oxidative stress in PNH, which might play a significant role in the pathophysiology of the disease. Indeed, in vitro treatment of PNH-RBC with antioxidants decreased their hemolysis [6].

Therefore, there is a rationale for treatment with antioxidants in order to reduce the oxidative stress and improve its clinical manifestations in PNH patients. One antioxidant is fermented papaya preparation (FPP), a natural health food product obtained by yeast biofermentation of carica papaya [7], which decreases oxidative stress both in vitro and in vivo [8].

Case presentation

A 36-year old woman was diagnosed in 1996 with PNH complaining of generalized weakness and recurrent episodes of nocturnal hemoglobinuria. The diagnosis was confirmed by Ham's test and flow cytometry. The patient received folic acid, iron supplement, and danazol without significant change in her average Hb level which was ~7.5 gm/dl with LDH ~2500 u/lit. Before receiving FPP, she had anemia (Hb= 7.4 gr/dl, MCV 95 fl), leukopenia (leukocyte (WBC)=1500/mcl), lactate dehydrogenase (LDH) up to 5300 u/l, indirect bilirubinemia, and elevated plasma Hb (Fig. 1). Serum haptoglobin was undetectable, serum ferritin and transferrin saturation were low, 7 ng/ml and 5%, respectively. A recent bone marrow disclosed erythroid hyperplasia.

FPP supplied as sachets, containing 3 g powder, by Osato Research Institute, Gifu, Japan, was given three times daily for 4 months. Following FPP therapy, Hb level increased by

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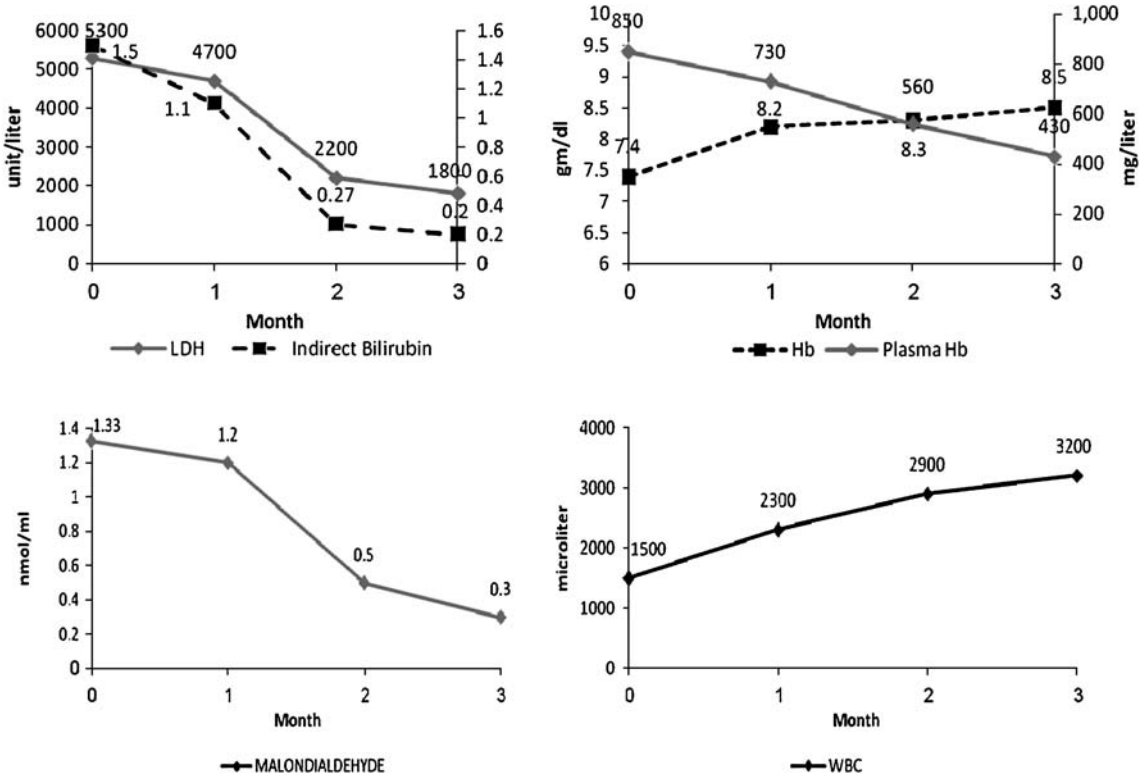

Fig. 1 Changes in Hb levels, WBC, and in hemolytic and oxidative stress parameters induced and maintained for 3 months following during administration of FPP

1 gr/dl, WBC to 3,200 per microliter, and all the hemolytic parameters have been significantly improved (Fig. 1).

Malondialdehyde levels, a product of lipid membrane peroxidation, were significantly decreased—which may reduce its mutagenic and leukemogenic effect [9]. The patient was symptomatically improved, with less fatigue and better performance.

Conclusion

The findings indicate a significant amelioration of hemolytic and oxidative stress parameters which was induced and sustained by FPP treatment in a patient with PNH. Antioxidants may serve as inexpensive adjuvant or alternative therapy in PNH.

Conflict of interest disclosure The authors declare no competing financial interest.

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