Fatigue Improvement after Eculizumab in Paroxysmal Nocturnal Hemoglobinuria: Apropos of a Case

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Abstract

A 54-year-old male presented with shortness of breath and was diagnosed with pulmonary emboli. Laboratory studies revealed hemolytic anemia. Flow cytometry showed a prominent white blood cell clone without CD59 in 85% (NV 0-3.0) and red blood cells with 8.5% CD59 absence (NV 0-3.0) confirming a diagnosis of paroxysmal nocturnal hemoglobinuria. Eculizumab was started to decrease the possibility of a thrombotic recurrence, with incidentally, a marked subjective improvement of symptomatology, as fatigue, was seen. We reviewed current literature regarding the improvement in fatigue seen in patients with paroxysmal nocturnal hemoglobinuria treated with eculizumab.

The different phenotypes seen in patients with paroxysmal nocturnal hemoglobinuria might be explained by selection and expansion of the abnormal clone which would render a population of cells into a heterogeneous combination of normal and abnormal cells. As an example, type I red blood cells are normal, type II red blood cells are partially deficient in GPI-proteins, and type III red blood cells are completely deficient in GPI-proteins [3]. The larger the number of type III red blood cells present, the worse the hemolysis seen in a particular patient. The fact that our patient’s CD59 was lower in red blood cells than in white blood cells might be counterintuitive; nevertheless a reasonable explanation would be that while both red and white blood cells carry the abnormality, red blood cells might be more prone to complement induced attack than white blood cells thus, when testing is performed, the CD59 red blood cell population has already been diminished due to hemolysis.

Eculizumab is an anti-C5 humanized monoclonal antibody which inhibits terminal complement mediated intravascular hemolysis in GPI-defective cells and is the first targeted disease-modifying therapy for paroxysmal nocturnal haemoglobinuria [4]. This antibody binds to the complement protein C5, halting the attachment of the terminal complement complex cascade (C5b-9). In clinical trials of eculizumab compared with baseline and placebo, eculizumab was well tolerated and increased health-related quality of life and fatigue scores and decreased intravascular hemolysis, levels of LDH, stabilizing hemoglobin and reaching packed red cell transfusion independence in more patients [5]. The pivotal study by Hillmen et al. [6] revealed significant improvements (p< 0.001) in the quality of life of patients receiving eculizumab. The seminal trials that evaluated the safety and efficacy of eculizumab, TRIUMPH and SHEPHERD, noted statistically significant improvement in the Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue instrument scores, by week 3 with p=0.009 and by week...
not the interaction between PNH and the immune system explains the improvement on fatigue remains to be seen [12]. Until the development of eculizumab, the management of PNH has mainly been symptomatic with transfusion support, folic acid nutritional support, anticoagulation after thromboembolic disease ensued, and allogeneic stem cell transplantation for selected cases. Eculizumab, despite the fact that it is not a curative therapy, provides a statistically significant improvement in fatigue and quality of life which are so critically important for patients with paroxysmal nocturnal hemoglobinuria.

References


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