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ABSTRACT N. PO69

WHOLE BLOOD THROMBIN GENERATION HYPERCOAGULABLE PROFILE IN A PATIENT WITH HEMOLYTIC CRISIS DUE TO PAROXYSMAL NOCTURNAL HEMOGLOBINURIA: A CASE REPORT.

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Background: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare acquired hematologic disorder characterized by intravascular hemolysis, bone marrow failure, and an increased risk of thrombosis. It is caused by a somatic mutation in the PIG-A gene, which results in a deficiency of glycosylphosphatidylinositol (GPI)-anchored proteins on the cell membrane, including the complement regulators CD55 and CD59, thus promoting complement activation and destruction of erythrocytes and platelets. Thrombosis is the main cause of mortality in PNH, often occurring at atypical venous sites. The introduction of complement inhibitors, such as eculizumab, has significantly reduced thrombotic events. However, assessment of coagulation by plasma thrombin generation tests has yielded conflicting results. Since blood cells play a key role in the pathophysiology of PNH, it is hypothesized that thrombin generation in whole blood (WB-TG) may provide a more accurate evaluation of the prothrombotic state in patients with PNH.

Case Report: We present the case of a 25-year-old woman, without significant medical history, admitted for a hemolytic crisis with hemoglobinuria triggered by influenza A virus infection, raising clinical suspicion of paroxysmal nocturnal hemoglobinuria (PNH). Indeed, hematological tests revealed normocytic anemia (Hb 77 g/L), mild thrombocytopenia, leukopenia, and marked hemolysis, characterized by elevated lactate dehydrogenase (LDH) levels (1.867 U/L) and nearly undetectable haptoglobin. The diagnosis of PNH was confirmed by flow cytometry, which identified a large PNH clone in granulocytes (89%), monocytes (86%), and erythrocytes (77%). The patient was treated with corticosteroids and antithrombotic prophylaxis with enoxaparin. During hospitalization, the patient's hemolytic symptoms and hematological parameters improved, and no thrombotic events occurred. However, whole blood thrombin generation (WB-TG) performed at admission revealed a hypercoagulable phenotype compared to 21 healthy controls. In the absence of thrombomodulin (TM), the patient showed a markedly increased endogenous thrombin potential (ETP) (2993 vs. 1609 nM·min; +86%), along with elevated peak thrombin concentration (308 vs. 199 nM, +58%) and velocity index (57 vs. 36, +58%). After TM addition, the anticoagulant response was diminished, as indicated by persistently elevated ETP (1832 vs. 895 nM·min; +105%), peak thrombin (199 vs. 123 nM, +62%), and velocity index (58 vs. 31, +87%). Lag time and time-to-peak were within reference ranges or only minimally prolonged. (Tab 1).

Conclusions: This case highlights how whole blood thrombin generation (WB-TG) may be a sensitive and reliable tool to identify hypercoagulability in patients with PNH, even in the absence of clinical thrombotic events. This approach allows consideration of the interaction between cellular and plasma components of blood, overcoming the limitations of plasma-based tests. WB-TG assessment may more effectively guide antithrombotic prophylaxis management, improving thrombotic risk stratification and optimizing therapeutic choices. Further studies are needed to confirm these findings and define the clinical role of WB-TG in the daily management of PNH.

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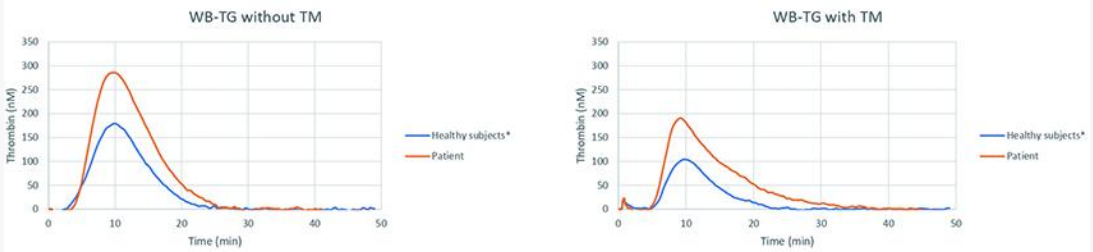
WB-TG profiles in PNH patient vs. healthy controls.



*median profile. WG-TG, whole blood thrombin generation; TM, thrombomodulin