Positivity of the Sugar-Water Test in the Screening for Paroxysmal Nocturnal Hemoglobinuria

To the Editor:

Paroxysmal nocturnal hemoglobinuria (PNH) is an acquired stem cell disorder of a clonal nature that leads to Coombs-negative intravascular hemolysis. For the diagnosis of PNH, it is required to detect affected erythrocytes that are susceptible to the autologous complement caused by a deficiency in complement regulatory membrane proteins such as decay-accelerating factor (DAF) and CD59. These proteins are anchored to the membrane via glycosylphosphatidylinositol (GPI). PNH cells do not produce the anchor and then the lack of the proteins has diagnostic value in PNH. To detect the affected erythrocytes, there are conventional hemolysis tests that use complement-mediated selective hemolysis of affected erythrocytes: acidified serum test (Ham’s test) and the sugar-water (SW) test. Recent advances in the research on abnormal hemolysis in PNH has brought new methods for the diagnosis: direct identification of affected cells by flow cytometry, detection of impaired synthesis of GPI anchor, and cytogenetic analysis of the abnormal expression of the PIG-A gene. Among the tests, the hemolysis tests are distinct because of their simplicity as a rapid assay that requires small amounts of blood but no special reagents or equipment. Above all, the SW test is highly sensitive and becomes positive before the detection of affected erythrocytes by flow cytometry (unpublished observation); thus, it is considered to be a practical screening test for PNH diagnosis.

Thus, we investigated the validity of the SW test for the screening of a large number of blood samples obtained from volunteers in Japan, specifically in the Far East, where PNH is regarded to be relatively common. We also expected to be able to assess an objective prevalence of PNH without depending on the clinical manifestations. Erythrocytes obtained from volunteers who underwent a physical examination at our medical center were subjected to the SW test and the blood samples positive for the test were further analyzed by flow cytometry with antibodies against DAF and CD59. The total number of volunteers was 23,465, consisting of 7,160 women 22 to 81 years old and 16,305 men 29 to 78 years old. Thirty-six (0.2%) were positive for the hemolysis test. However, flow cytometry showed that there were no affected cells in the 36 specimens. The SW test eventually gave a result of 0.2% false-positive. Moreover, laboratory data of 41 patients with PNH experienced in our hospital during the past 33 years showed that virtually all of the patients were positive for the SW test, except a case with coexisting congenital C9-deficiency whose erythrocytes showed negative results only when autologous serum was used in the SW test. These findings indicate that both false-negative and false-positive results were rare in the SW test. By demonstrating the real score concerning sensitivity and specificity, we reaffirm that the SW test is still the most appropriate test for screening of PNH.

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