resistant NOTCH1-mutated clone is at risk of acquiring further progression-associated mutations. Besides the known t(14;19)(q32;q33)/IGH-BCL3,8-10 we also identified dic(9;14)(q34;q32)/IGH-NOTCH1, which so far has not been reported in B-cell leukemia/lymphoma, as a novel genomic aberration capable of triggering RS.

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Persistently high quality of life conferred by coexisting congenital deficiency of terminal complement C9 in a paroxysmal nocturnal hemoglobinuria patient

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Surprisingly, the patient had C3d-bound erythrocytes (Figure 1C) that often appear in PNH patients on eculizumab and are susceptible to extravascular hemolysis. Thus, the patient manifests extremely low levels of both intra- and extravascular hemolysis. It is interesting to verify whether ordinary PNH patients harbor dormant extravascular hemolysis. Judging from the fluorescence intensity of C3d-positive erythrocytes, the amount of C3d on the PNH erythrocytes of our patient appears less than that of some PNH patients on eculizumab (Figure 1C; current report). In contrast, C3d+ erythrocytes were undetectable in PNH patients before eculizumab treatment (Figure 1C). The amount of C3d on erythrocytes may inversely correlate with the intensity of intravascular hemolysis. It then led us to speculate that extravascular hemolysis is too rapid to allow extravascular clearance of C3d-bound PNH erythrocytes in vivo. It is also theoretically possible that eculizumab-associated extravascular hemolysis is controllable by decreasing the dose of eculizumab. The C3d deposition could also be affected by the altered expression of erythrocyte glycolipids. In general, infection amplifies both intravascular hemolysis of PNH and extravascular hemolysis of hereditary spherocytosis. Eculizumab may not completely eliminate the infection-associated precipitation of hemolysis in PNH patients having both types of hemolysis.

The findings in our exceptional PNH patient surely promote unveiling of complex pathophysiology and contribute to the establishment of a better terminal complement-targeted therapy in PNH.

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