resistant NOTCH1-mutated clone is at risk of acquiring further progression-associated hits. Besides the known t(14;19)(q32;q13)/IGH-BCL3,5,6-10 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.

To the editor:

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

Paroxysmal nocturnal hemoglobinuria (PNH) clone bears a PIGA mutation and fails to express glycosylphosphatidylinositol-linked membrane proteins such as complement-regulatory CD55 and CD59, leading to complement-mediated intravascular hemolysis and thrombosis. The advent of eculizumab, an inhibitor of terminal complement C5, provides good quality of life (QOL) by preventing hemolysis and thrombosis,1,2 and may improve prognosis of PNH.1A). The high QOL may reflect that the C9-deficiency prevents reactions by generation of C5a and C5b-8.7 Currently, virtually all membrane attack complex (C5b-9) formation but allows immune

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Contribution: K.D.K. and I.W. designed and performed the research, analyzed data, and wrote and approved the manuscript; L.M. analyzed data and wrote and approved the manuscript; A.B. and C.G. treated the patient, contributed vital patient information, and approved the manuscript; J.F.F. performed array CGH, analyzed data, and approved the manuscript; P.V. analyzed data and wrote and approved the manuscript; and J.C. designed the research, analyzed data, and wrote and approved the manuscript.

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Correspondence: Iwona Wlodarska, Center for Human Genetics, KU Leuven, Gasthuisberg, Herestraat 49, Box 602, B-3000 Leuven, Belgium; e-mail: iwona.wlodarska@uzleuven.be.

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Surprisingly, the patient had C3d-bound erythrocytes (Figure 1C) that often appear in PNH patients on eculizumab 4,5 and are susceptible to extravascular hemolysis.7 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 report4). In contrast, C3d+ erythrocytes were undetectable in PNH patients before eculizumab treatment (Figure 1C).4 The amount of C3d on erythrocytes may inversely correlate with the intensity of intravascular hemolysis. It then led us to speculate that intravascular 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.8 In general, infection amplifies both intravascular hemolysis of PNH9 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.

Nobuyoshi Hanaoka
Department of Hematology/Oncology, Wakayama Medical University, Wakayama, Japan
Yoshiko Murakami
Research Institute for Microbial Diseases, and WPI Immunology Frontier Research Center, Osaka University, Osaka, Japan
Masahide Nagata
Nagata ENT Clinic, Kumamoto, Japan
Shoichi Nagakura
Department of Hematology/Oncology, National Hospital Organization Kumamoto Medical Center, Kumamoto, Japan
Yuji Yonemura
Department of Blood Transfusion Medicine and Cell Therapy, Kumamoto University, Kumamoto, Japan
Takashi Sonoki
Department of Hematology/Oncology, Wakayama Medical University, Wakayama, Japan
Taroh Kinoshita
Research Institute for Microbial Diseases, and WPI Immunology Frontier Research Center, Osaka University, Osaka, Japan
Hideki Nakakuma
Department of Hematology/Oncology, Wakayama Medical University, Wakayama, Japan

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Correspondence: Hideki Nakakuma, Department of Hematology/Oncology, Wakayama Medical University, 811-1 Kimiidera, Wakayama 641-8510, Japan; e-mail: hnakakum@wakayama-med.ac.jp.
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Nobuyoshi Hanaoka, Yoshiko Murakami, Masahide Nagata, Shoichi Nagakura, Yuji Yonemura, Takashi Sonoki, Taroh Kinoshita and Hideki Nakakuma

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