OC 11.3 Anti-idiotypic antibodies against ADAMTS13 autoantibodies are present in patients after acute episodes of immune-mediated Thrombotic Thrombocytopenic Purpura (iTTP)

S. R. Heeb, M. Schaller, J. A. Kremer Hovinga
Department Of Hematology And Central Hematology Laboratory And Department For Biomedical Research, Inselspital, Bern University Hospital and University of Bern, Bern, Switzerland

Objectives: A severe ADAMTS13 deficiency caused by ADAMTS13 autoantibodies is the hallmark of iTTP. The presence of ADAMTS13 immune complexes years after acute episodes point at an ongoing autoimmune process balanced by as yet unknown adaptive mechanisms. Failure to uphold these mechanisms might result in relapses, which are frequently seen in iTTP patients. We hypothesized that anti-idiotypic antibodies against ADAMTS13 autoantibodies might constitute such an adaptive mechanism.

Methods: Splenic mononuclear cells of two iTTP patients, splenectomized after a relapsing disease course, were used to generate IgG_1 Fab κ/λ libraries by phage display. Expressed phages were screened for binding to two separate pools of anti-ADAMTS13 Fabs (Schaller et al., Blood 2014; pooled according to their CDR3 motifs). ADAMTS13 autoantibody-specific anti-idiotypic phages were sequenced to determine their immunoglobulin variable heavy (IGV_H) and light (IGV_L) chain genes.

Results: A total of 15 sequenced anti-idiotypic Fabs, yielded 14 productive IGV_H chains, with IGHV3–23*01 shared by both patients (3/14 Fabs). Four of the 14 IGV_H were paired with a productive IGV_L chain (three κ, with IGKV1–39*01 shared by both patients, and one λ). Anti-idiotypic Fabs with paired productive IGV_H and IGV_L chains were detected only for the pool of ADAMTS13 autoantibodies of CDR3 motifs 1/2.

Conclusion: Our results indicate, that in both iTTP patients analyzed, the IgG_1 repertoire contains a distinct set of ADAMTS13 autoantibody-specific anti-idiotypic antibodies. Functional analysis of these anti-idiotypic Fabs as well as screening of patients' plasmas for the presence of ADAMTS13 autoantibody-specific anti-idiotypic antibodies is ongoing.

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