Can molecular markers help in the diagnosis and management of WM?

Cécile Tomowiak, Stéphanie Guidez, Stéphanie Poulain, Xavier Leleu

Waldenström macroglobulinemia (WM) was first described by Jan Gosta Waldenström in 1944, as a distinct B-cell lymphoproliferative disorder characterized by bone marrow infiltration of lymphoplasmacytic cells along with production of an IgM monoclonal protein in the serum. It can be associated with various complications related to tumor infiltration or to the serum monoclonal component. Biological markers are essential for the diagnosis of WM, for prognosis determination, monitoring of response to therapy and progression, and possibly even in the decision of the optimal treatment; indeed, in recent years, genomic characterization of WM has led to the identification of MYD88 and CXCR4 mutations that can be critical for the diagnosis, prognosis and therapeutic options for WM. The recent finding of MYD88 L265P mutation by Treon et al. (Boston, MA, USA) in about 90% of cases of WM made it a major diagnostic marker of the disease that was implemented to the new criteria in the last IWMF recommendations. On the contrary, mutations of CXCR4, the second most frequent somatic mutation, were identified in approximately 30% of WM patients. Multiple CXCR4 mutations were all described in the carboxyl (C) terminal domain, the CXCR4 C1013G mutation being the most frequent recurrent CXCR4 mutation. Most of CXCR4 mutations coexist with MYD88 L265P mutations. While the MYD88 L265P mutation has a role in WM cell proliferation and survival, CXCR4 mutation has been implicated in tumor progression, more aggressive disease features and drug resistance.

In conclusion, molecular markers have become key genomic markers in the diagnosis and prognosis of WM, respectively MYD88 L265P mutation and CXCR4 mutations. Other mutations are under investigation with a probable prognosis impact, CD79 and Tp53.