THE MONOCLONAL GAMMOPATHY WITH UNDETERMINED SIGNIFICATION AND OTHER PREMYELOMA STATES: SOME PATHOGENESIS DATA AND FOLLOW UP.

Dan Colita, Adriana Colita, Daniel Coriu
Fundeni Clinic of Hematology, Bucharest

Multiple myeloma (MM) is a plasma-cell neoplasm that accounts for 10% of hematologic diseases. It involves adults with a median age at onset of 69 years. Fewer than 2% of patients are younger than age 40 at diagnosis. MM evolves from premalignant conditions named monoclonal gammopathy of undetermined significance (MGUS) and smouldering multiple myeloma (SMM). These precursor diseases of MM are asymptomatic but have in common with the MM the same genetic events, the presence of a serum monoclonal protein and of clonal marrow plasmocytes in the bone marrow. MGUS and its derivative, the MM, are in fact multiple subtypes accordingly to the immunoglobulin isotype of the monoclonal protein. The most well characterized MGUS are IgG (69%), IgA (11%) and biclonal (3%). They are followed by light chain MGUS and, in a smaller proportion the IgD, the IgE and the nonsecretory variety. About 17% of all MGUS is the IgM subtype, an apart subcathegory which engenders the rare IgM myeloma variety and a different disease: Waldenström's macroglobulinemia. The risk of progression to MM from MGUS is 1% per year and for SMM is 10% in the first 10 years after the diagnosis. These risks of progression are not uniform. The cases MGUS are stratified by some risk factors (e.g. non-IgG isotype, serum M protein concentration and free light chains ratio) each is worth for 1 point. At 20 years of follow up, the risk of progression for patients with MGUS with 0, 1, 2 or 3 factors is 5%, 21%, 37% and 58 % respectively. For SMM, the risk factors include BM plasma cells > 10% (1 pt.), serum M protein concentration > 3g/dL (1 pt.) and a skewed FLC-ratio. The cumulative risk of progression at 10 years is 50%, 65%, 84% respectively. The clonal progression of genetic and molecular abnormalities seconded by the tissular depositions of the monoclonal protein are the common pathogenic factors of these three disease states suggesting a spectrum continuum process. The consensus on the atitude is the watch and wait strategy or, at the most the limit the therapy within the frame of clinical trials.