Do patients with IgM related disorders have a different amyloid presentation and course?

Dr Ashutosh Wechalekar

Systemic AL amyloidosis is a rare disorder of protein misfolding caused by an underlying B-cell disorder - 6% of cases with AL amyloidosis have IgM associated disease. Due to the rarity of IgM related AL amyloidosis, its pathology, underlying pathophysiology and natural course remain poorly understood. Patients with IgM associated AL amyloidosis have a disease course that may be different from plasma cell dyscrasia related AL amyloidosis. A significant proportion of patients with IgM related AL amyloidosis have underlying lymphoplasmacytic lymphoma/Waldenstrom's macroglobulinaemia but in a third of all cases, the bone marrow does not show clear evidence of an underlying lymphoid infiltrate. The presenting serum free light chain levels in IgM AL amyloidosis are significantly lower than non-IgM cases. There appears to be a higher proportion of patients with kappa light chain amyloidosis in IgM disease than non-IgM disease. There is higher incidence of peripheral neuropathy, lymph node involvement and lung involvement. Cardiac involvement is less prevalent. In AL amyloidosis, the extent of heart involvement dominates the clinical outcomes. This also appears to be the case in IgM related amyloidosis with advanced heart involvement but in cases with less severe cardiac amyloidosis, this does not appear to have such a major impact on outcomes. Peripheral and autonomic neuropathy do not have a major prognostic impact in non-IgM AL amyloidosis but are independent prognostic markers for outcomes in IgM AL amyloidosis. Some patients appear to have a more indolent disease course. IgM related AL amyloidosis is a distinct subtype of AL amyloidosis with a different underlying pathology, pattern of organ involvement, prognostic markers and treatment outcomes.