Advances in the Diagnosis and Management of Systemic Amyloidosis

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The past ten years have witnessed significant progress in the clinical management of systemic amyloidoses, thanks to the increasing availability of refined diagnostic techniques, the identification of novel prognostic markers for risk-stratification and the development of more effective agents that suppress or reduce the circulating amyloidogenic precursors. Such improvements have been paralleled by a greater awareness of this group of diseases in the medical community, overall leading to earlier recognition and more tailored treatments. Early, accurate diagnosis is the key to effective therapy, and early "red-flags" should raise the clinical suspicion of systemic amyloidosis and trigger the appropriate diagnostic procedures. Unequivocal identification of the amyloidogenic protein may require advanced technologies and expertise and mass spectrometry-based proteomic techniques are now considered gold standard for amyloid typing. New imaging methods are also under development for improving the assessment of organ involvement. The most common type, immunoglobulin light chain amyloidosis (AL), is caused by clonal plasma cells that produce misfolded light chains, with a reported incidence of 8.9 per million person years. The patients with IgM-associated AL amyloidosis represent a small subgroup (5-7%) characterized by distinct clinical and laboratory features. Patients are older than non-IgM patients, with higher frequency of lymph-node involvement and less severe heart and renal damage. Most of the patients had underlying Iymphoma, mainly of Iymphoplasmocytic subtype. Prognosis is dominated by the extent of cardiac involvement, and cardiac biomarkers directs the choice of therapy. The goals of therapy are prompt elimination of the misfolded amyloidogenic light chains, minimization of treatment toxicity, and support of the function of target organs. Virtually all patients with AL amyloidosis die because of heart failure or sudden death. Therefore, it is essential that hematologic response translates into stabilization or improvement of cardiac function to provide significant benefit in quality of life and survival. Treatment of IgM-associated amyloidosis is based on regimes developed specifically for Waldenström's macroglobulinemia. Similarly to that observed in non-IgM patients with AL amyloidosis, also in this population hematologic response to chemotherapy greatly improves survival. In the near future, amyloid diseases will be treated with combination cytotoxic, targeted, and immunologic approaches that reduce protein precursor production, prevent aggregation, and induce fibril resorption.