Advances in Amyloidosis

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AL amyloidosis is a rare acquired disease in which a monoclonal free light chain deposits as aggregated extracellular fibrils and causes organ dysfunction. Amyloidosis includes: AA amyloidosis due to chronic inflammation, β2 amyloidosis seen in dialysis, senile amyloidosis which is more and more frequently diagnosed, inherited forms and those related to light chain deposits: AL amyloidosis. In this form there is most of the time a plasma cell clone that infiltrates the bone marrow to a modest extent and transformation to overt myeloma occurs very infrequently.

Initial investigation should confirm the diagnosis of amyloidosis on tissue biopsy and this should be followed by amyloidosis typing. The careful distinction between AL amyloidosis and other forms is very critical because chemotherapy will not have any benefit outside AL. Immunochemistry can help mainly for AA amyloidosis and some hereditary forms. In cases of doubt ultra structural immunochemistry, DNA analysis and/or amyloid fibril characterization by mass spectrometry may be necessary.

In systemic amyloidosis, deposits can affect any part of the body except the brain and lead to a wide range of tissue and organ dysfunction with extremely varied clinical presentation.

The most common cause of death in amyloid is cardiac, either due to progressive congestive cardiomyopathy or sudden death. Serum levels of serum troponin T and NT-Pro BNP are predictive of survival and are the basis of the Mayo Clinic staging system.

Survival in this disease is directly depending on hematological response which should be monitor with the FLC assay that provides a direct measure of the fibril-precursor protein.

Despite great progress since 2000, optimal treatment is still widely debated, particularly on the role of high dose treatment with autologous stem cell transplant (ASCT). Recommendations among the French network for AL amyloidosis (AL) is to first adapt treatment to disease severity evaluated by the Mayo Clinic staging system and then on hematological responses. Mayo 1 and 2 patients receive melphalan and dexamethasone (MDex). Bortezomib is added for refractory patients, after one cycle in patients with cardiac involvement (Mayo 2) and after 3 cycles for patients without (Mayo 1). Patients with severe cardiac disease (Mayo 3) are given a combination of weekly bortezomib, oral cyclophosphamide and dexamethasone (VCD).

This simple risk-adapted and response-tailored treatment can give a high response rate and a very good survival even in a multicenter setting. Other myeloma new drugs, particularly IMIDs, could be used as salvage treatment for non responders.