Workup of the WM patient with Amyloidosis

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Immunoglobulin light chain amyloidosis is a rare complication of immunoglobulin M monoclonal gammopathies and Waldenström's macroglobulinemia. Early diagnosis is crucial in order to establish effective treatment before irreversible organ damage has occurred. The diagnosis of amyloidosis requires the demonstration of amyloid deposits in tissues using Congo red staining or electron microscopy (EM). The availability of alternative, less invasive, sites can spare the biopsy of the organ involved. In a series of 597 consecutive patients with suspected systemic amyloidosis referred to our center, abdominal fat aspirate (AFA) had 82% sensitivity. The combination of AFA with the Congo red staining of bone marrow biopsy allows the detection of amyloidosis in almost 90% of patients. The biopsy of a minor salivary gland can detect amyloid deposits in 58% of subjects with negative AFA. Once the presence of the deposits has been established, it is vital to reach unequivocal amyloid typing, since treatment is different in different types of amyloidosis, and mistyping can lead to catastrophic therapeutic mistakes. The clinical presentation rarely allows discriminating different types of amyloidosis (e.g. macroglossia and periorbital purpura, typical of AL amyloidosis, are present in approximately 10% of patients only). Light microscopy immunohistochemistry has a poor diagnostic performance in AL amyloidosis. At our center immuno EM approaches 100% specificity. Protein identification by mass spectrometry is the gold standard for amyloid protein identification, being now feasible on clinical biopsy samples. Hereditary amyloidosis should be ruled out by DNA analysis. In AL amyloidosis the demonstration of the amyloidogenic LC is essential for diagnosis and assessment of response to treatment. The amyloid forming clone is usually small and a combination of high-resolution techniques, including serum and urine immunofixation and the free LC assay, is needed to grant maximum sensitivity. A monoclonal IgM is present in 5-7% of patients with AL amyloidosis. Subjects with IgM-AL amyloidosis usually are older (median age 68 vs 61 yrs in non-IgM AL), present with a usually small IgM spike associated more frequently to LC kappa at low concentration. The patients with AL amyloidosis associated to IgM gammopathy present less frequent and less severe heart involvement (lower cardiac biomarkers) and kidney involvement (lower urinary protein conc.) and more frequent lymph node and lung involvement compared to non-IgM AL amyloidosis.

Early diagnosis and accurate typing, refined patients stratification and novel therapies, conjugating tolerability with rapid efficacy, monitored with cardiac biomarkers are changing the natural history of AL amyloidosis.