When should you suspect amyloidosis and what work-up should you do?

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Several clinical hints should raise the suspicion of systemic amyloidosis, such as the presence of heart failure with preserved ejection fraction and thickened ventricular walls with low voltages at ECG. Kidney involvement is characterized by proteinuria and progressive renal failure. Fatigue and weight loss are common. The presence of axonal sensorimotor polyneuropathy (carpal tunnel syndrome is present in 50% of patients) should suggest the diagnosis, as well as the increase of cardiac and renal biomarkers in patients with MGUS. The presence of prototypic signs such as macroglossia and periorbital purpura can immediately lead to the right diagnosis. However, such signs are uncommon and, more importantly, appear late in the course of the disease, frequently when the organ damage caused by the amyloid process is already irreversible. The search for serum and urine monoclonal protein is necessary, and if there are signs of cardiac involvement, bone tracers labeled with technetium localize avidly to transthyretin cardiac amyloidosis, while their uptake by cardiac AL amyloidosis is usually absent or modest. These tracers may help in differentiating between AL and ATTR amyloidosis. Abdominal fat aspirate, can detect amyloid in more than 80% of patients, if negative, labial salivary glands may be biopsied. If these biopsies are negative and there is clinical suspicion of cardiac involvement cardiac MRI can be diagnostic. The involved organ can then be biopsied, keeping in mind that liver biopsy may result in fatal bleeding. Once amyloid has been detected, it is essential to determine precisely which protein forms the deposits in order to select the appropriate therapy. Mass spectrometry-based proteomics is now extensively used to unequivocally identify the protein causing the disease. Other technologies can be complementary such as immune electron microscopy, developed at our center, or immunohistochemistry, available in specialized centers. Several technologies are required to characterize the amyloidogenic clone. The identification and quantification of the amyloid protein requires serum and urine immunofixation followed by FLC measurement. Mass spectrometry is now emerging as a sensitive and accurate technology for light chain identification and quantification. Analysis of AL plasma cells with interphase FISH showed that the (11;14) translocation is the most commonly observed abnormality.