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Amyloidosis

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Amyloidosis is an uncommon plasma-cell dyscrasia with an incidence of eight patients per million per year. It is often difficult to recognize because of the myriad symptoms and vague nature of the clinical presentation. Symptoms include fatigue, dyspnea, edema, paresthesias, and weight loss. Clinical syndromes at presentation include nephrotic-range proteinuria with or without renal insufficiency, cardiomyopathy, hepatomegaly, symptomatic peripheral neuropathy, and autonomic failure. Recent advances have occurred in evaluation of patients by using the free light chain assay and new prognostic assessments with cardiac biomarkers. Newly developed therapeutic strategies, involving high-dose and intermediate-dose chemotherapy, have evolved in the last 3 years. This paper reviews a diagnostic pathway clinicians can use to diagnose the disorder, assess a patient's prognosis, and logically plan a therapeutic strategy.

Key words: amyloid; amyloidosis; cardiomyopathy; monoclonal gammopathy; multiple myeloma; nephrotic syndrome; stem-cell transplantation.

Amyloidosis results from the extracellular deposition of fibrillar amyloid protein (Figure 1).[1] Amyloid is defined by the tinctorial properties of binding of Congo red dye and green birefringence under polarized light.[2] X-ray diffraction microscopy demonstrates that amyloid is a protein that configures as a β-pleated sheet rather than the normal α-helical structure of physiologic proteins.[3] Amyloidosis is a generic term and includes all forms of systemic amyloidosis, those related to light chain deposits, amyloid A protein, and inherited forms, which include transthyretin, apolipoprotein, lysozyme, and fibrinogen. It also includes the forms of localized amyloidosis that are seen in the brain in Alzheimer disease, genitourinary tract,

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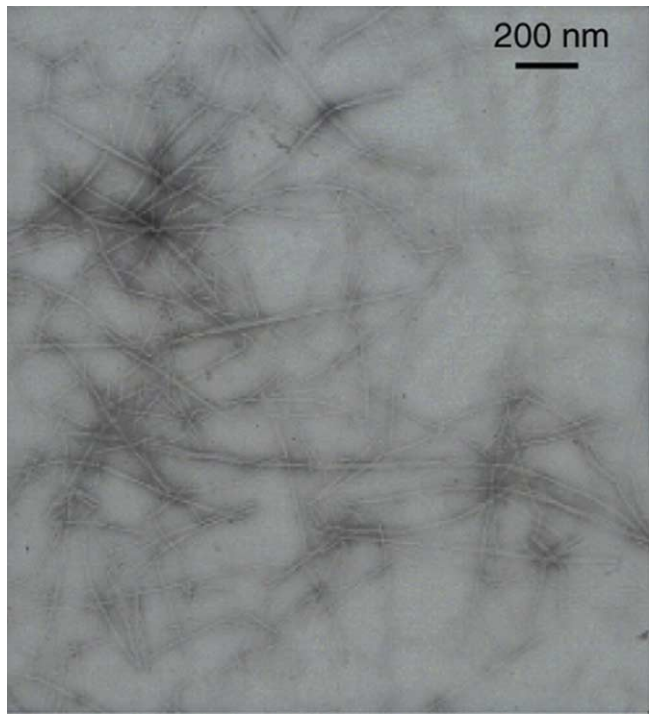

Figure 1. Electron micrograph demonstrating the fibrillar ultrastructure of amyloid.

tracheobronchial tree, and skin.[4] The form of amyloidosis that is associated with the shortest survival and poorest outcome is primary, also known as immunoglobulin light chain amyloidosis (AL). A structural subunit of this form of amyloid is the monoclonal (M) immunoglobulin light chain derived from plasma cells or lymphoplasmacytic cells, usually in the bone marrow.[5]

The symptoms of the disorder are vague. They include fatigue, edema, and weight loss, and are generally not helpful in the formulation of an appropriate differential diagnosis.[6] Occasional patients are recognized initially by the hematologist because they have an M protein with a small percentage of plasma cells in the bone marrow[7], and the disease is mislabeled as atypical multiple myeloma with no clear-cut explanation for the fluid retention, weight loss, and fatigue. Because there is no diagnostic blood test, radiograph, or scan, a heightened awareness of this entity is essential to identify patients. Patients can present in several ways. Patients whose disease is ultimately diagnosed because of nephrotic syndrome frequently are treated empirically with high-dose corticosteroids for the possibility that they may have minimal change disease[8], membranous nephropathy, or membranoproliferative glomerulonephropathy. Often, patients with nephrotic syndrome develop dramatic increases in lipid values and are treated for hypercholesterolemia without recognition that it is due to heavy proteinuria.

Patients with cardiac amyloid frequently fail to develop cardiomegaly or interstitial pulmonary edema and have no ischemic symptoms. Therefore, the normal chest radiograph offers no clues as to the etiology of fatigue and dyspnea, and these patients

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