Yet another amyloidosis

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Systemic amyloidosis is a syndrome of protean manifestations and many pathophysiologies, united by the histopathologic demonstration of extracellular deposition of Congo red-positive fibrillar material that shows apple green birefringence under polarized light microscopy.[1] Its clinical features vary depending on the site of amyloid deposition and the particular protein of which amyloid is comprised. Symptomatic deposition of amyloid may involve the heart, the liver, the kidneys, the stomach and intestines; the central, peripheral, or autonomic nervous systems; the lungs or upper airway; or the skin.[1] Familial Mediterranean fever is an autosomal recessive disorder of amyloid deposition.[2]

Since it can present in so many different ways, amyloidosis is a favorite topic for case reports and clinical pathologic conferences (CPCs). A search on the New England Journal of Medicine website for clinical cases identified 562 publications in that journal where amyloidosis was either the diagnosis or a key element of the differential diagnosis extending back into the 1940s, with many of these in the feature Case Records of the Massachusetts General Hospital. This author has personally been the discussant at two CPCs at different medical schools where the diagnosis turned out to be amyloidosis.

The proteins most acknowledged as causes of amyloidosis are immunoglobulin light chains,[3] serum amyloid protein A,[4] and transthyretin.[5] In the current issue of the *Journal of Investigative Medicine*, Mann and colleagues[6] present a review article discussing the clinical features, pathogenesis, and current understanding of an under-recognized but relatively frequent amyloidosis disorder caused by the deposition of leukocyte chemotactic factor 2 (LECT-2).

LECT-2 amyloidosis (ALECT-2) is one of the most common causes of renal amyloidosis, and less frequently, of hepatic amyloidosis. Involvement of other organ systems has been reported but is uncommon. ALECT-2 renal involvement appears to have a less aggressive clinical course than other forms of renal amyloidosis. It has a characteristic pattern of tissue deposition, occurring primarily as diffuse involvement of the renal cortex rather than of the medullary interstitium or the glomerulus. Hepatic involvement also exhibits a characteristic pattern of deposition in the periportal parenchyma and around the periphery of the portal triad and central venules.[6]

It is reasonable to expect that ALECT-2 will become more widely recognized in the future. LECT-2 is a neutrophil chemotactic factor produced in the liver and is part of the inflammatory response to hepatic fat deposition. Predisposing factors to increased LECT-2 production appear to include obesity, metabolic syndrome, and non-alcoholic steatohepatitis—disorders that are certainly on the increase. Although ALECT-2 has been described in many different ethnic groups, it appears to be particularly common in individuals of Latinx ancestry, one of the faster growing components of the US population.

Mann and colleagues have provided a great service to the medical community by their concise yet thorough review of a clinical disorder that deserves to be more frequently considered.

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