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Editorial

LECT2 – A New Cause of Hepatic Amyloidosis

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Editorial

Amyloidosis is caused by an abnormal deposition and accumulation of insoluble protein fibrils in multiple organs, often leading to diverse clinical presentations, and possible organ failure. On Congo-Red staining, amyloid fibrils form characteristic beta-pleated sheets that typically show apple, green birefringence upon polarization under light microscopy. The kidney is the most common organ affected in systemic amyloidosis. The liver is involved less frequently than the kidney. In this editorial we present a recently discovered amyloid protein - LECT2 (leukocyte chemotactic factor 2) that has been documented to affect the kidney and the liver.

Of more than 30 types of amyloid protein fibrils discovered thus far, LECT2 is one of the most recently described. It was initially reported to present with slowly progressive renal failure and nephrotic syndrome [1,2].

In the United States, LECT2 protein has been found to be especially prevalent among people of Hispanic ethnicity [1]. In an autopsy series, LECT2 amyloid deposits were identified within the kidney in 3.1% of Hispanics, and could represent an important but under-recognized etiology of chronic kidney disease in this population [1,3]. Two large case series focusing on renal amyloidosis identified LECT2 as the second and third most common form of renal amyloidosis respectively [3,4]. LECT2 fibrils are found in the glomeruli, renal vessels, and interstitium. Other organs including the liver, spleen, adrenals, and lungs but not myocardium or brain have been reported to be involved with LECT-2 amyloid protein [1,5].

A recent large case series identified LECT2 as the second most common form of hepatic amyloidosis [6]. In this series LECT2 accounted for up to 25% of hepatic amyloid cases. LECT2 is synthesized mainly by the liver and is considered to be a hepatokine. The exact biological function of LECT2 is not precisely known. In the liver, it acts as is an eutrophilic chemotactic factor. It also plays a role in hepatocyte regeneration [6]. Increased expression of LECT2 has been found in hepato cellular tumors [7]. The LECT2 gene has been mapped to chromosome 5q31.1-q32 by fluorescence in situ hybridization. This region contains a cluster of cytokine genes that include IL-4, IL-5, and IL-9 [8].

Recently it was discovered that LECT2 may play an important role in insulin resistance and may promote atherosclerosis [9]. As such, it is also suggested to play a role in the development of fatty liver and obesity [10].

Hepatic amyloid, when identified, is usually located in the sinusoids, portal tracts, and arterioles. Various morphological patterns of amyloid including linear, globular and mixed types have been identified. The Globular Hepatic Amyloid (GHA) sub-type is composed of round to oval globules, 5 to 40 micrometer in diameter that are found within the space of Disse as well as aggregated within the portal tracts [11]. Chandran et al. found that GHA, although uncommon, is highly sensitive and specific for LECT2 amyloidosis and was also found more often in Hispanics [12]. LECT2 has been described in a patient with non-cirrhotic portal HTN [13]. It is possible that deposition of GHA in the vascular spaces of the liver can cause obstruction of the blood flow at the sinusoidal level resulting in non-cirrhotic portal hypertension [14].

The diagnosis of LECT2 amyloid involves the use of immuno histochemical staining and laser micro dissection with mass spectrometry (more accurate) in addition to demonstrating typical green birefringence in Congo-Red stained sections [15,16].

Being a newly discovered protein fibril that causes amyloidosis, the current state of knowledge regarding LECT2 and liver disease is a work in progress. More research is needed to clarify its role and significance regarding hepatic amyloidosis. Clinicians should be aware of its potential role as a cause of hepatic and renal disease (especially in Hispanics) and special tests such as immunostaining and laser micro dissection with mass spectrometry should be performed in cases where routine testing fails to characterize the amyloid fibril type.

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