Serum CXCL5 Detects Early Hepatocellular Carcinoma and Indicates Tumor Progression

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Abstract

Chemokines or chemotactic cytokines play a pivotal role in the immune pathogenesis of liver cirrhosis and hepatocellular carcinoma (HCC). Nevertheless, comprehensive cytokine profiling data across different etiologies of liver diseases are lacking. Chemokines might serve as diagnostic and prognostic biomarkers. In our study, we analyzed serum concentrations of 12 inflammation-related chemokines in a cohort of patients (n = 222) with cirrhosis of different etiologies and/or HCC. We compared 97 patients with cirrhosis and treatment-naïve HCC to the chemokine profile of 125 patients with cirrhosis but confirmed absence of HCC. Nine out of twelve chemokines were significantly elevated in sera of cirrhotic patients with HCC compared to HCC-free cirrhosis controls (CCL2, CCL11, CCL17, CCL20, CXCL1, CXCL5, CXCL9, CXCL10, CXCL11). Among those, CXCL5, CXCL9, CXCL10, and CXCL11 were significantly elevated in patients with early HCC according to the Barcelona Clinic Liver Cancer (BCLC) stages 0/A compared to cirrhotic controls without HCC. In patients with HCC, CXCL5 serum levels were associated with tumor progression, and levels of CCL20 and CXCL8 with macrovascular invasion. Importantly, our study identified CXCL5, CXCL9, and CXCL10 as universal HCC markers, independent from underlying etiology of cirrhosis. In conclusion, regardless of the underlying liver disease, patients with cirrhosis share an HCC-specific chemokine profile. CXCL5 may serve as a diagnostic biomarker in cirrhotic patients for early HCC detection as well as for tumor progression.