

Abstract

Previously, we demonstrated unique protein expression patterns in 20-week-Schistosoma mansoni-infected CBA/J mice with moderate splenomegaly syndrome (MSS) or hypersplenomegaly syndrome (HSS). To better understand the development of severe pathology, we compared the two-dimensional differential in-gel electrophoresis (2D-DIGE) proteomic signatures of livers from uninfected mice and mice infected for 6, 8, 12, or 20 weeks and found significant changes in collagen isoforms, interleukin-2 (IL-2), cytokeratin 18, hydroxyproline, S. mansoni phosphoenolpyruvate carboxykinase, major urinary protein isoforms, and peroxiredoxin 6. Cytokeratin 18, hydroxyproline, and connective tissue growth factor (CTGF) were chosen for analysis in mouse and human sera using targeted biochemical assays. Consistent with the liver analysis, cytokeratin 18, CTGF, and hydroxyproline were significantly elevated in sera from mice with HSS compared to those from uninfected mice or mice with MSS. Moreover, cytokeratin 18 and CTGF were found to be markers for subjects with hepatosplenic and intestinal schistosomiasis, respectively, while serum hydroxyproline was a strong indicator of fibrosis for severe HS. These findings indicate that schistosome-associated changes to the liver can be detected in the serum and reveal the potential for cytokeratin 18 to be used as a diagnostic marker for early detection of hepatosplenic schistosomiasis.