

Original Article

Association between immune-dysfunction and hepatic fibrosis in patients

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Abstract: This report was described the relationship between impaired immunocompetence and liver fibrosis progression in patients. The recruited suffers were recorded the medical history during therapeutic periods, which diseased condition was diagnosed through blood serum testing and hepatic biopsy for further examinations. Representatively, the liver functional enzymes, (such as ALT, AST) and immune cell counts (including neutrophil leucocytes, platelets) were significantly elevated, while the albumin content and hemoglobin number were decreased. As seen in pathological picture, the intracellular collagen and inflammatory infiltration were observed in the liver. In addition, respective biomarker of hepatitis B surface antigen (HBsAg), a surface antigen of the hepatitis B virus (HBV), was immune-positively expressed in the liver cells, as well as of cytokeratins levels (such as CK18, 19) were up-regulated. Here the histopathological observations illustrate that hypo-immune features promote the accumulation of hepatic collagen and the induction of cytokeratin formation that may promote the progression of liver disease. Further, the clinicopathologic evidence suggests the possible cytokeratin biomarker for the diagnosis of HBV-infected liver fibrosis.

Keywords: Liver fibrosis immune, collagen, cytokeratin

Introduction

Hepatofibrosis is featured by excessive connective tissue depositing in the liver during wound healing. The inducement of hepatic fibrogenesis is chronic invasion, especially in inflammatory stress, such as hepatitis [1]. As shown in clinical observations, virus-infected hepatocytes can alter lipid homeostasis and signal pathways and therefore cause accumulation of oxidative stress and inflammatory infiltration [2, 3]. These profibrogenic mediators could promote the development to liver fibrosis. Some reports indicate that hepatitis-infected patient with immunodeficiency is implicated in inducing a faster development of hepatic fibrosis over time [4]. In clinical treatment, pharmacological intervention seems to be a conventional management of liver fibrosis, leaving increase of adverse effects [5]. Therefore, clinical observation warrants conducting and selecting representative biomarkers in pathological diagnosis

before making the effective prescriptions. In this report, we focus on the highlights on clinical biochemistry detection and histopathological examination to investigate the relationship between immune-dysfunction and liver fibrosis in patients, and to identify a potential candidate marker for screening fibrosis progression in the liver.

Patients and methods

The subjects (n = 4) with diseased livers were registered prior to receiving drug therapy. Routinely, all patients were subjected to clinical diagnosis, including serological test and pathological inspection. As a statement, all the procedures were according to the Ethical Guidelines issued in the Declaration of Helsinki.

Methodologically, liver samples were collected via biopsy and embedded in paraffin as blocks. 5 µm-sectioned liver specimen was conducted

Immune-deregulation relates to hepatofibrosis

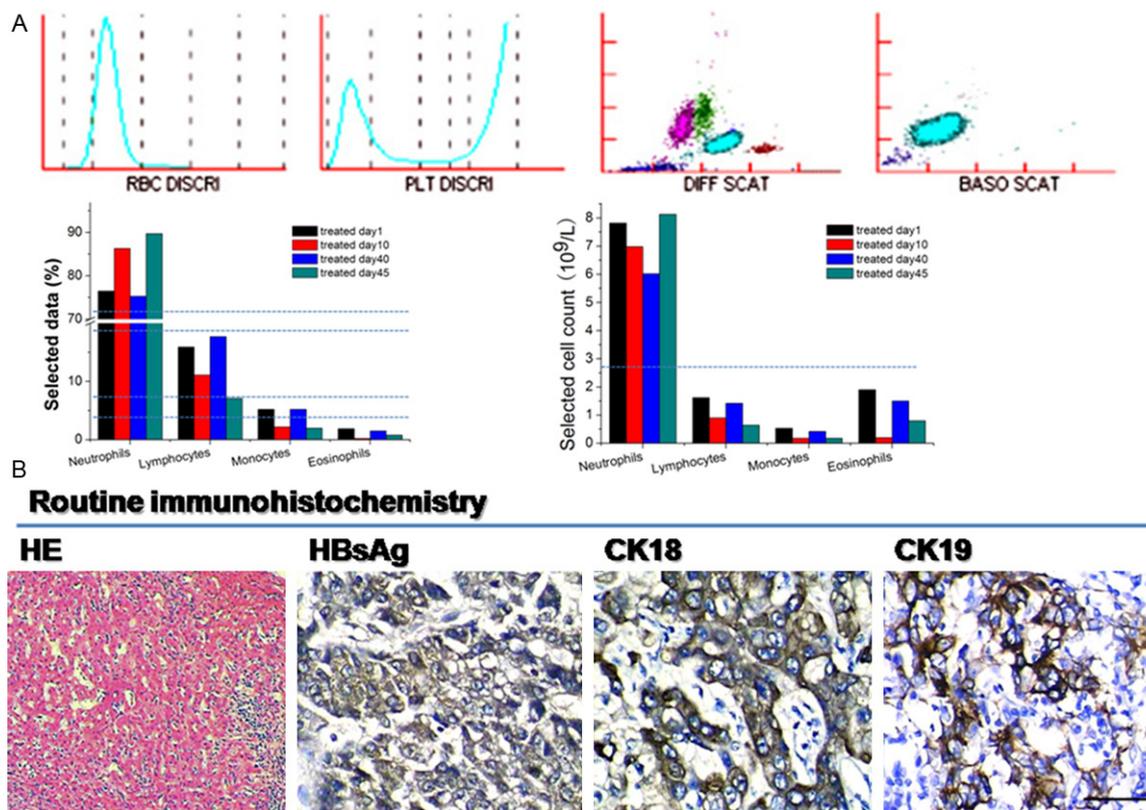


Figure 1. A. The analyzed data from representative patient showed the abnormally profiling in blood immune cells when compared to the clinical standards in use (dashed distinctions near the bars). B. Microstructure images exhibited representative immunochemical stains during liver fibrosis progression (Immunohistochemistry; scale bar = 50 mm). HE staining displayed that outcome of inflammatory infiltration and collagen deposition in the liver. Immuno-labeled positive cells of HBsAg were strongly expressed in liver cells, whereas the immunoactivity for CK18, 19 was widespread distributed around the fibrogenesis liver when the diseased liver developing.

immunohistochemistry assay. In brief, the sliced liver sample was blocked with non-fat milk solution for 1 h, and then was incubated with primary antibodies (1:100; Fuzhou Maixin Biotech. Co., Ltd.) at 4°C overnight before further being incubation of secondary antibodies for 1 h at room temperature. Following steps, antigen-antibody complex was exposed to 3, 3'-diaminobenzidine for visible coloration prior to the nuclei being counter-staining with haematoxylin.

Results

Archiving diseased patient features

As diagnosed, all subjects were tested serologically, with the consequences of significantly elevated ALT and AST levels, and notably increased immunopositive hepatitis B surface antigen (HBsAg). In parallel, demographic characterization of the patients showed the average age was 58.6 with 3 males and 1 female.

In addition, the plasma levels of immune cells, such as neutrophil leukocytes, platelets, were notably increased in a time-dependent phenomenon. However, the hemoglobin content was reduced during the diseased development (**Figure 1A**).

Representative immunophenotypes

Routine staining by HE exhibited that HBV-infected liver widespread deposited the cellular infiltration around the fibrous area.

To identify the characterization and location of immune-markers in liver fibrosis, immunohistochemistry was performed on serial sectioned liver samples. More visibly, HBsAg-immunopositivity cells were labeled in infected liver cells, as brown endochylema location. immunoactive cells for cytokeratins CK18, 19 were identified unevenly distributed in hepatic epithelia, which the positive cells were labeled in cytoplasm (**Figure 1B**).

Discussion

Published studies indicate that the progression of liver fibrosis likely relates to body immune tolerance, which is a promotive factor to damage liver cells and further cause hepatocirrhosis [6]. During liver fibrosis, pathological alteration causes by liver inflammation cascades and results in excess synthesis of extra cellular matrix (ECM) and collagen fibers to abnormally increase. In the cytoplasm, cytokeratin modulates a complex cell biology network that is mainly involved in cell movement and differentiation [7]. As a trend, the subsets of cytokeratin, such as CK18, 19, function as some terminal cell differentiation and the developmental process [8]. Thus, clinical direction of CK18, 19 may be as the possible markers for screening the fibrosis development, especially in HBV-infected patient.

In our current observations, HBV-induced liver fibrosis patients show a significant immune insufficient associated with inflammatory stress, in which was serologically defined and pathologically checked. Basically, the findings provide applicable evidences that the relation between the presence of immune deficit and progression of hepatic fibrosis.

In addition, widespread CK18, 19-immunoreactive cells suggest that HBV-infected liver cause the predisposition of epithelia proliferation and collagenization. Thereby, reduction of hepatic collagen accumulation via enhancement of immune ability can combat the malignant tendency from liver damage to fibrosis.

As limited, further investigation with a large number of patients warrants to conduct on future scientific study.

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Disclosure of conflict of interest

None.

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