Volume 3, Issue 11, November 2025 ISSN (E): 2938-3765

THE ROLE OF CYTOKINES IN HEPATOCELLULAR INFLAMMATION

Zokirkhodjaev Sh. Y.
Tashkent State Medical University, Uzbekistan

Abstract
Hepatocellular inflammation is a central feature of various liver diseases and is primarily mediated by cytokines, which are key regulators of immune and inflammatory responses. This article reviews the role of pro-inflammatory and anti-inflammatory cytokines in the pathogenesis of liver injury, focusing on their effects on hepatocyte function, immune cell recruitment, and fibrogenesis. Understanding the balance between these cytokines is crucial for the development of targeted therapeutic strategies aimed at controlling liver inflammation and preventing progression to chronic liver disease and cirrhosis.

Keywords: Cytokines, Hepatocellular inflammation, Liver injury, Pro-inflammatory cytokines, Anti-inflammatory cytokines, Fibrogenesis.

Introduction

Currently, chronic hepatitis is one of the most widespread liver diseases globally and attracts significant attention due to its progression to fibrosis, liver cirrhosis, and hepatocellular carcinoma. These diseases require timely diagnosis, thorough monitoring, and the development of effective treatment protocols. According to international public health data, approximately 1% of the world's population is infected with hepatitis C virus (HCV), while 5% is infected with hepatitis B virus (HBV). In Europe, co-infection is observed in 3% of the population, and acute viral hepatitis is registered in about 5% of the population [1,2].

The prevalence of chronic hepatitis B varies by geographic region: high (>8% in Africa, Asia, and the Western Pacific), intermediate (2–7% in Southern and Eastern Europe), or low (<2% in Western Europe, North America, and Australia) [29]. Each year, liver cirrhosis develops in 2–5% of patients with chronic hepatitis [3]. At present, the role of the cytokine system in chronic liver diseases and its interaction with other regulatory systems of the body is being widely investigated [4]. It is known that the immune system is regulated genetically; therefore, viral infections can become persistent and lead to chronic hepatitis partly due to immunogenetic factors [5–7]. Thus, some individuals are resistant to viral infection, while others are predisposed to disease progression [8,9]. It has been established that the liver injury in HCV and HBV infections is not associated with direct hepatotoxicity of the viruses but results from immune-mediated inflammation and accelerated fibrogenesis [10,11]. Under physiological conditions, cytokines regulate the activity of hepatic stellate cells (Ito cells), which play the primary role in liver fibrogenesis. These cells produce both profibrotic and antifibrotic mediators, maintaining balance. Antifibrotic mediators include metalloproteinases such as collagenase, gelatinase, and stromelysin. Metalloproteinase activity is controlled by specific inhibitors produced by stellate cells. Regardless of etiology, liver damage

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

triggers the release of large amounts of cytokines such as interleukin-1 (IL-1) and tumor necrosis factor-α (TNF-α). These cytokines activate stellate cells, leading to the production of platelet-derived growth factor (PDGF) and transforming growth factor β1 (TGF-β1), which are crucial drivers of disease progression. TGF-β regulates regenerative processes, promotes collagen and extracellular matrix synthesis, and stimulates the transformation of Ito cells into fibroblasts. Excessive collagen deposition in the space of Disse disrupts sinusoidal blood flow and contributes to hepatocyte necrosis. Recent studies have demonstrated the role of cytokines in complications of liver cirrhosis such as portal hypertension, hepatic encephalopathy, variceal bleeding, and multiple organ failure. Increased intestinal permeability in cirrhotic patients enhances endotoxin translocation from gram-negative bacteria into the bloodstream. Normally, endotoxins are neutralized by Kupffer cells; however, in cirrhosis, their accumulation leads to oxidative stress, lipid peroxidation, increased TNF-α production, inflammation, necrosis, and apoptosis. Increased TNF-α stimulates the overproduction of IL-1, IL-6, IL-8, which promote hepatocyte necrosis, apoptosis, and fibrogenesis. Experimental studies in mice showed that TNF-α may directly induce portal hypertension. Together with IL-8, it activates reactive oxygen species and nitric oxide production, contributing to tissue damage and multi-organ dysfunction. Recent findings revealed that elevated serum levels of pro-inflammatory cytokines (TNF-α, IL-1, IL-6) along with decreased anti-inflammatory cytokines (IL-4, IL-10) are strongly associated with complications such as portal hypertension, hepatic encephalopathy, ascites, and spontaneous bacterial peritonitis [12].

Thus, in liver cirrhosis, the balance between pro-inflammatory and anti-inflammatory cytokines is disrupted. Pro-inflammatory cytokines play a crucial role in cirrhosis decompensation and development of complications such as portal hypertension, ascites, hepatic encephalopathy, and liver failure.

References

1. Бондаренко А.Л. Неблагоприятные прогностиче-ские иммунологические и иммуногенетические факторы формирования цирроза печени у больных хроническим гепатитом В / Бондаренко А.Л., Барамзина С.В. // Росс. журн. гастроэнтерол., гепатол., колопр-октол.— 2004.— № 4.— С. 54—59.
2. Interleikin-1beta gene polymorphism associated with hepatocellular carcinoma in hepatitis B virus infection /Hirankkarn N., Kimkong I., Kummee P // World J. Gastroenterol.— 2006.— Vol. 12, N 5.— P. 776—779.
3. European Association for the Study of the Liver EASL Clinical Practice Guidelines: Management of chronic hepatitis B. J. Hepatol..-2009.-№ 50(2).-P.227–242.
4. Астахин А. В., и соавт. Роль цитокинов и интерферона α в патогенезе хронических диффузных заболеваний печени. А. В. Астахин и соавт. Вестник РАМН, 2004, № 4, С. 19–23.
5. Покровский В. И. Хронический гепатит С: современные представления о пато- и морфогенезе. концепция антивирусной стратегии гепатоцитов. Бюллетень экспериментальной биологии и медицины. 2003, Т. 135, № 4, С. 364–3 76.
6. Ярилин А. А. Система цитокинов и принципы ее функционирования в норме и при патологии. Иммунология. 1997, № 5, С. 7–14.

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

7. Белобородова Э. И., Абдрашитов Р. Ф., Белобородова Е. В., Бурковская, В.А. и соавт. Диагностическая ценность определения сывороточных маркеров фиброза печени при хроническом вирусном гепатите. Клиническая медицина. 2007, № 9, С. 61–63.
8. Абдукадырова М. А. Прогностические маркеры хронизации вирусного гепатита С. Иммунология. 2002, № 1, С. 47–50.
9. Абдурахманов, Д. Т. Вирус гепатита В в патологии человека. Клиническая фармакология и терапия. 2002, № 1, С. 48–56.
10. Рачковский М. И., Черногорюк Г. Э., Белобородова Э. И., Белобородова Е. В. и соавт. Оценка прогностической роли альфа-фетопротеина при циррозе печени: результаты 3-летнего наблюдения. Современные проблемы науки и образования. 2013, № 5, С. 303–304.
11. Рачковский М. И., Черногорюк Г. Э., Белобородова Э. И., Белобородова Е. В. и соавт. Оценка прогностической роли альфа-фетопротеина при циррозе печени: результаты 3-летнего наблюдения. Современные проблемы науки и образования. 2013, № 5, С. 303–304.
12. Li X., Geng M., Peng Y., Meng L., Lu S. Molecular immune pathogenesis and diagnosis of COVID-19. J Pharm Anal 2020;10(2):102–8.
13. Zakirhodjaev Sh.Ya. Talibdjanova M.X. Chronic Liver Diseases and Humoral Factors of Immunity. Евразийский научный вестник. Voluma 33. P.17-23.

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5