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Correlation Between NLRP3 Inflammasome and GP73 Levels and Hepatitis B Cirrhosis with Esophageal Varices Rupture

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Abstract: *Objective:* To investigate the correlation between NOD-like receptor family protein 3 (NLRP3) inflammasome and Golgi protein 73 (GP73) levels and hepatitis B cirrhosis with esophageal varices (EV) rupture. *Methods:* The subjects of this study were 145 patients with hepatitis B cirrhosis and varices who were treated in our hospital in recent years. Endoscopic examination was performed on the patients. The patients were divided into two groups according to whether there was EV rupture: rupture group and non-rupture group. The correlation between plasma NLRP3 and GP73 levels and hepatitis B cirrhosis with EV rupture was analyzed. *Results:* Through observation, comparing the levels of NLRP3 and GP73 between the two groups, the levels of NLRP3 and GP73 were significantly higher in the rupture group than in the non-rupture group ($P < 0.05$). Logistic regression analysis showed that NLRP3 and GP73 levels and Child-Pugh classification were related risk factors of hepatitis B cirrhosis with EV rupture. *Conclusion:* NLRP3 inflammasome and GP73 levels are closely related to hepatitis B cirrhosis with EV rupture. The corresponding evaluation aids in predicting EV rupture and bleeding in patients with hepatitis B cirrhosis.

Keywords: Hepatitis B cirrhosis; Esophageal varices; NLRP3 inflammasome; GP73; Correlation

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1. Introduction

Liver cirrhosis is a transition period from chronic liver disease to liver cancer. The co-existence of liver cirrhosis with other diseases affects the survival period and quality of life of patients. Esophageal varices (EV) are considered a serious complication of liver cirrhosis. Patients often present with massive hematemesis without symptoms or tarry stools. Clinical studies have shown that NOD-like receptor family protein 3 (NLRP3) is associated with the occurrence of various diseases and highly expressed in liver cell injury, which may be associated with liver cell apoptosis and related to vascular aging and vascular rupture [1]. Golgi protein 73 (GP73) is a new type of serum marker that has been confirmed to be highly correlated with liver cirrhosis [2] and liver cancer in recent years. It has high sensitivity to liver cell damage [3] and a certain relationship with the occurrence of EV [4]. Therefore, NLRP3 and GP73 may be associated with liver cirrhosis and EV rupture [5] and may become relevant markers for predicting the risk of EV rupture [6].

The main cause of liver cirrhosis in China is hepatitis B [7]. In this study, 145 patients with hepatitis B cirrhosis complicated with varices in our hospital were selected to determine the correlation between the levels of NLRP3 inflammasome and GP73 and hepatitis B cirrhosis with EV rupture.

2. Materials and methods

2.1. General information

The subjects of this study were 145 patients with hepatitis B cirrhosis and varices admitted to the Department of Infectious Diseases and Gastroenterology of Shaanxi Provincial People's Hospital from January 2020 to December 2022. The diagnosis complied with the Chinese Guidelines for the Diagnosis and Treatment of Liver Cirrhosis (2019 Edition) and the Chinese Guidelines on the Management of Liver Cirrhosis [8]. The patients underwent endoscopic examination and then divided into two groups according to the presence or absence of EV rupture, namely the rupture group and the non-rupture group. There were 75 patients in the rupture group, including 52 male and 23 female patients, age ranging from 41 to 60; there were 70 patients in the non-rupture group, including 51 male and 19 female patients, with age ranging from 42 to 62. There were no significant differences in the baseline data of the two groups of patients ($P > 0.05$). The research protocol was approved by the Ethics Committee of Shaanxi Provincial People's Hospital, and all the patients signed the informed consent.

2.2. Methods

Venous blood was extracted from each patient and placed in a 5 mL vacuum anticoagulant tube. The anticoagulant tube was inverted twice to ensure sufficient contact between the blood and the tube wall. After standing for 1 hour, a pipette was used to extract the upper layer of plasma, and it was then stored in an environment of -80°C. Every 6 months, concentration detection was performed, and the levels of NLRP3 and GP73 in the two groups of patients were detected by enzyme-linked immunosorbent assay (ELISA).

2.3. Statistical analysis

Statistical software SPSS 21.0 was used to process the relevant data in this study; the measurement data were expressed as mean ± standard deviation, and *t*-test was performed. $P < 0.05$ indicates statistically significant difference.

3. Results

3.1. NLRP3 and GP73 levels

Comparing the levels of NLRP3 and GP73 between the two groups, the rupture group had significantly higher NLRP3 and GP73 levels than the non-rupture group ($P < 0.05$). See **Table 1** for details.

Table 1. Comparison of NLRP3 and GP73 levels between the two groups of patients

Group	Number of cases	NLRP3 (ng/L)	GP73 (ng/L)
Rupture group	75	614.62 ± 59.25	183.85 ± 22.61
Non-rupture group	70	546.26 ± 67.12	131.05 ± 21.32
t	–	6.152	14.443
P	–	< 0.001	< 0.001

3.2. Multivariate analysis of liver cirrhosis with EV rupture

Multivariate analysis showed that Child-Pugh classification, NLRP3, and GP73 are related risk factors of liver cirrhosis with EV rupture. See **Table 2** for details.

Table 2. Multivariate logistic regression analysis of liver cirrhosis with EV rupture

Variable	beta	SE	Wald χ^2 value	*P*-value	OR (95%CI)
Child-Pugh classification	2.269	0.785	1.748	0.017	1.839 (1.516–2.589)
NLRP3	2.201	0.783	4.069	0.005	1.993 (1.846–2.765)
GP73	0.063	0.146	16.745	< 0.001	1.865 (1.487–2.697)

Abbreviations: χ^2, chi-square; OR, odds ratio; SE, standard error.

4. Discussion

When chronic liver disease is not effectively controlled [9], it gradually develops into liver cirrhosis, resulting in a more serious degree of liver fibrosis, which promotes an increase in portal venous pressure and blood flow in the gastric or esophageal vessels [10]. Varices [11], which may progress to EV rupture and bleeding, is a risk factor that threatens the life of patients with liver cirrhosis [12]. For patients with rupture and bleeding caused by portal hypertension, they are usually in the decompensated stage of liver cirrhosis and are prone to various complications. Early diagnosis and appropriate intervention can improve the survival rate of patients and disease effect. In order to improve the early diagnostic efficiency of liver cirrhosis with EV rupture, we selected 145 patients with hepatitis B cirrhosis and varices in our hospital as the research subjects [13].

In the human immune system, inflammasome is a relatively important component, most of which are proteolytic complexes, which can recognize pathogens and then transfer signals to promote cell activation and release related inflammatory factors, playing a certain anti-inflammatory effect. NLRP3 is an important member of the inflammasome family that can recognize endogenous and exogenous pathogens and signaling pathways. Studies have shown that excessive intraluminal pressure contributes to the expression of NLRP3 and is closely related to vascular endothelial injury and angiotensin II (AngII) dysfunction [14]. GP73, on the other hand, is a transmembrane glycoprotein in the Golgi apparatus. Unlike NLRP3, which is basically not expressed in normal human tissues, the expression of GP73 decreases if the disease progresses into liver cirrhosis. The increase is most significant in connective tissues and liver cells near cirrhotic nodules [15]. Our results showed that the levels of NLRP3 and GP73 in the rupture group were significantly higher than in the non-rupture group ($P < 0.05$). The reasons are as follows: (i) the number of patients with Child-Pugh C in the rupture group was significantly higher, indicating that the liver reserve capacity of the rupture group was weaker and the liver cirrhosis was relatively more serious, which may be the cause of the rupture; (ii) EV rupture may be due to the increased local vascular pressure, leading to inflammatory response and thus the increase in NLRP3 and GP73 levels.

In order to analyze the correlation between plasma NLRP3 and GP73 levels and hepatitis B cirrhosis with EV rupture, logistic regression analysis was conducted in this study [16]. The results showed that NLRP3 and GP73 levels and Child-Pugh classification are risk factors of hepatitis B cirrhosis with EV rupture. Analysis of the reason may be that NLRP3, as an inflammasome, not only identifies local vascular inflammation, but also promotes inflammatory response, thus causing damage to vascular endothelium. GP73 may be associated with the triggering of inflammatory reactions. A high expression of GP73 is associated with the degree of damage to the nucleus and cell structure, promoting the destruction of local blood vessels, which may be an independent cause of hepatitis B cirrhosis with EV rupture [17].

In conclusion, there is a close relationship between plasma NLRP3 and GP73 levels and hepatitis B cirrhosis with EV rupture, and this evaluation is conducive to the prediction of EV rupture and bleeding in patients.

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Disclosure statement

The authors declare no conflict of interest.

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