

• 临床研究 •

乙肝病毒相关慢加急性肝衰竭患者中 PMN-MDSC 的表达及意义

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[摘要] 目的: 探讨乙肝病毒相关慢加急性肝衰竭(hepatitis B virus-related acute-on-chronic liver failure, HBV-ACLF)患者中多核型髓源性抑制细胞(polymorphonuclear myeloid-derived suppressor cell, PMN-MDSC)的表达及意义。方法: 选取2022年9月—2023年8月皖南医学院弋矶山医院收治的HBV-ACLF患者40例为研究组, 同期在该院诊治或体检的慢性乙肝(chronic hepatitis B, CHB)患者20例、健康对照(healthy control, HC)10例为对照组, 收集临床资料, 留取血标本。流式细胞术检测入院当日外周血PMN-MDSC频率, 比较研究组和两个对照组外周血PMN-MDSC频率的差异。采用Spearman检验分析HBV-ACLF外周血PMN-MDSC频率与炎症指标、疾病严重度的相关性。分别根据是否合并或继发感染及随访期第28天预后情况对HBV-ACLF患者分组, 比较各组外周血PMN-MDSC频率的差异。结果: HBV-ACLF组外周血PMN-MDSC频率显著高于CHB组和HC组(P 均 <0.001), CHB组和HC组之间PMN-MDSC频率差异无统计学意义。HBV-ACLF外周血PMN-MDSC频率与白细胞计数、中性粒细胞淋巴细胞比值、降钙素原水平、国际标准化比值、总胆红素水平、Child-Turcotte-Pugh评分、终末期肝病模型评分均呈正相关($r=0.347, 0.799, 0.506, 0.450, 0.462, 0.470, 0.481, P$ 均 <0.05), 与淋巴细胞计数呈负相关($r=-0.428, P < 0.01$)。40例HBV-ACLF患者中, 合并感染18例, 继发感染17例, 28 d预后差21例, 其外周血PMN-MDSC频率均高于对照组患者, 差异有统计学意义(P 均 <0.001)。结论: HBV-ACLF患者外周血富集PMN-MDSC, 其频率与感染风险、疾病严重度及患者短期预后密切相关。

[关键词] 髓源性抑制细胞; 乙型肝炎病毒; 慢加急性肝衰竭; 感染; 预后**[中图分类号]** R557.1**[文献标志码]** A**[文章编号]** 1007-4368(2024)06-838-07

doi: 10.7655/NYDXBNSN231142

Expression and significance of polymorphonuclear myeloid-derived suppressor cells in patients with HBV-related acute-on-chronic liver failure

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[Abstract] **Objective:** To investigate the expression and significance of polymorphonuclear myeloid-derived suppressor cells (PMN-MDSC) in patients with hepatitis B virus-related acute-on-chronic liver failure (HBV-ACLF). **Methods:** A total of 40 HBV-ACLF patients admitted to Yijishan Hospital of Wannan Medical College from September 2022 to August 2023 were selected as the study group, while 20 patients with chronic hepatitis B (CHB) and 10 healthy controls (HC) diagnosed or undergoing examinations at the same hospital during the same period were collected as the two control groups. Clinical data were collected and blood samples were obtained. Flow cytometry was used to detect the frequency of peripheral blood PMN-MDSC on the day of admission, and to compare the differences in the frequency of PMN-MDSC between the study group and the two control groups. Spearman's correlation analysis was used to investigate the correlation between the frequency of PMN-MDSC and inflammation markers or disease severity. HBV-ACLF patients were further grouped based on whether they had concurrent or secondary infections and the prognosis on day 28 of follow-up, and the differences in PMN-MDSC frequency among groups were compared. **Results:** The frequency of PMN-MDSC in HBV-ACLF

[基金项目] 国家自然科学基金(82370604); 安徽省高校自然科学类科学研究重点项目(2022AH051213); 安徽省卫生健康科研项目(AHWJ2022b054); 皖南医学院重点项目科研基金(WK2022ZF10)

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group was significantly higher than that in the CHB group and the HC group ($P < 0.001$ for both), whereas there was no significant difference in the PMN-MDSC frequency between the CHB and HC groups ($P > 0.05$). The frequency of PMN-MDSC in HBV-ACLF patients was positively correlated with the white blood cell count, neutrophil-to-lymphocyte ratio, procalcitonin, international normalized ratio, total bilirubin, Child-Turcotte-Pugh score, and the model of end-stage liver disease score ($r=0.347, 0.799, 0.506, 0.450, 0.462, 0.470, 0.481$, respectively, all $P < 0.05$), and negatively correlated with the lymphocyte count ($r=-0.428, P < 0.01$). Among the 40 HBV-ACLF patients, 18 had concurrent infections, 17 had secondary infections, and 21 had poor prognosis on day 28, with their peripheral blood PMN-MDSC frequencies significantly higher than those of the control group patients (all $P < 0.001$). **Conclusion:** PMN-MDSC are enriched in HBV-ACLF patients and the frequency of PMN-MDSC in peripheral blood is closely related to infection risk, disease severity, and short-term prognosis of patients.

[Key words] myeloid-derived suppressor cell; hepatitis B virus; acute-on-chronic liver failure; infection; prognosis

[J Nanjing Med Univ, 2024, 44(06): 838-844]

慢加急性肝衰竭(acute-on-chronic liver failure, ACLF)是以慢性肝病为基础、急性肝内外损伤为诱因、伴有多器官衰竭和早期高病死率的一组临床综合征^[1]。我国是乙型肝炎病毒(hepatitis B virus, HBV)感染高负担地区, HBV相关ACLF(HBV-ACLF)是临床最常见的肝衰竭类型。HBV-ACLF患者28 d病死率高达40%, 目前普遍认为, T淋巴细胞等免疫细胞的功能紊乱及伴随的细菌(真菌)感染, 是造成HBV-ACLF进展和患者早期高病死率的重要原因^[1, 4-5]。除肝移植外, 尚缺乏有效降低HBV-ACLF患者病死率的干预措施^[2-3]。因此, 有必要深入研究HBV-ACLF患者细胞免疫紊乱的发生机制和潜在干预靶点。

髓源性抑制细胞(myeloid-derived suppressor cell, MDSC)是一群病理激活、表型异常的髓系来源细胞, 可通过多种途径抑制T淋巴细胞等免疫细胞的增殖、活化和迁移。根据来源及形态特征, MDSC分为单核型MDSC(monocytic MDSC, M-MDSC)和多核型MDSC(polymorphonuclear MDSC, PMN-MDSC)两大亚群, 其中PMN-MDSC主要通过分泌过量活性氧自由基、精氨酸酶-1和前列腺素2发挥免疫抑制功能^[6-7]。外周血PMN-MDSC表达水平在败血症、活动性结核病等细菌感染病患者中显著升高, 并与疾病严重程度、患者预后密切相关^[8-10], 但关于HBV-ACLF患者中PMN-MDSC表达及意义的报道不多。本研究探讨HBV-ACLF患者外周血PMN-MDSC表达水平及其与继发感染风险、疾病严重程度及患者短期预后的关联, 为HBV-ACLF早期干预策略的优化提供思路。

1 对象和方法

1.1 对象

纳入2022年9月—2023年8月皖南医学院弋矶山医院收治的HBV-ACLF患者40例(HBV-ACLF

组), 慢性乙型肝炎(chronic hepatitis B, CHB)患者20例(CHB组), 同时选取本院健康体检者10例作为健康对照(healthy control, HC)组。HBV-ACLF的纳入标准参照中华医学会《肝衰竭诊治指南(2018版)》^[11]; CHB的纳入标准参照中华医学会《慢性乙型肝炎防治指南(2022年版)》^[12]。排除标准: ①年龄 < 18 岁或 > 80 岁; ②妊娠期女性; ③合并其他病因所致慢性肝病, 或重叠感染其他肝炎病毒; ④合并肝细胞癌(hepatocellular carcinoma, HCC)等恶性肿瘤或严重肝外器质性疾病; ⑤使用免疫抑制剂治疗肝外器质性疾病; ⑥住院时间 < 5 d导致重要临床资料缺失; ⑦28 d访视期内失访。比较HBV-ACLF组和CHB组及HC组基线时(入院当日)外周血MDSC频率的差异。分析HBV-ACLF外周血PMN-MDSC频率与炎症指标、预后评分的相关性。分别根据基线时合并感染、住院期间继发感染及访视期第28天预后情况对HBV-ACLF患者进行分组, 比较各组外周血PMN-MDSC频率的差异。本研究符合2013年修订的《赫尔辛基宣言》的要求, 研究方案经皖南医学院伦理委员会审核批准[(2023)伦审第(164)号], 所有研究对象均签署知情同意书。

1.2 方法

1.2.1 资料收集

采集所有研究对象的住院资料(或健康体检资料), 包括: ①性别和年龄; ②肝硬化病史; ③白细胞计数(white blood cell count, WBC)、中性粒细胞计数(neutrophil count, NEUT)、淋巴细胞计数(lymphocyte count, LYMT)、中性粒细胞淋巴细胞比值(neutrophil-to-lymphocyte ratio, NLR)、降钙素原(procalcitonin, PCT)、国际标准化比值(international normalized ratio, INR)、总胆红素(total bilirubin, TBil)、氨基丙转氨酶(alanine aminotransferase, ALT)、白蛋白

(albumin, ALB)、血肌酐(creatinine, CRE)、乙肝表面抗原(hepatitis B surface antigen, HBsAg)、乙肝e抗原(hepatitis B e antigen, HBeAg)、HBV脱氧核糖核酸(deoxyribonucleic acid, DNA)等辅助检查结果;④腹水评分(1分:无腹水;2分:少量腹水;3分:中~大量腹水)和肝性脑病评分(1分:无肝性脑病;2分:1~2级肝性脑病;3分:3~4级肝性脑病)。根据基线数据,计算HBV-ACLF患者的Child-Turcotte-Pugh(CTP)评分和终末期肝病模型(model for end-stage liver disease, MELD)评分,具体公式参照相关文献^[13]。

1.2.2 流式细胞术检测外周血MDSC频率

基线时,使用EDTA抗凝管采集外周血静脉血5 mL,采用人淋巴细胞分离液(Axis-shield公司,挪威)和密度梯度离心法分离外周血单个核细胞(peripheral blood mononuclear cell, PBMC),1 mL磷酸缓冲盐溶液(phosphoric acid buffer salt solution, PBS)重悬细胞,0.4%台酚蓝计数并调整细胞浓度为 2×10^6 个/mL。采用流式细胞术检测PBMC中PMN-MDSC频率,主要步骤包括:①取100 μ L PBMC悬液(2×10^5 个细胞)加入5 mL流式管中,分别加入APC-HLA-DR、FITC-CD11b、Alexa Fluor700-CD33、PE-Cy7-CD14和PE-CD15流式单抗(Biolegend公司,美国)各2 μ L,避光孵育20 min;②加入2 mL PBS吹打混匀细胞,离心、弃上清,并重复该步骤1次;③加入流式鞘液200 μ L重悬细胞,使用贝克曼公司Cytotoflex S流式细胞仪检测外周血MDSC频率(PBMC中MDSC占比),PMN-MDSC标记策略为HLA-DR^{low}CD11b⁺CD33⁺CD14⁻CD15⁺细胞,M-MDSC标记策略为HLA-DR^{low}CD11b⁺CD33⁺CD14⁺CD15⁻细胞。

1.2.3 细菌真菌感染诊断标准及患者短期预后评估

临床医师综合患者临床表现、感染标志物、影像学检查、微生物学培养、宏基因组二代测序及经验性抗感染疗效,对合并/继发细菌真菌感染进行诊断,各部位感染的具体诊断标准参照《终末期肝病合并感染诊治专家共识(2021年版)》^[14]。访视期第28天评估HBV-ACLF患者的预后情况,患者短期预后差定义为:28 d访视期内死亡,或放弃治疗自动出院,或接受肝移植手术。

1.3 统计学方法

采用SPSS 22.0和GraphPad Prism 9.5对数据进行统计分析。计数资料以例数(百分比)[$n(\%)$]表示,组间比较采用 χ^2 检验。正态分布计量资料以均数 \pm 标准差($\bar{x} \pm s$)表示,两组比较采用独立样本 t 检验,多组比较采用单因素方差分析。非正态分布计

量资料以中位数(四分位数)[$M(P_{25}, P_{75})$]表示,两组比较采用Mann-Whitney U 检验,多组比较采用Kruskal-Wallis检验。变量间相关性分析采用Spearman检验。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 3组研究对象基线特征比较

HBV-ACLF组性别构成、年龄、WBC、NEUT和CRE相比HC和CHB组,差异无统计学意义(P 均 > 0.05)。HBV-ACLF组NLR、INR和TBil均显著高于HC和CHB组;LYMT和ALB均低于HC和HBV组,差异有统计学意义(P 均 < 0.001)。与CHB组比较,HBV-ACLF组肝硬化患者比例、合并细菌感染患者比例和PCT均升高,差异有统计学意义(P 均 < 0.01);但2组HBsAg、HBeAg、HBV DNA和ALT水平比较,差异无统计学意义(P 均 > 0.05 ,表1)。

2.2 3组外周血MDSC频率的比较

HBV-ACLF组、CHB组、HC组外周血M-MDSC频率分别为2.20%(1.41%, 3.01%)、1.41%(0.90%, 1.92%)和0.57%(0.43%, 0.67%),整体差异有统计学意义($H=29.672, P < 0.001$);HBV-ACLF组外周血M-MDSC频率高于CHB组和HC组,差异有统计学意义(P 均 < 0.05);CHB组外周血M-MDSC频率高于HC组,差异有统计学意义($P=0.008$,图1A)。HBV-ACLF组、CHB组、HC组外周血PMN-MDSC频率分别为3.77%(1.35%, 5.11%)、0.67%(0.55%, 0.82%)和0.50%(0.40%, 0.59%),整体差异有统计学意义($H=44.401, P < 0.001$);HBV-ACLF组外周血M-MDSC频率高于CHB组和HC组,差异有统计学意义(P 均 < 0.001);CHB组和HC组外周血PMN-MDSC频率比较,差异无统计学意义($P=0.421$,图1B)。

2.3 HBV-ACLF外周血PMN-MDSC频率与炎症指标、疾病严重度的相关性分析

Spearman检验显示,HBV-ACLF患者外周血PMN-MDSC频率与炎症指标WBC、NLR、PCT表达水平均呈正相关($r=0.347, 0.799, 0.506, P$ 均 < 0.05),与LYMT呈负相关($r=-0.428, P < 0.01$,图2A~D)。HBV-ACLF外周血PMN-MDSC频率与疾病严重度指标INR、TBil、CTP评分、MELD评分均呈正相关($r=0.450, 0.462, 0.470, 0.481, P$ 均 < 0.01 ,图2E~H)。

2.4 HBV-ACLF外周血PMN-MDSC频率与患者合并或继发感染、短期预后的关系

40例HBV-ACLF患者中,入院时合并感染共计

表1 3组研究对象基线特征比较

Table 1 Comparison for the baseline characteristics among the three groups of subjects

Variable	HC(n=10)	CHB(n=20)	HBV-ACLF(n=40)	Statistic	P
Male[n(%)]	7(70.0)	16(80.0)	34(75.0)	$\chi^2=1.228$	0.541
Age(years, $\bar{x} \pm s$)	39.0 \pm 5.6	40.0 \pm 10.0	45.0 \pm 12.0	$F=2.837$	0.066
Cirrhosis[n(%)]	-	6(30.0)	29(72.5)	$\chi^2=9.909$	0.002
With infection[n(%)]	-	3(15.0)	18(45.0)	$\chi^2=4.038$	0.045
HBsAg[n(%)]	-	-	-	$\chi^2=0.330$	0.848
<500 U/mL	-	5(25.0)	9(22.5)		
500-5 000 U/mL	-	6(30.0)	15(37.5)		
>5 000 U/mL	-	9(45.0)	16(40.0)		
HBeAg positive[n(%)]	-	9(45.0)	15(37.5)	$\chi^2=0.313$	0.576
HBV DNA[n(%)]	-	-	-	$\chi^2=1.321$	0.517
<200 U/mL	-	6(30.0)	15(37.5)		
200-20 000 U/mL	-	5(25.0)	13(32.5)		
>20 000 U/mL	-	9(45.0)	12(30.0)		
WBC($\times 10^9/L$, $\bar{x} \pm s$)	7.1 \pm 1.2	5.9 \pm 1.3	6.2 \pm 2.6	$F=1.134$	0.328
NEUT($\times 10^9/L$, $\bar{x} \pm s$)	4.1 \pm 0.9	3.4 \pm 1.0	4.4 \pm 2.3	$F=1.776$	0.177
LYMT($\times 10^9/L$, $\bar{x} \pm s$)	2.4 \pm 0.3*	1.9 \pm 0.5*	1.2 \pm 0.4	$F=35.608$	<0.001
NLR($\bar{x} \pm s$)	1.7 \pm 0.4*	2.0 \pm 0.5*	4.1 \pm 2.3	$F=13.854$	<0.001
PCT[ng/mL, $M(P_{25}, P_{75})$]	-	0.23(0.15, 0.36)	0.60(0.47, 0.79)	$Z=-4.298$	<0.001
INR[$M(P_{25}, P_{75})$]	1.0(0.9, 1.0)*	1.0(0.9, 1.1)*	2.1(1.8, 2.5)	$H=51.250$	<0.001
TBil[$\mu\text{mol/L}$, $M(P_{25}, P_{75})$]	10(6, 11)*	21(16, 30)*	309(249, 405)	$H=53.267$	<0.001
ALT[U/L, $M(P_{25}, P_{75})$]	16(9, 25)*	120(91, 271)	133(57, 929)	$H=53.267$	<0.001
ALB(g/L, $\bar{x} \pm s$)	48.0 \pm 1.8*	47.0 \pm 3.7*	35.0 \pm 4.7	$F=23.140$	<0.001
CRE($\mu\text{mol/L}$, $\bar{x} \pm s$)	67 \pm 15	69 \pm 11	71 \pm 24	$F=0.171$	0.843

Compared with the HBV-ACLF group, * $P < 0.05$.

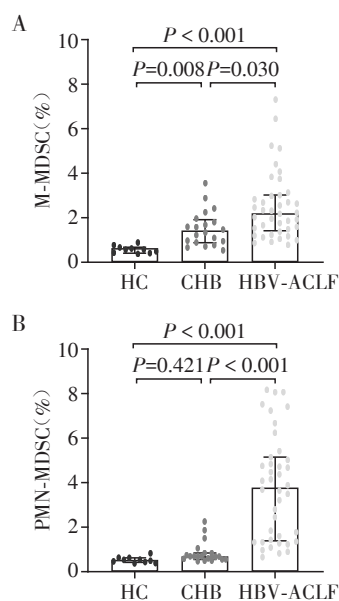


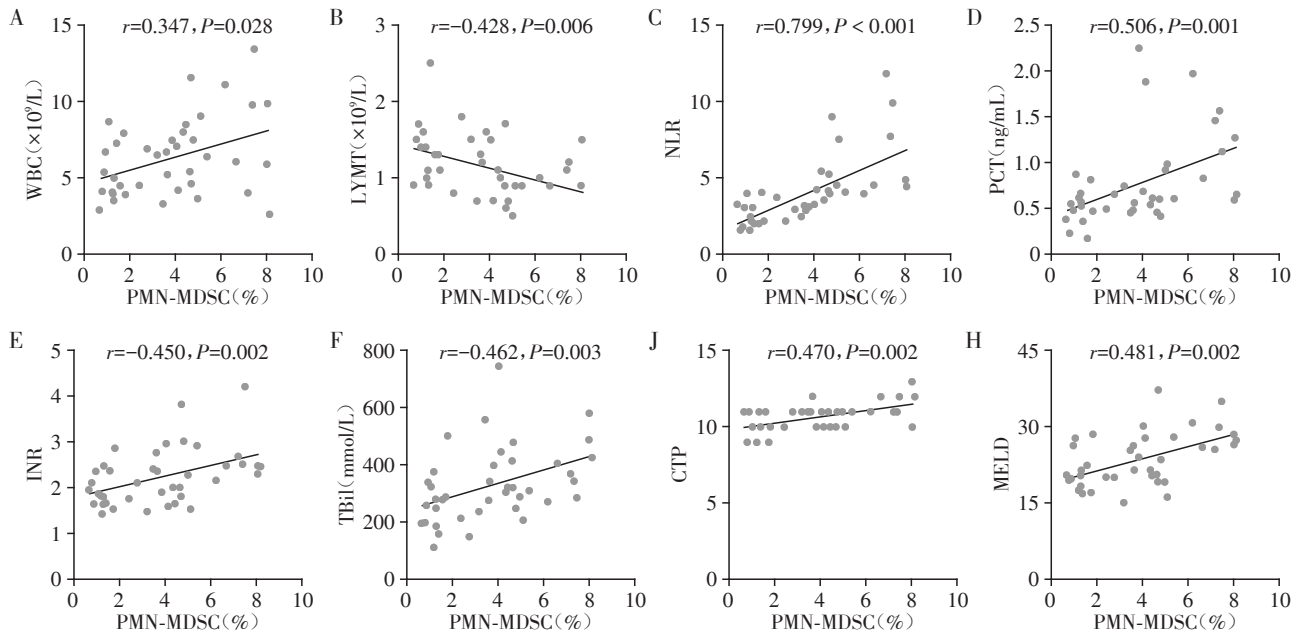
图1 3组研究对象外周血M-MDSC频率(A)、PMN-MDSC频率(B)的比较

Figure 1 Comparison of peripheral blood M-MDSC frequency (A) and PMN - MDSC (B) frequency among the three groups of subjects

18例[细菌感染16例(88.9%),细菌真菌混合感染2例(11.1%)],其外周血PMN-MDSC频率高于对照组[5.22%(4.08%, 7.44%) vs. 1.50%(1.18%, 3.77%)],差异有统计学意义($Z=-1.268, P < 0.001$, 图3A)。住院期间继发感染共计17例[细菌感染8例(47.1%),细菌真菌混合感染9例(52.9%)],二次感染12例(70.6%)],其外周血PMN-MDSC频率高于对照组[5.02%(3.97%, 7.47%) vs. 1.74%(1.24%, 4.15%)],差异有统计学意义($Z=-3.737, P < 0.001$, 图3B)。全部HBV-ACLF患者中,28 d预后差患者共计21例(死亡14例,自动出院5例,接受肝移植手术2例),其外周血PMN-MDSC频率高于对照组[5.02%(4.42%, 7.32%) vs. 1.33%(1.09%, 2.42%)],差异有统计学意义($Z=-5.349, P < 0.001$, 图3C)。

3 讨论

M-MDSC和PMN-MDSC在表型分子、诱导因素、免疫抑制介质等特征上存在不同程度差异,MDSC亚群构成取决于病原种类、机体免疫应答特征、疾



A-D: Spearman correlation analysis of peripheral blood PMN-MDSC frequency with inflammation markers such as WBC(A), LYMT(B), NLR(C), and PCT(D) in HBV-ACLF patients. E-H: Spearman correlation analysis of peripheral blood PMN-MDSC frequency with disease severity markers such as INR(E), TBil(F), CTP score(G), and MELD score(H) in HBV-ACLF.

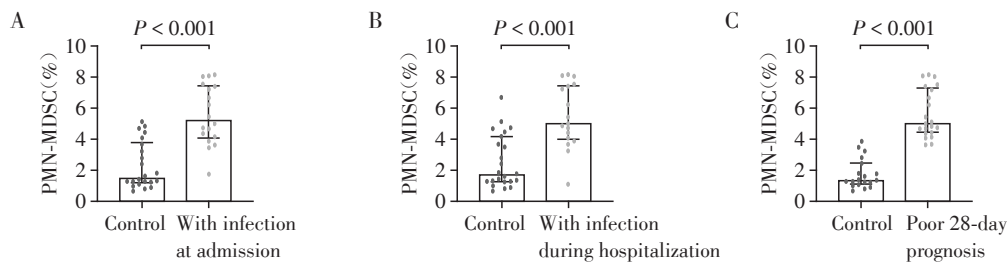
图2 HBV-ACLF患者外周血PMN-MDSC频率与炎症指标、疾病严重度的Spearman相关性分析

Figure 2 Spearman correlation analysis of peripheral blood PMN-MDSC frequency with inflammation markers and disease severity in HBV-ACLF patients

病阶段等因素^[6-7]。HBV是一种嗜肝病毒,通过持续诱导适应性免疫应答和固有免疫应答,造成肝细胞损伤及伴随的肝脏炎症、纤维化乃至癌变^[11]。多项研究表明,M-MDSC是CHB患者体内MDSC主要亚群,HBsAg和HBeAg是M-MDSC扩增的重要诱导因素;M-MDSC可通过分泌一氧化氮、精氨酸酶-1、白介素-10等,抑制HBV特异性CD4⁺/CD8⁺T淋巴细胞的增殖和活化,导致HBV持续感染与疾病进展^[15-17]。当CHB发展至终末期肝病阶段,患者体内免疫微环境更加复杂,MDSC表达水平和亚群构成亦发生一

定变化。Zeng等^[18]研究表明,HBV-ACLF外周血MDSC水平明显高于CHB,外周血MDSC频率与TBil、INR、ALT水平呈明显正相关,与HBsAg、HBeAg、HBV DNA水平无相关性。Nan等^[19]研究表明,乙型肝炎肝硬化所致HCC患者外周血和肝脏中PMN-MDSC水平明显高于非HCC患者。

本研究比较了3组研究对象两群MDSC表达水平差异,结果显示,HBV-ACLF外周血两群MDSC频率均高于CHB组和HC组,且HBV-ACLF组外周血PMN-MDSC频率明显高于CHB组;CHB组外周血



A: Comparison of the PMN-MDSC frequencies between patients with infection at admission (n=18) and the controls (n=22). B: Comparison of the PMN-MDSC frequencies between patients with infection during hospitalization (n=17) and the controls (n=23). C: Comparison of the PMN-MDSC frequencies between patients with poor 28-day prognosis (n=21) and the controls (n=19).

图3 入院时合并感染、住院期间继发感染及28d预后差HBV-ACLF患者与对照组外周血PMN-MDSC频率比较

Figure 3 Comparison of PMN-MDSC frequencies in peripheral blood between HBV-ACLF patients with co-infection on admission, secondary infection during hospitalization, and poor 28-day prognosis and controls

M-MDSC频率明显高于HC组,但2组PMN-MDSC频率接近。在此基础上,本研究分析了HBV-ACLF组外周血PMN-MDSC频率与炎症指标、合并细菌感染的关系,发现HBV-ACLF组外周血PMN-MDSC频率与WBC、NLR、PCT呈正相关(与NLR的相关性最高),与LYMT呈负相关,且LYMT在HBV-ACLF、CHB和HC中呈递减趋势;40例HBV-ACLF患者中,基线时合并细菌感染者18例(45.0%),其外周血PMN-MDSC频率明显高于对照组。结合相关文献,以上结果提示PMN-MDSC扩增于HBV-ACLF阶段而非CHB阶段,HBV-ACLF外周血PMN-MDSC富集加重了T淋巴细胞的增殖、活化障碍,细菌感染可能是HBV-ACLF患者体内PMN-MDSC扩增的重要诱因。

目前普遍认为,细菌感染是HBV-ACLF发生、发展的重要肝外因素,通过诱发内毒素血症、炎症细胞因子风暴及伴随的全身炎症反应综合征,导致凝血系统等肝外器官功能衰竭^[20]。多项研究表明,与无细菌感染HBV-ACLF患者相比,合并细菌感染者病情进展更快,短期病死率更高^[3,14,20]。Darcy等^[8]研究表明,败血症患者体内富集PMN-MDSC,外周血PMN-MDSC频率与疾病严重程度呈正相关。Ruan等^[9]研究表明,与M-MDSC相比,外周血PMN-MDSC频率与败血症患者免疫耐受状态相关性更好,PMN-MDSC持续高水平更有助于预测二次感染风险。本研究发现,HBV-ACLF外周血PMN-MDSC频率与INR、TBil、CTP评分、MELD评分均呈正相关;40例HBV-ACLF患者中,住院期间继发细菌感染者17例(42.5%),其中二次感染占70.6%,继发细菌感染者外周血PMN-MDSC频率明显高于对照组患者;并且所有真菌感染均在细菌感染基础上发生,基线感染谱中真菌感染占比仅为11.1%,继发感染谱中真菌感染占比提升至52.9%,提示PMN-MDSC表达上调加重了HBV-ACLF患者体内免疫抑制微环境,导致二次感染与疾病进展。本研究进一步比较了不同预后HBV-ACLF患者外周血PMN-MDSC水平,发现28d预后差的患者外周血PMN-MDSC频率明显高于预后好的患者,提示外周血PMN-MDSC频率可作为HBV-ACLF患者短期预后评估的免疫炎症指标之一。

本研究存在以下不足:①HBV-ACLF样本量偏少,可能造成一定的统计偏倚,也不利于计算外周血PMN-MDSC频率评估患者短期预后的临界值;②尽管在细菌真菌感染诊断中严格遵从了相应规范、标准,但由于HBV-ACLF患者存在不同程度的

细胞免疫功能障碍,加上腹腔积液、外周血等微生物培养的阳性率不高且耗时偏长,对合并或继发细菌真菌感染的判读可能不够准确。今后需通过增加样本量、应用新型病原学诊断方法(如靶向二代测序、细菌核酸检测)等进一步研究。

综上所述,本研究发现,HBV-ACLF患者外周血PMN-MDSC富集,其频率与继发感染风险、疾病严重程度及患者短期预后密切相关。本研究有助于完善HBV-ACLF细胞免疫紊乱的形成机制,并为HBV-ACLF干预措施的优化提供理论依据。

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[收稿日期] 2023-12-07

(本文编辑: 戴王娟)

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