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肝硬化患者感染性休克的病原学特征及危险因素分析

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摘要 目的:探讨肝硬化患者感染性休克的病原学特征,并分析其危险因素。**方法:**回顾性分析 2012 年 1 月-2015 年 4 月期间本院收治的 640 例肝硬化患者的临床资料,分析肝硬化患者感染性休克发病率及感染部位分布,并分析感染性休克病原学特征,采用单因素和多因素 logistic 回归分析感染性休克的危险因素。**结果:**640 例肝硬化患者感染性休克发病率为 14.38%,感染部位分布于腹腔及消化道和肺部;共分离培养病原菌 96 株,包括革兰阴性杆菌 52 株(54.17%)、革兰阳性球菌 18 株(18.75%)、真菌 26 株(27.08%)。单因素分析结果显示,肝硬化患者并发感染性休克与年龄、抗生素、消化道出血、住院时间及肝性脑病有关($P<0.05$),与性别、血清白蛋白、侵入性操作无关($P>0.05$)。多因素 logistic 回归分析结果显示,年龄 ≥ 60 岁、抗生素使用、消化道出血、肝性脑病及住院时间 >30 d 均为肝硬化患者感染性休克的危险因素 ($P<0.05$)。**结论:**感染性休克患者病原菌以革兰阴性杆菌为主,年龄 ≥ 60 岁、抗生素使用、消化道出血、肝性脑病及住院时间 >30 d 为肝硬化患者感染性休克的危险因素,应根据病原学特征及其危险因素采取相关措施,减少肝硬化患者感染性休克的发病风险。

关键词:肝硬化;感染性休克;病原学;分布;危险因素

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Etiological Characteristics and Risk Factors of Septic Shock in Patients with Liver Cirrhosis

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ABSTRACT Objective: To explore the etiological characteristics of septic shock in patients with liver cirrhosis, and to analyze the risk factors. **Methods:** The clinical data of 640 patients with liver cirrhosis, who were treated in Chongqing Three Gorges Central Hospital from January 2012 to April 2015, were retrospectively analyzed; the incidence and location of infectious shock, and the etiological characteristics in the patients with liver cirrhosis were also analyzed. The risk factors of septic shock was analyzed by single factor and multivariate logistic regression analysis. **Results:** The incidence of septic shock in 640 patients with liver cirrhosis was 14.38%, the site of infection was located in the abdominal cavity, digestive tract and lungs. A total of 96 strains of pathogenic bacteria were isolated and cultured, including 52 strains (54.17%) of gram negative bacilli, 18 strains (18.75%) of gram positive cocci, 26 strains (27.08%) of fungi. Single factor analysis showed that age, antibiotics, gastrointestinal bleeding, hospitalization time and hepatic encephalopathy were relevant to the septic shock in the patients with liver cirrhosis ($P<0.05$), the sexes, serum albumin, invasive procedure were not relevant ($P>0.05$). Multivariate logistic regression analysis showed that age ≥ 60 years, the use of antibiotics, gastrointestinal bleeding, hepatic encephalopathy and hospitalization time >30 d were influencing factors for the septic shock in patients with liver cirrhosis ($P<0.05$). **Conclusion:** Gram negative bacilli are the main pathogens in the patients with septic shock; the age ≥ 60 years, the use of antibiotics, gastrointestinal bleeding, hepatic encephalopathy and hospitalization time >30 d are influencing factors for the septic shock in the patients with liver cirrhosis. So relevant measures should be taken according to the etiological characteristics and risk factors in order to reduce the risk of septic shock in the patients with liver cirrhosis.

Key words: Liver cirrhosis; Septic shock; Etiological; Distribution; Risk factors

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前言

肝硬化是临床常见的一种或多种病因长期反复作用形成

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的慢性进行性肝病,处于肝病患者免疫力低下阶段^[1,2]。据统计^[3],全世界范围内,每年死于肝硬化的患者高达 50 万,仅次于心脏病、癌症、中风等疾病。肝硬化发病原因存在多方面,主要有酒精肝、病毒性肝炎、自身免疫性肝炎等^[4]。感染是肝硬化患者常见的并发症之一,肝硬化患者的住院感染率平均约为 30%,而由于感染导致的肝硬化死亡患者占比超过 30%^[5]。肝硬化患者出现感染性休克的原因在于患者肝脏代偿功能下降,肝硬化患者常伴随发生多种免疫功能缺陷疾病,对病原体的抵抗

功能较差,机体各组织器官容易受到多种病原菌的侵袭^[6],进一步导致患者解毒功能下降,一旦存在体液、细胞等免疫系统功能下降,则患者极易出现病原菌感染而导致感染性休克,休克过程中肝硬化患者的肝脏缺血,进一步损伤肝功能^[7]。我国是肝病患者数量较多的国家之一,但是对于肝硬化并发感染的系统性调查研究并不多见,因此研究肝硬化并发感染性休克成为临床热点之一^[8,9]。本研究主要对2012年1月-2015年4月期间因肝硬化来我院接受治疗的640例肝硬化患者出现感染性休克的病例资料进行回顾性分析,记录感染性休克患者病原菌感染的相关临床特征,分析其危险因素,从而针对性提出预防控制措施,现将本研究内容报道如下。

1 资料与方法

1.1 临床资料

回顾性分析2012年1月-2015年4月期间内因肝硬化接受治疗的640例患者的临床资料。纳入标准:所有研究对象均符合病毒性肝炎防治方案中肝硬化相关诊断标准^[10],排除标准:①临床患者资料不完整;②合并患有心、肾等重大脏器病变患者;③合并患有其他免疫缺陷疾病患者;④入组前3个月使用免疫调节剂的患者。其中包括男性387例,女性253例,年龄21-75岁,平均年龄(56.7±4.63)岁,肝硬化类型:病毒性肝炎性肝硬化472例、胆汁淤积性肝硬化63例、隐源性肝硬化56例、酒精性肝硬化49例。

1.2 感染性休克诊断标准^[11]

①诊断依据包含患者临床特征,对患者脓性分泌物及外周血进行相关病原菌培养,实验室检测结果证实出现感染性休克:白细胞计数、血细胞压积、血红蛋白、血尿素氮和肌酐值等增高,病原菌培养结果显示阳性结果;②参考Fry MOD标准,判定患者出现多器官功能障碍综合征;③参考美国胸科学会和危重病医学会联席会议诊断标准,证实患者出现全身炎症反应综合征;④参考Montgomery诊断标准判断患者出现不可逆器官功能衰竭,根据以上4项判断感染性休克。

1.3 病原菌检测方法

取患者的腹水,采用法国生物梅里埃公司生产的VITEK-60全自动微生物分析系统进行细菌培养,并使用其配套的细菌鉴定卡鉴定病原菌。使用革兰氏染色法对细菌进行鉴别,标本固定后,初染使用碱性染色结晶紫,媒染使用碘液,然后使用95%的乙醇脱色,最终使用稀释5倍的复红进行复染,结果中显示紫色的细菌为革兰氏阳性菌,显示红色的为革兰氏阴性菌。真菌鉴定使用纸片扩散法,根据不同的抑菌圈来判定真菌的类型,质控真菌由北京中检维康技术有限公司提供。

1.4 调查方法

回顾性分析患者相关临床资料,调查表内容主要包括患者年龄、性别、是否存在侵入性操作、有无抗菌药物预防服用、有无消化道出血、患者血清白蛋白水平、是否存在肝性脑病以及住院时间,分析患者感染性休克发病与上述指标间是否存在相关性。

1.5 研究方法

统计640例肝硬化患者发生感染性休克的例数,以及主要的感染部位;分析感染性休克患者分离培养的病原菌的分布状况,并采用单因素和多因素logistic回归分析感染性休克的发

病因素。

1.6 统计分析

采用SPSS20.0进行分析处理,计数数据以率的形式表示,组间对比采用 χ^2 检验,危险因素分析采用logistic回归分析,以 $P<0.05$ 表示差异存在统计学意义。

2 结果

2.1 感染性休克发病率及感染部位分布

640例肝硬化患者出现感染性休克92例,发病率高达14.38%,主要感染部位分布在腹腔及消化道和肺部,见表1。

表1 患者主要感染部位分布及构成比

Table 1 Distribution and composition ratio of primary infection site in patients

Infection site	Infection cases	百分比 Percentage (%)
Abdominal cavity and digestive tract	41	44.57
Lungs	25	27.17
Trauma	11	11.96
Urinary tract	6	6.52
Skin soft tissue	5	5.43
Blood	2	2.17
Biliary tract	1	1.09
Other	1	1.09
Total	92	100.00

2.2 病原菌分布状况

所有感染性休克患者共分离培养病原菌96株,革兰阴性杆菌52株,占比54.17%,包括大肠埃希菌18株,铜绿假单胞菌13株,肺炎克雷伯菌8株,鲍氏不动杆菌7株,其他6株;革兰阳性球菌18株,占比18.75%,包括金黄色葡萄球菌9株,肠球菌属6株,表皮葡萄球菌3株;真菌26株,占比27.08%,包括白假丝酵母菌22株,其他4株,见表2。

表2 肝硬化患者感染性休克病原菌的分布及构成比

Table 2 Distribution and composition ratio of septic shock pathogenic bacteria in patients with cirrhosis

Pathogenic bacteria	Strains	Percentage (%)
Gram negative bacteria	52	54.17
<i>Escherichia coli</i>	18	18.75
<i>Pseudomonas aeruginosa</i>	13	13.54
<i>Klebsiella pneumoniae</i>	8	8.33
<i>Acinetobacter baumannii</i>	7	7.29
Other	6	6.25
Gram positive cocci	18	18.75
<i>Staphylococcus aureus</i>	9	9.38
<i>Enterococcus</i>	6	6.25
<i>Staphylococcus epidermidis</i>	3	3.13
Fungus	26	27.08
<i>Candida albicans</i>	22	22.92
Other	4	4.17
Total	96	100.00

2.3 感染性休克患者发病单因素分析

住院时间及肝性脑病有关($P<0.05$),与性别、血清白蛋白、侵入肝硬化患者并发感染性休克与年龄、抗生素、消化道出血、性操作无关($P>0.05$),数据如下表 3 所示。

表 3 感染性休克患者的单因素分析及构成比

Table 3 Single factor analysis and composition ratio of patients with septic shock disease

Factors		Total number of cases	Number of infections	Percentage (%)	χ^2	P
Gender	Male	387	56	14.47	1.203	0.089
	Female	253	36	14.23		
Age (years)	≥ 60	412	67	16.26	2.652	0.049
	<60	228	25	10.96		
Serum albumin (g/L)	>35	126	12	9.52	0.956	0.394
	28-35	338	37	10.95		
	<28	176	43	24.43		
Antibiotic	Have	211	25	11.85	2.846	0.024
	Not have	429	67	15.62		
Invasive procedure	Have	209	31	14.83	1.566	0.195
	Not have	431	61	14.15		
Gastrointestinal bleeding	Have	325	62	19.08	3.564	0.000
	Not have	315	30	9.52		
Hepatic encephalopathy	Have	217	54	24.88	5.689	0.000
	Not have	423	38	8.98		
Hospitalization time(d)	≤ 30	368	41	11.14	3.057	0.015
	>30	272	51	51		

2.4 多因素 logistic 回归分析

将年龄、抗生素使用、消化道出血、肝性脑病及住院时间纳入多因素 logistic 回归方程,结果显示,年龄 ≥ 60 岁、抗生素使用、消化道出血、肝性脑病及住院时间 $>30d$ 均为肝硬化患者感染性休克的危险因素($P<0.05$),数据如下表 4 所示。

表 4 多因素 logistic 回归分析

Table 4 Multivariate logistic regression analysis

Factors	β	OR	95%CI	P
Age ≥ 60 years	1.627	4.275	3.231-5.897	0.001
Use of antibiotics	1.764	4.692	3.163-5.616	0.000
Gastrointestinal bleeding	1.248	2.341	1.387-4.391	0.021
Hepatic encephalopathy	1.989	5.325	3.689-8.112	0.000
Hospitalization time >30 d	1.696	4.123	3.356-5.462	0.000

3 讨论

由单个或多种病因长期反复作用对肝部造成弥漫性肝损伤即为肝硬化^[12],肝硬化患者处于免疫力低下的状态下极易感染,虽然在过去几十年的时间里治疗效果明显,但是依然存在大量的细菌感染,患者的死亡率依然居高不下,肝硬化合并感染的患者不仅会增加住院时间,而且浪费大量的医疗资源^[13]。肝硬化患者一旦感染,容易休克,感染性休克是临床上较为常见的一种急性危重疾病,临床上,感染性休克主要由微生物及其产生的毒素等导致患者出现脓毒症综合征并伴随休克症状,该病发病迅速,进展较快,患者常出现组织缺氧、缺血,多器官功能异常,机体代谢出现紊乱,甚至导致多器官功能衰竭,病死率较高^[14,15]。肝硬化患者出现感染可能性较高,感染发生后,导

致患者机体内出现毒性代谢产物较高,肝脏需要代谢细菌产生的大量毒素,肝硬化患者自身肝脏功能降低,因此导致患者出现器官功能减弱,肝脏等器官功能进一步下降,导致患者治疗效果较差,影响预后^[16,17],此外感染中的致病菌诱发的临床症状不易察觉,给临床诊断带来了一定的难度^[18]。因此,探讨肝硬化患者合并感染性休克的病原学及危险因素,并采取积极应对措施,降低肝硬化感染性休克的病死率,具有非常实际的重要意义。

在本研究中,共纳入 640 例肝硬化患者,其中包含感染性休克患者 92 例,发病率为 14.38%,回顾性分析肝硬化并发感染性休克患者进行临床资料,结果分析表明所有感染性休克主要感染部位分布在腹腔、肺部以及消化道、血液等,分析原因可能是肝硬化并发感染性休克患者肝细胞内巨噬细胞、中性粒细胞等减少,机体内体液、细胞免疫力下降,导致患者出现肺部感

染。此外,患者肠道内菌群失调,胃肠功能下降,且门脉高压时,患者胃肠道淤血,肠道屏障损伤,导致患者出现肠道、腹腔部位感染^[20,21]。

本研究显示,慢性乙肝患者存在革兰阴性杆菌、革兰阳性球菌及真菌感染,所有感染性休克患者中共分离培养得到病原菌 96 株,分别为革兰阴性杆菌 52 株(54.17%)、革兰阳性球菌 18 株(18.75%)、真菌 26 株(27.08%)。肝硬化患者主要感染部位在肺部,病原菌为革兰阴性杆菌,包括大肠埃希菌、肺炎克雷伯菌等,其中主要为大肠埃希菌,其次为肺炎克雷伯菌^[22,23],主要是由于肝硬化患者胃肠道内菌群失衡,而造成肠黏膜屏障功能下降及细菌发生移位导致的,同时大肠埃希菌是机体中正常的菌群,但是当机体免疫力下降时,容易诱发肠外感染及呼吸道感染^[24,25]。此外还包括真菌感染,主要为白假丝酵母菌,由于院内抗生素滥用等因素,导致机体内菌群失调,从而导致真菌感染^[26]。对肝硬化患者并发感染性休克进行危险因素分析^[27,28],主要为年龄 ≥ 60 岁、抗生素使用、消化道出血、肝性脑病及住院时间 >30 d,针对上述危险因素,可采取相应措施^[29,30]:(1)肝硬化患者应进行积极检查,对症支持治疗,同时对肝脏功能进行监测;对基础疾病进行积极治疗,能够显著提高肝功能,纠正患者血红蛋白水平;(2)针对药敏试验结果,针对性进行抗生素治疗,但要避免长期使用抗生素,防止病原菌出现耐药性;(3)对肝硬化并发肝性脑病患者需要进行原发病治疗,解除诱因,降低其他并发症发病风险,此外,需要积极治疗肠道出血等;(4)为减少肝硬化患者医院感染机会,除进行常规治疗外,则应减少住院时间,病房空气保持流通,按照病种进行积极隔离治疗。

综上所述,肝硬化患者合并感染性休克发病率较高,临床应从合理使用抗菌药物,控制消化道出血,减少肝性脑病,减少住院时间等方面预防感染的发生。

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