

肝硬化患者血清和腹水CA125升高

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Elevation of serum and ascites CA125 levels in liver cirrhosis

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Abstract

AIM: To evaluate the range of serum and ascitic cancer antigen(CA) 125 levels in patients with liver cirrhosis and to explore possible factors associated with CA 125 elevation.

METHODS: A total of 70 patients were studied. Group I consisted of 30 patients with liver cirrhosis with or without ascites. Group II consisted of 30 patients with digestive malignant tumors with or without ascites. And group III consisted of 10 patients with benign (but not cirrhotic) ascites. CA 125 levels were measured in sera of all the patients and also simultaneously in ascitic fluids of 15 patients.

RESULTS: Serum CA125 levels in 87 % patients from group I were elevated, especially in those with ascites (95 % vs 38 % in patients without ascites, $P < 0.01$) irrespective of the etiology of cirrhosis. Serum CA 125 levels were correlated with Child-Pugh scores ($r = 0.38$) but it was marginally significant ($P = 0.06$). All the patients with ascites from group II and group III had elevated serum CA 125 levels. There was no difference in serum CA 125 levels among patients with ascites from group I (275 ± 175 kU/L), group II (368 ± 190 kU/L) and group III (396 ± 287 kU/L), neither did ascitic CA 125 levels ($P > 0.05$), but serum CA 125 levels were significantly higher than those of patients without ascites from group I (72 ± 83 kU/L) and group II (83 ± 42 kU/L). The levels of serum CA 125 were lower than, but correlated with that of ascites CA 125 (198 ± 108 kU/L vs 460 ± 234 kU/L, $r = 0.58$, $P = 0.026$). The elevation of serum CA 125 in malignant ascites was more often accompanied with abnormalities of other tumor markers compared with that in benign ascites (90 % vs 6 %, $P < 0.01$). Among the 38 patients with only serum CA125 elevation but not accompanied with a rise of other tumor markers, 36 (95 %) were diagnosed as benign ascites.

CONCLUSION: The elevation of serum CA 125 is common in liver cirrhosis patients. It is correlated with the amount of ascites, and possibly insufficiency of liver function. Serum CA 125 probably derives from ascites. It usually predicts benign disease if the elevation of serum or ascites CA 125 is not accompanied with a rise of other tumor markers.

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摘要

目的: 研究肝硬化患者血清和腹水CA125升高的情况、原因及临床意义。

方法: 共有70例患者入选, 分成3组: 组1(Group I), 肝硬化伴或不伴腹水患者30例, 组2(Group II), 消化系统肿瘤伴或不伴腹水患者30例, 组3(Group III), 除肝硬化外其他良性疾病引起的腹水患者10例. 检测所有患者血清CA125(15例患者同时检测腹水CA125), 并与病因、腹水、Child分级等指标作相关分析. 同时检测AFP、CEA和CA19-9等肿瘤标记物。

结果: 87%的Group I患者存在血清CA125异常升高, 伴腹水的患者血清CA125异常发生率显著高于不伴腹水的患者(95% vs 38%, $P < 0.01$). 血清CA125的水平与Child-Pugh评分相关(但不具显著性, $r = 0.38$, $P = 0.06$), 而与肝硬化的病因无关. Group II伴腹水和Group III的患者血清CA125明显升高, 但Group I伴腹水患者、Group II伴腹水患者和Group III患者之间的血清CA125水平无显著差异($P > 0.05$), 分别为 275 ± 175 kU/L、 368 ± 190 kU/L和 396 ± 287 kU/L, 均显著高于Group I和Group II不伴腹水的患者的血清CA125水平(分别为 72 ± 83 kU/L和 83 ± 42 kU/L, $P < 0.05$). 血清CA125显著低于腹水CA125 (198 ± 108 kU/L vs 460 ± 234 kU/L), 二者呈线性相关($r = 0.58$, $P = 0.026$); 90%的恶性腹水患者血清CA125的升高伴有其他肿瘤标记物的异常, 而良性腹水患者极少伴其他指标的异常(仅2%, $P < 0.01$). 38例患者仅血清CA125异常, 其中有36例(95%)为良性腹水。

结论: 肝硬化患者血清CA125的异常升高很常见, 其水平与腹水有关, 也可能与肝功能不全有关, 但与腹水的病因、良恶性等无关. 血清CA125可能来源于腹水. 血清CA125单项异常多提示良性、而非恶性疾病。

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0 引言

癌抗原 CA125 在妇科肿瘤、尤其是卵巢癌的诊断和预后中的作用已经得到公认^[1-9]. 有学者发现, 非肿瘤疾病如肝硬化患者也可出现血清 CA125 升高^[10-15]. 我们研究肝硬化患者血清和腹水 CA125 的变化情况, 以探讨其升高的原因和临床意义.

1 材料和方法

1.1 材料 I 组: 1999/2001 年住院肝硬化患者 30 (男 15, 女 15) 例, 平均年龄 65 ± 16 岁, 其中乙型肝炎后肝硬化 20 例, 丙型肝炎后肝硬化 5 例, 酒精性肝硬化 5 例. Ia: 无腹水, 8 例; Ib: 中少量腹水, 9 例; Ic: 大量腹水, 13 例. II 组: 恶性肿瘤伴或不伴腹水患者 30 (男 16, 女 14) 例, 平均年龄 50 ± 15 岁, 其中: IIa: 原发性肝癌 10 例, 均有大量腹水; IIb: 胃癌和胰腺癌 10 例, 有大量腹水; IIc: 胃癌和胰腺癌 10 例, 无腹水. III 组: 良性腹水患者 10 (男 4, 女 6 例), 平均年龄 45 ± 9 岁, 其中嗜酸性胃肠炎 3 例, 布加综合征 3 例, 低白蛋白血症 4 例. 所有患者均同时行妇科查体、B 超和 CT 除外妇科肿瘤疾病.

1.2 方法 对所有患者进行 B 超检查, 按腹水的深度划分为大量、中少量. 液性暗区厚度小于 3 cm 为中少量, 大于 3 cm 为大量. 对有腹水的患者在做腹水穿刺时, 同时检测腹水和血清 CA125, 并查其他肿瘤指标, 包括癌胚抗原 CEA, 甲胎蛋白 AFP 和糖抗原 CA19-9, 采用酶联免疫黏附法(ELISA), 试剂盒均购自 Roche. 以大于正常值上限 2 倍者为异常升高.

统计学处理 分别采用 t 检验, χ^2 检验和线性相关回归分析.

2 结果

2.1 肝硬化患者血清 CA125 与 Child 分级和腹水的关系 肝硬化患者 30 例 Child A 级 9 例, B 级 12 例, C 级 9 例. 血清 CA125 异常升高者占 26 例(87%), 其中 A 级 7/9 (78%), B 级 10/12 (83%), C 级 9/9 (100%), 三者相比, 无显著性差异($P > 0.05$). 按血清 CA125 水平的高低排列, C 级(330 ± 287 kU/L)大于 B 级(207 ± 152 kU/L)大于 A 级(169 ± 158 kU/L), 但三者之间无显著性差异($P > 0.05$). 血清 CA125 与 Child 评分具有一定的相关性($r = 0.38$, $P = 0.06$), 但不具显著性. 我们同时将肝硬化患者血清 CA125 分别与其相应的血清转氨酶、血氨水平、前胶原 III 肽和 IV 型胶原、胆固醇、转氨酶、凝血酶原时间、血清白蛋白等指标做相关分析, 结果均无统计学意义. Ia 组中血清 CA125 异常升高者占 38%, Ib + Ic 组中占 95%, 具有显著性差异($P < 0.01$). Ia 组(72 ± 83 kU/L, $n = 8$)血清 CA125 的水平显著低于 Ib 组(328 ± 238 kU/L, $n = 9$, $P < 0.01$)和 Ic 组(255 ± 152 kU/L, $n = 13$, $P < 0.01$), 而 Ib 组和 Ic 组之间的血清 CA125 水平无显著性差异($P > 0.05$).

2.2 恶性腹水患者血清、腹水 CA125 的比较 IIa 组(375 ± 192 kU/L)与 IIb 组(346 ± 187 kU/L)的血清 CA125 水平无显著性差异($P = 0.16$), 但均显著高于 IIc 组(83 ± 42 kU/L, $P < 0.01$). 将 IIa、IIb 组合并后, 分别与 III 组以及 Ib+Ic 组患者相比较(表 1), 血清、腹水 CA125 水平均无显著性差异($P > 0.05$). IIa+IIb 组(恶性腹水)患者血清 CA125 均有升高, 但同时有 CA19-9, CEA 和 AFP 至少一项异常升高者 18 例(90%), 而 Ib+Ic + III 组(良性腹水)患者中仅有 2 例同时伴有 CA19-9 升高(6%), 具有显著性差异($P < 0.01$). 38 例血清 CA125 单项升高的患者中, 有 36 例(95%)为良性疾病.

表 1 腹水患者血清、腹水 CA125($\bar{x} \pm s$, kU/L)的比较

分组别	血清 CA125	腹水 CA125 ^a
IIa + IIb	368 ± 190 ($n = 20$)	434 ± 278 ($n = 4$)
III	396 ± 287 ($n = 10$)	462 ± 254 ($n = 4$)
Ib+Ic	275 ± 175 ($n = 22$)	435 ± 207 ($n = 7$)

^a $P < 0.05$, vs 血清.

2.3 腹水 CA125 与血清 CA125 的关系 有 15 例患者同时测定腹水和血清 CA125, 腹水 CA125 显著高于血清 CA125 (460 ± 234 kU/L vs 198 ± 108 kU/L, $P = 0.005$), 二者之间显著相关($r = 0.58$, $P = 0.026$, 见图 1).

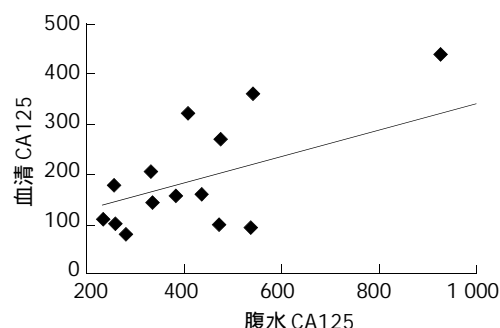


图 1 血清 CA125 与腹水 CA125 的相关.

3 讨论

本研究显示, 87% 的肝硬化患者血清 CA125 异常升高, 有腹水的患者高达 95%. 我们还发现, 肝硬化患者血清 CA125 的升高与腹水的存在相关, 而与肝硬化的病因、腹水的原因以及良恶性无关. 肝硬化患者血清 CA125 升高的具体机制尚不清楚, 肝硬化时常伴肝功能不全, 结果导致肝脏对血清 CA125 的清除能力下降, 可能成为血清 CA125 异常升高的原因之一. 本研究中有 38% 的无腹水的肝硬化患者血清 CA125 异常升高, 而且血清 CA125 水平与 Child-Pugh 分级轻度相关, 均支持此假说. 但另一方面, 肝硬化患者伴腹水时血清 CA125 异常发生率和异常水平显著高于无腹水患者; 肝硬化患者血清 CA125 水平低于腹水, 与腹水 CA125 呈正相关. 我们曾对 3 例大量腹水的肝硬化患者进行腹水穿刺, 同

时检测穿刺前后的血清CA125的变化,发现腹水穿刺后,血清CA125的水平有明显下降.肝硬化患者血清CA125的水平随腹水的长消而增减,腹水完全消退后,血清CA125也恢复正常^[16].以上结果均支持血清CA125可能来源于腹水.免疫组化研究发现腹膜间皮细胞CA125呈现高表达^[17-19],因此,腹水可能刺激腹膜,使其产生CA125增加,通过腹膜屏障,以一定的比例吸收进入血循环,引起血清CA125升高.

各种原因的腹水均可导致血清CA125升高,而与腹水的良恶性无关.良恶性腹水的患者之间血清CA125水平并无差异,而且结核性腹水、心功能不全以及创伤造成的腹水患者血清CA125同样明显增加^[20-24],因此,血清CA125的异常升高并不一定提示恶性肿瘤,尤其是在肝硬化患者.传统认为血清CA125是一种妇科肿瘤标记物,因此,肝硬化腹水尤其是女性患者,血清CA125的异常升高会误导临床诊断,有时甚至会造成不必要的剖腹探查.我们的研究发现,如果在检测CA125的同时检测其他几种肿瘤标记物,如CEA、AFP和CA19-9等,则很容易区分良恶性腹水.血清CA125单项异常常提示良性腹水,而恶性腹水常伴有其他更特异性的肿瘤标记物的异常.

此外,考虑到肝硬化患者血清CA125的升高与腹水有关,并且血清CA125的升高早于腹水的出现,故有学者认为血清CA125的升高可预测腹水的发生,其敏感性甚至高于B超^[16],提示血清CA125有可能成为监测肝硬化患者腹水消长的一项有用指标.

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