

胆总管结石对血清CA19-9的影响

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■背景资料

CA19-9是临床常用的肿瘤标志物,对引起阻塞性黄疸的胰腺癌、胆管癌等均有一定的诊断价值。但一些良性疾病合并阻塞性黄疸时,也可以引起CA19-9升高。本文结合胆总管结石患者相关临床资料,分析治疗前的肿瘤标志物CA19-9、CEA与总胆红素、直接胆红素的关联性,以及治疗前后CA19-9变化与总胆红素、直接胆红素变化的关联性。

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Elevated serum CA19-9 levels in patients with common bile duct stones

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Abstract

AIM: To observe changes in serum carbohydrate antigen 19-9 (CA19-9) and carcinoembryonic antigen (CEA) levels in patients with common bile duct stones.

METHODS: A total of 68 patients with surgically confirmed common bile duct stones were included in the study. The correlations of serum CEA and CA19-9 with total bilirubin and direct bilirubin were analyzed. For 20 patients whose serum CA19-9 levels were twice more than the upper limit of normal values, a consistent follow-up was conducted to analyze the correlations of the difference between preoperative and postoperative serum CA19-9 levels with total bilirubin and direct bilirubin.

RESULTS: Significant correlations were noted

between serum CA19-9 and total bilirubin and direct bilirubin ($r = 0.813$ and 0.786 , respectively; both $P = 0.000$) in patients with common bile duct stones. No significant correlations were noted between serum CEA and total bilirubin and direct bilirubin. The difference between preoperative and postoperative serum CA19-9 levels has significant correlations with total bilirubin and direct bilirubin ($r = 0.787$ and 0.806 , respectively; both $P = 0.000$).

CONCLUSION: Elevated serum CA19-9 levels are noted in patients with concurrent common bile duct stones and obstructive jaundice. In these patients, serum CA19-9 as a tumor marker has a poor specificity.

Key Words: Common bile duct stone; Obstructive jaundice; CA19-9

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摘要

目的: 探讨胆总管结石对血清CEA、CA19-9的影响。

方法: 回顾经ERCP或手术证实、治疗的胆总管结石患者68例,分析血清CEA,特别是血清CA19-9与胆总管结石患者总胆红素、直接胆红素的相关性;并对20例血清CA19-9值超过正常上限两倍以上患者统一时间进行随访,分析治疗前后血清CA19-9变化值与总胆红素、直接胆红素变化值的相关性。

结果: 血清CA19-9与总胆红素、直接胆红素存在明显相关性($r = 0.813, 0.786$, 均 $P = 0.000$);血清CEA与总胆红素、直接胆红素不存在相关性;治疗前后血清CA19-9变化值与总胆红素、直接胆红素变化值存在明显相关性($r = 0.787, 0.806$, 均 $P = 0.000$)。

结论: 胆总管结石合并阻塞性黄疸时,可导致血清CA19-9升高,此时血清CA19-9作为肿瘤标志物的特异性差。

■同行评议者

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关键词: 胆总管结石; 阻塞性黄疸; CA19-9

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0 引言

糖类抗原CA19-9在上消化系统肿瘤细胞中普遍表达^[1], 其测定是临床上诊断恶性胰胆疾病的可靠手段^[2]. 但是, 很多的良性疾病也可以导致血清CA19-9升高^[3-9]. 本文结合胆总管结石患者接受ERCP或手术治疗前后的情况, 对胆总管结石导致血清CA19-9升高进行分析.

1 材料和方法

1.1 材料 收集2004-01/2009-08华中科技大学同济医学院附属同济医院经ERCP或者外科手术治疗的胆总管结石患者68例, 其中男40例, 女28例, 年龄17-83(平均54)岁. 所用病例均无肿瘤病史及罹患肿瘤的依据. 术前均进行相关的影像学检查(包括腹部超声、CT或者MRI检查)提示存在胆总管结石, 再经ERCP或者手术证实及治疗.

1.2 方法 术前检查此类患者的胆红素等生化指标、血清CEA(本院参考值: 0-5 $\mu\text{g/L}$)及CA19-9(本院参考值: 0-37 kU/L)等肿瘤标志物. 对血清CA19-9升高超过正常值上限两倍以上(CA19-9>74 kU/L)的患者进行随访. 根据血清总胆红素的水平, 将所有患者分成3组: 重度黄疸组(总胆红素大于170 $\mu\text{mol/L}$)、轻-中度黄疸组(总胆红素介于34-170 $\mu\text{mol/L}$)、无明显黄疸组(总胆红素小于34 $\mu\text{mol/L}$), 并统计患者的血清总胆红素、直接胆红素、CEA、CA19-9值.

统计学处理 应用统计软件包SPSS18.0, 计量资料数据用 $\text{mean} \pm \text{SD}$ 表示, 进行近似 t 检验或配对 t 检验及相关性分析, $P < 0.05$ 为差异有统计学意义.

2 结果

2.1 血清CA19-9、CEA与血清总胆红素、直接胆红素的关系 血清CA19-9与血清总胆红素、直接胆红素明显相关($r = 0.813$, $P = 0.000$; $r = 0.786$, $P = 0.000$). 血清CEA与血清总胆红素、直接胆红素不相关($r = 0.061$, $P = 0.622$; $r = 0.109$, $P = 0.378$, 表1).

2.2 黄疸程度不同组间血清CA19-9、CEA值的比较 重度黄疸组与轻-中度黄疸组、重度黄疸组与无明显黄疸组、轻-中度黄疸组与无明显黄

疸组之间血清CA19-9的水平均有统计学意义($t = 4.415$, $P = 0.003$; $t = 4.894$, $P = 0.002$; $t = 2.326$, $P = 0.028$). 重度黄疸组与轻-中度黄疸组、重度黄疸组与无明显黄疸组、轻-中度黄疸组与无明显黄疸组血清CEA的水平均无统计学意义($t = 0.701$, $P = 0.504$; $t = 1.111$, $P = 0.302$; $t = 1.378$, $P = 0.175$).

2.3 治疗前、后血清CA19-9变化分析 治疗后, 随着血清总胆红素及直接胆红素的下降, 血清CA19-9值也明显下降, 血清CA19-9的变化值($640.69 \text{ kU/L} \pm 709.00 \text{ kU/L}$)与总胆红素变化值($144.45 \mu\text{mol/L} \pm 92.71 \mu\text{mol/L}$)、直接胆红素变化值($93.93 \mu\text{mol/L} \pm 62.30 \mu\text{mol/L}$)存在明显相关($r = 0.078$, 0.806 , 均 $P = 0.000$).

3 讨论

CA19-9属于I型糖类抗原, 主要分布于正常胎儿胰腺、胆囊、肝、肠等组织, 成人则存在于胰、胆管上皮处, 以唾液黏蛋白形式存在于血清中, 含量甚微. 自从Korproski等^[10]发现人类结肠肿瘤细胞产生CA19-9以来, 血清CA19-9作为临床常用的肿瘤标志物, 应用于胰腺癌、胆管癌、结肠癌、胃癌等恶性疾病的诊断、治疗、预后和复发的判断^[11-22]. 但也发现, 临床上很多良性疾病可以引起CA19-9升高^[3-9]. 原因可能是与半抗原结合的载体, 在组织损伤或破坏时, 神经苷脂增加, 进入血液循环, 这时单克隆抗体只识别抗原, 导致假阳性增加^[23]. 本文的资料显示, 胆总管结石引起CA19-9升高, 与总胆红素及直接胆红素明显相关, 而且总体趋势而言, 这种CA19-9的升高随着黄疸的程度增加而增加, 又随着黄疸的下降而下降. 这说明阻塞性黄疸可引起CA19-9值的升高, 这与有关文献^[3,8,9,24-29]提示良性疾病引起阻塞性黄疸可导致CA19-9升高的报道相符. 因而在阻塞性黄疸时, 血清CA19-9作为肿瘤标志物的特异性差, 这与相关文献^[16,19,30,31]报道CA19-9作为胰腺癌、胆管癌等的肿瘤标志物特异性不高相符. 在解除阻塞性黄疸后, 血清CA19-9又可以恢复到正常水平, 这与Marrelli等^[28]的报道相符. 因而血清CA19-9值升高而并无黄疸或者黄疸程度不足以解释时, 或者黄疸减退后CA19-9值仍保持高值甚或有增加趋势时, 仍需警惕肿瘤的可能性.

癌胚抗原(CEA)在1965年由Gold等^[32]和Chen等^[34]进行了描述, 是临床常用的肿瘤标志物, 也应用于消化系统恶性疾病, 包括引起阻塞性

■ 研发前沿

阻塞性黄疸可引起血清CA19-9升高, 如何在阻塞性黄疸的情况下, 客观评价血清CA19-9的临床意义, 是困扰临床医生的一个难点.

■相关报道

Marrelli等报道, 良性疾病引起的阻塞性黄疸中, 61%的患者有CA19-9升高. 在解除阻塞性黄疸的患者中, 38例恶性肿瘤中有18例患者, 以及几乎所有的良性疾病患者CA19-9下降. 在成功解除阻塞性黄疸的情况下, CA19-9保持不变或者测量值大于90 kU/L, 强烈提示恶性原因所致的阻塞性黄疸.

表 1 各组患者血清CA19-9、CEA、总胆红素及直接胆红素水平

分组	n	总胆红素($\mu\text{mol/L}$)	直接胆红素($\mu\text{mol/L}$)	CEA($\mu\text{g/L}$)	CA-199(kU/L)
重度黄疸组	8	252.65 \pm 60.65	172.10 \pm 33.54	2.95 \pm 7.05	1263.70 \pm 719.73
轻-中度黄疸组	27	83.87 \pm 35.83	49.86 \pm 24.73	2.43 \pm 0.92	123.51 \pm 231.29
无明显黄疸组	33	12.83 \pm 7.05	3.90 \pm 3.00	2.14 \pm 0.65	9.09 \pm 9.41

黄疸的胰腺癌、胆管癌的诊断、治疗、预后及复发的评估^[17,22,30,33-38]. 本研究中, 即使合并明显黄疸的胆总管结石患者, 血清CEA也在正常范围, 血清CEA与总胆红素、直接胆红素也无明显关联. 鉴于CEA对引起阻塞性黄疸的恶性肿瘤有一定的灵敏性和特异性, 在阻塞性黄疸时, 血清CEA的检测, 可能有利于良、恶性疾病的鉴别.

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■同行评价

胆总管结石合并阻塞性黄疸时,血清CA19-9升高十分常见,本文回顾分析认为血清CA19-9作为肿瘤标记物的特异性差,对临床具有一定的指导意义。

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• 消息 •

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