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血清及胸腔积液中 CA19-9、SCC-Ag 及 CYFRA21-1 对肺癌诊断意义的对比研究 *

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摘要 目的:探讨肺癌患者血清及胸腔积液中的糖蛋白抗原 19-9(CA19-9)、鳞状细胞癌抗原(SCC-Ag)和细胞角蛋白 19 片段(CYFRA21-1)对肺癌的诊断意义。**方法:**选取 2016 年 1 月到 2017 年 6 月在我院接受治疗的肺癌患者 67 例作为肺癌组,另选取我院同期收治的肺良性病变患者 55 例纳入良性病变组。采用电化学发光法检测并对比两组患者血清及胸腔积液中的 CA19-9、SCC-Ag 和 CYFRA21-1 水平,比较所有研究对象血清及胸腔积液中 CA19-9、SCC-Ag 和 CYFRA21-1 的阳性率并分析其诊断价值。**结果:**肺癌组患者血清及胸腔积液中的 CA19-9、SCC-Ag 和 CYFRA21-1 水平显著高于良性病变组,有统计学差异($P<0.05$)。CA19-9、SCC-Ag 和 CYFRA21-1 在胸腔积液中的阳性率高于在血清中的阳性率,有统计学差异($P<0.05$)。胸腔积液中 CA19-9、SCC-Ag 和 CYFRA21-1 单项检测对肺癌的灵敏度显著高于血清检测,血清及胸腔积液中 CA19-9、SCC-Ag 和 CYFRA21-1 三项联合检测的灵敏度、特异性、阳性预测值均高于单项检测,差异均有统计学意义($P<0.05$)。**结论:**肺癌患者血清及胸腔积液中 CA19-9、SCC-Ag 和 CYFRA21-1 呈现高表达,三项指标联合检测可提高诊断肺癌的灵敏度、特异性和阳性预测值。

关键词:肺癌;糖蛋白抗原 19-9;鳞状细胞癌抗原;细胞角蛋白 19 片段;诊断价值

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Comparative Study of CA19-9, SCC-Ag and CYFRA21-1 in Serum and Pleural Effusion in the Diagnosis of Lung Cancer*

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ABSTRACT Objective: To investigate the diagnostic significance of glycoprotein antigen 19-9 (CA19-9), squamous cell carcinoma antigen (SCC-Ag) and cytokeratin 19 fragment (CYFRA21-1) in serum and pleural effusion in patients with lung cancer. **Methods:** 67 cases of lung cancer patients treated in our hospital from January 2016 to June 2017 were selected as lung cancer group, and 55 cases of benign pulmonary lesions treated in our hospital during the same period were selected benign lesions group. The levels of CA19-9, SCC-Ag and CYFRA21-1 in serum and pleural effusion in two groups were detected by Electrochemiluminescence Method and compared. The positive rates of CA19-9, SCC-Ag and CYFRA21-1 in serum and pleural effusion of all patients were compared and the diagnostic value was analyzed. **Results:** The levels of serum and pleural effusion CA19-9, SCC-Ag and CYFRA21-1 in lung cancer group were significantly higher than that in benign lesions group, the differences were statistically significant ($P<0.05$). The positive rate of CA19-9, SCC-Ag and CYFRA21-1 in pleural effusion were significantly higher than that in serum, the differences were statistically significant ($P<0.05$). The sensitivity of pleural effusion CA19-9, SCC-Ag and CYFRA21-1 single detection of lung cancer were significantly higher than that in serum, and serum and pleural effusion CA19-9, SCC-Ag and CYFRA21-1 three joint detection sensitivity, specificity, positive predictive value were significantly higher than that of single detection, the differences were statistically significant ($P<0.05$). **Conclusion:** The expression of CA19-9, SCC-Ag and CYFRA21-1 in serum and pleural effusion of patients with lung cancer is highly expressed. The joint detection of three indicators can improve the sensitivity, specificity and positive predictive value of the diagnosis of lung cancer.

Key words: Lung cancer; Glycoprotein antigen 19-9; Squamous cell carcinoma antigen; Cytokeratin 19 fragment; Diagnostic value

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前言

肺癌是全球范围内最为常见的恶性肿瘤,多发于支气管粘膜上皮,是一种实质性脏器癌症^[1]。在2010年世界卫生组织(WHO)发布的癌症报告中显示,全世界在2008年有161万例左右的肺癌新发病例,有138万例患者因肺癌而死亡,其发病率和病死率居恶性肿瘤第一位^[2-4]。我国工业化不断发展、周围环境不断恶化,吸烟人数不断上升、老龄化社会的到来,这些都可提升肺癌的发病率,导致我国肺癌患者数量呈现逐年增加的趋势,对我国人民的生命健康构成巨大威胁,如何预防肺癌、诊断肺癌、治疗肺癌已成为医务人员的研究重点^[5,6]。肺癌患者早诊断早治疗可以有效提升治疗效果,使其预后得到很大的改善,生存时间明显延长,由此可见,准确的诊断对于肺癌患者而言具有重要的意义^[7]。目前临床上对于肺癌患者常用的检测方法有计算机断层扫描、核磁共振、超声、胸片、血清或胸腔积液肿瘤标志物检测等非侵袭式检查,还有病理活检、胸腔穿刺术、纤维支气管镜、淋巴结活检、胸膜活检等侵袭式检查^[8,9]。侵袭式检查能直接检查病变部位的情况,具有较高的准确性,但往往操作较为复杂,且会给患者带来一定的痛苦,而非侵袭式检查中的血清或胸腔积液肿瘤标志物检测具有取样方便、操作简单等特点,目前已在临床上较多运用^[10,11]。本研究旨在探讨肺癌患者血清及胸腔积液中的糖蛋白抗原19-9(carbohydrate antigen 19-9,CA19-9)、鳞状细胞癌抗原(squamous cell carcinoma antigen,SCC-Ag)和细胞角蛋白19片段(cytokeratin 19 fragment,CYFRA21-1)对肺癌的诊断意义,以为临床诊断肺癌提供参考,现报道如下。

1 资料与方法

1.1 一般资料

选取2016年1月到2017年6月在我院接受治疗的肺癌患者67例作为肺癌组,纳入标准:(1)所有患者均经胸膜穿刺活检、细胞学检验、淋巴结活检确诊为原发性肺癌;(2)患者及其家属对本研究知情同意;(3)年龄>22岁。排除标准:(1)合并

有其他恶性肿瘤者;(2)合并有严重器质性疾病者;(3)可导致CA19-9水平升高的疾病者;(4)资料不全者。肺癌组男38例,女29例,年龄26-73岁,平均年龄(46.34±8.77)岁,肿瘤类型:腺癌30例,鳞癌27例,肺泡细胞癌7例,其他3例。另选取我院同期收治的肺良性病变患者55例纳入良性病变组,其中男30例,女25例,年龄23-74岁,平均年龄(46.81±9.05)岁,疾病类型:炎性胸腔积液25例,结核性胸腔积液22例,结缔组织疾病8例。两组患者的一般资料无明显差异($P>0.05$),可进行组间比较。本研究的内容符合医院管理委员会的相关条例,并已批准通过。

1.2 检测方法

于清晨抽取所有研究对象在空腹状态下的静脉血5 mL,并行胸腔穿刺抽取5 mL胸腔积液。将收集到的样本进行3000 r/min的离心运动,10 min后采集上清液待测。采用电化学发光法检测CA19-9、SCC-Ag和CYFRA21-1水平,电化学发光免疫分析仪购自美国罗氏公司,试剂为配套试剂。所有检测项目均由我院资深的检验医师操作。阳性判定标准:CA19-9超过37 U/mL、SCC-Ag超过1.5 ng/mL、CYFRA21-1超过3.3 ng/mL时认为检验结果为阳性。

1.3 相关计算公式

灵敏度=真阳/(真阳+假阴)×100%;特异性=真阴/(真阴+假阳)×100%;阳性预测值=真阳/(真阳+假阳)×100%。

1.4 统计学方法

选用SPSS19.0对所有数据进行统计分析,CA19-9、SCC-Ag水平等计数资料以率(%)表示,进行 χ^2 检验,CYFRA21-1阳性率等计量资料以($\bar{x} \pm s$)表示,进行t检验,检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 两组患者血清中的CA19-9、SCC-Ag和CYFRA21-1水平比较

肺癌组患者血清中的CA19-9、SCC-Ag和CYFRA21-1水平显著高于良性病变组,有统计学差异($P<0.05$),具体见下表。

表1 两组患者血清中的CA19-9、SCC-Ag和CYFRA21-1水平比较($\bar{x} \pm s$)
Table 1 Comparison of serum CA19-9,SCC-Ag,CYFRA21-1 levels between the two groups($\bar{x} \pm s$)

Groups	n	CA19-9(U/mL)	SCC-Ag(ng/mL)	CYFRA21-1(ng/mL)
Lung cancer group	67	28.72± 6.61	3.24± 2.52	10.64± 7.61
Benign lesions group	55	11.64± 2.37	1.53± 0.65	2.31± 1.42
t	-	17.447	4.693	7.610
P	-	0.000	0.000	0.000

2.2 两组患者胸腔积液中的CA19-9、SCC-Ag和CYFRA21-1水平比较

肺癌组患者胸腔积液中的CA19-9、SCC-Ag和CYFRA21-1水平显著高于良性病变组,有统计学差异($P<0.05$),具体见下表。

2.3 所有患者血清及胸腔积液中CA19-9、SCC-Ag和CYFRA21-1阳性率情况

CA19-9、SCC-Ag和CYFRA21-1在胸腔积液中的阳性率

高于在血清中的阳性率,有统计学差异($P<0.05$)。具体见下表。

2.4 血清及胸腔积液中CA19-9、SCC-Ag和CYFRA21-1对肺癌患者的诊断价值

胸腔积液中CA19-9、SCC-Ag和CYFRA21-1单项检测对肺癌的灵敏度高于血清检测,有统计学差异($P<0.05$);血清及胸腔积液中CA19-9、SCC-Ag和CYFRA21-1三项联合检测的衡量指标均高于单项检测,有统计学差异($P<0.05$),具体见下表。

表 2 两组患者胸腔积液中的 CA19-9、SCC-Ag 和 CYFRA21-1 水平比较($\bar{x} \pm s$)Table 2 Comparison of pleural effusion CA19-9, SCC-Ag, CYFRA21-1 levels between the two groups($\bar{x} \pm s$)

Groups	n	CA19-9(U/mL)	SCC-Ag(ng/mL)	CYFRA21-1(ng/mL)
Lung cancer group	67	30.84 $\pm$ 7.27	4.89 $\pm$ 2.84	38.62 $\pm$ 14.38
Benign lesions group	55	13.52 $\pm$ 3.21	1.63 $\pm$ 0.71	8.17 $\pm$ 5.26
t	-	17.555	8.112	14.217
P	-	0.000	0.000	0.000

表 3 所有患者血清及胸腔积液中 CA19-9、SCC-Ag 和 CYFRA21-1 阳性率情况[n(%)]

Table 3 The positive rates of serum and pleural effusion CA19-9, SCC-Ag, CYFRA21-1 among all the patients[n(%)]

Position	n	CA19-9	SCC-Ag	CYFRA21-1
Serum	122	45(36.89)	48(39.34)	54(44.26)
Pleural effusion	122	62(50.82)	64(52.46)	76(62.30)
χ^2	-	4.810	4.225	7.969
P	-	0.028	0.040	0.005

表 4 血清及胸腔积液中 CA19-9、SCC-Ag 和 CYFRA21-1 对肺癌患者的诊断价值(%)

Table 4 Diagnostic value of serum and pleural effusion CA19-9, SCC-Ag and CYFRA21-1 in patients with lung cancer(%)

Position	Measure index	CA19-9	SCC-Ag	CYFRA21-1	Joint detection
Serum	Sensitivity	53.73 (36/67) [#]	59.70 (40/67) [#]	64.18 (43/67) [#]	89.55 (60/67)
	Specificity	83.64 (46/55) [#]	85.45 (47/55) [#]	80.00 (44/55) [#]	90.91 (50/55)
	Positive predictive value	80.00 (36/45) [#]	83.33 (40/48) [#]	79.63(43/54) [#]	92.31 (60/65)
	Sensitivity	77.61 (52/67) ^{*#}	79.10 (53/67) ^{*#}	74.63 (50/67) ^{*#}	91.04 (61/67)
Pleural effusion	Specificity	81.82 (45/55) [#]	80.00 (44/55) [#]	52.73 (29/55) [#]	89.10 (49/55)
	Positive predictive value	83.87 (52/62) [#]	82.81 (53/64) [#]	65.79 (50/76) [#]	91.04 (61/67)

Note: Compared with serum sensitivity detection, *P<0.05; Compared with joint detection, [#]P<0.05.

3 讨论

由于肺癌患者在患病初期临床症状不明显,甚至有部分患者身体无任何不适,即使后期病情发展,其临床症状的轻重和出现的早晚仍然取决于病理类型、有无转移、肿瘤发生部位、有无并发症以及患者的耐受性等因素,因此早期较难根据患者的临床表现诊断疾病,待患者疾病发展至晚期时,错过了手术的最佳时机,影响患者的治疗和预后,因此探究诊断肺癌的相关方法成为近年来医务工作者的研究重点^[12-14]。肿瘤标志物是一类能够反映肿瘤是否存在和生长状况的物质,与恶性肿瘤发生、发展密切相关。肿瘤标志物主要有肿瘤细胞直接分泌、肿瘤细胞的基因表达合成、机体对肿瘤的异常反应产生等几种来源^[15,16]。血清肿瘤标志物的主要类型有:癌胚抗原类、激素类、糖蛋白类、酶类。肿瘤标志物检测属于非侵袭性检测,具有操作简便、经济性好、微创、无射线危害等优点^[17-19]。相关研究显示^[20],通过检测肿瘤标志物的表达情况,对肿瘤的诊断、病情、治疗、预后有一定程度的指导作用。汪广杰^[19]等人对 1021 名肺癌患者血清 CA19-9、癌胚抗原、糖类抗原 125 及糖类抗原 15-3 水平进行检测,结果发现四种血清肿瘤标志物在肺癌患者血清中显著升高,且四项指标联合检测的特异度高达 100%,临床上对四项指标进行检测利于疾病的诊断。

本研究结果显示,肺癌组患者血清和胸腔积液中的 CA19-9、SCC-Ag 和 CYFRA21-1 水平显著高于良性病变组($P<0.05$),这说明 CA19-9、SCC-Ag 和 CYFRA21-1 在肺癌患者的血清和胸腔积液中高表达,可能对疾病有一定的预测作用。分析其中原因,CA19-9 是一种糖蛋白抗原,主要从癌细胞株分离而来,当机体发生癌变时,会导致血清及胸腔积液中的 CA19-9 的水平明显上升。已有研究证明^[21-23],消化道肿瘤的病情程度和血清 CA19-9 水平存在相关性,且 CA19-9 在乳腺癌、卵巢癌、前列腺癌、子宫内膜癌等恶性肿瘤患者的血清中呈现高表达,除此之外 CA19-9 在糖尿病等少数非肿瘤疾病也能够导致 CA19-9 水平升高。SCC-Ag 最早在宫颈癌患者的癌变组织中发现,正常组织中表达极低,在恶性病变的上皮细胞中含明显增加,尤其在鳞状上皮细胞中,判断非鳞癌的准确性较高。吴红波等人的研究显示^[24,25],SCC-Ag 在鳞癌、腺癌、小细胞肺癌、大细胞肺癌和肺部良性病变的患者血清中阳性率分别为 68.00%、14.29%、18.18%、20.00%、2.22%,可见 SCC-Ag 在肺癌中呈现高表达,尤其是鳞癌。CYFRA21-1 对鳞癌、腺癌最为敏感,除此之外,良性肝病、肾衰竭可引起血清中 CYFRA21-1 水平轻微升高,但很少超过 10 ng/mL^[26]。同时研究还显示,胸腔积液中 CA19-9、SCC-Ag 和 CYFRA21-1 单项检测对肺癌的灵敏度高于血清检测($P<0.05$);血清及胸腔积液中 CA19-9、

SCC-Ag 和 CYFRA21-1 三项联合检测的灵敏度、特异性、阳性预测值均高于单项检测($P<0.05$)。这说明三项指标在胸腔积液中的灵敏度高于血清检测,且三项指标联合检测具有更好的诊断价值。分析其中原因,可能是胸腔积液中的肿瘤标志物不需要经过血管运转,而血液中的肿瘤标志物被血液稀释,导致其在一定体积内的血清中变化程度被弱化,进而降低了诊断价值^[27,28]。CA19-9、SCC-Ag 和 CYFRA21-1 三种指标除了在肺癌患者中高表达,在良性病变的患者中水平也会有一定程度的升高,并且每个指标都会在一些不同的疾病中出现表达异常,而联合检测可以综合多种标志物的特性,有效减少了其他因素造成的误差,因而可以有效增加敏感度、特异性和阳性预测值^[29,30]。

综上所述,肺癌患者血清及胸腔积液中 CA19-9、SCC-Ag 和 CYFRA21-1 水平高于良性病变肺癌患者,并且三项指标联合检测可提高肺癌的诊断价值,临床上可在诊断肺癌时对三项指标进行监测。

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