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化学发光免疫分析在肿瘤标志物检测中的应用

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摘要 简要介绍了肿瘤标志物的一般概念及化学发光免疫分析的原理,综述了近年来化学发光免疫分析在主要的肿瘤标志物检测中的应用进展,并对化学发光免疫分析研究肿瘤标志物今后的发展提出展望。

关键词 化学发光免疫分析; 肿瘤标志物

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The application of chemiluminescent immunoassay in evaluation of tumor markers

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Abstract The theory of tumor markers and chemiluminescent immunoassay was introduced briefly. The recent application of chemiluminescent immunoassay in evaluation of tumor markers was reviewed, and the development of its application in evaluation of tumor markers in future was also viewed.

Key words chemiluminescent immunoassay; tumor markers

1 前言

肿瘤标志物(tumor markers)是1978年在美国国立癌症研究所召开的人类肿瘤免疫诊断会议上提出的,次年在英国第七届肿瘤发生生物学和医学会议上被大家确认,肿瘤标志物的检测对肿瘤辅助诊断及判断肿瘤预后、转归、评价疗效都具有重要的临床意义。

基于放射免疫分析的基本原理, Halman 在1977年将酶的化学发光与免疫反应结合起来,建立了化学发光免疫分析(chemiluminescent immunoassay, CLIA)方法。CLIA的基本原理是将发光物质或酶标记在抗原或抗体上,免疫反应结束后,加入氧化剂或酶底物而发光,通过测量发射光强度,根据标准曲线测定待测物的浓度。CLIA以其灵敏度高、仪器价格低、可实现自动化、使用简便、安全、无放射性污染等优势,倍受人们的青

睐,成为标记免疫分析的一个重要方向。

2 化学发光免疫分析在肿瘤标志物检测中的应用

2.1 糖脂或糖蛋白类标志物(CA系列)

Yan G等^[1]分别用化学发光酶免疫分析、酶联免疫分析和免疫放射分析等方法检测CA125,并对比分析了其在临床上的应用价值,发现在诊断卵巢癌时,化学发光酶免疫分析是检测CA125水平的较好的方法。Candido Dos Res FJ等^[2]用CLIA检测上皮卵巢肿瘤患者血清和囊液中的CA125和血管内皮生长因子水平,结果表明,分析患者血清中的CA125和囊液中的血管内皮生长因子水平是区分良性和恶性上皮卵巢肿瘤的好方法。Fujiwara H等^[3]用CLIA仪检测CA199,建立了分析CA199的新方法。CA199可作为胰腺、肝、胆囊肿瘤的标志物。王文耀等^[4]用CLIA检测了胰腺癌患者血浆中的CA199水平,并用聚合酶链反应检测K-ras基因,结果发现联合分析分子肿瘤标志物和蛋白肿瘤标志物比单独分析蛋白肿瘤标志物更灵敏。

2.2 同工酶类标志物

Arai K等^[5]用吡啶酯作为标记物,建立了一步

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夹心法 CLIA 检测前列腺酸性磷酸酶的新方法。

2.3 激素类标志物

Oed M 等^[6]用自动 CLIA 仪检测人绒毛膜促性腺激素, 结果表明, 该方法的精密度、线性关系、回收率和敏感性都较好。

2.4 肿瘤相关抗原

Adachi T 等^[7]用 CLIA 检测前列腺特异性抗原, 并探讨了其在前列腺癌检测中的临床应用意义, 认为前列腺特异性抗原可用来筛选前列腺癌, 但不能区分前列腺癌和良性前列腺增生。而 Wesseling S 等^[8]用 CLIA 仪检测 tPSA(总前列腺特异性抗原)和 fPSA(游离前列腺特异性抗原), 认为 fPSA/tPSA 可区分前列腺癌和良性前列腺增生。此外, Sanchez C 等^[9]用电化学发光免疫分析检测膀胱癌患者尿样中的 CYFRA21-1(细胞角蛋白 19 片段), 结果表明, 检测 CYFRA21-1 水平可作为膀胱镜检查的辅助。Deng YF 等^[10]也用电化学发光免疫分析检测了人头部和颈部鳞细胞癌的 CYFRA21-1, 并探讨了其临床意义, 发现 CYFRA21-1 不但对诊断有意义, 而且对患者的病情追踪有意义。

2.5 其他

Nomura F 等^[11]用电化学发光免疫分析检测肝小细胞癌患者的血清 DCP (des- γ -羧基凝血酶原)水平, 发现 DCP 对甲胎蛋白诊断肝癌起辅助作用; 而 Shimada M 等^[12]也用该方法检测了肝癌组织和非肝癌组织中的 DCP 水平, 结果表明 DCP 水平在肝致癌中起重要作用; Shimizu A 等^[13]用同样的电化学发光系统检测 DCP 水平, 认为 DCP 水平可作为肝硬化患者肝癌的标志物。最近, Geiger DU 等^[14]将 AMPPD[3-(2'-螺金刚烷)-4'-甲氧基-4-(3'-磷酸氧基)-苯基-1,2-环氧乙烷]作为标记物, 用全自动微粒子化学发光免疫分析仪检测血清中 cTnI(心肌肌钙蛋白 I)含量, 结果发现 cTnI 可作为反映心肌细胞损伤高度灵敏与特异的标志物。

3 结论

快速、准确地检测肿瘤标志物有重要的临床应用价值。目前国内用 CLIA 方法研究肿瘤标志物的成果并不是很多, 而国外很多人用该方法研究肿瘤标志物并讨论了其临床应用价值。同一个标志物可用不同的方法检测, 同一方法可分析不同的肿瘤标志物, CLIA 以其高的灵敏度和简便的仪器操作而

占优势。因此, 今后 CLIA 研究肿瘤标志物将有以下发展趋势: (1)寻找更敏感、更特异的新恶性肿瘤标志物, 寻求最合理的多种标志物的联合检测的组合; (2)研究开发新恶性肿瘤标志物的 CLIA 法即 CLIA 试剂盒, 以便临床上更迅速、准确、灵敏地检测肿瘤标志物。相信 CLIA 在肿瘤标志物临床检测中的应用, 会更好地推动恶性肿瘤研究的发展。

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4 结束语

总之,随着国际相关机构及各国的相关部门制定的法律法规或标准的不断完善,¹³¹I治疗技术也将得到不断提高和推广。参照国内外辐射危害标准界限,对服用¹³¹I患者的周围人群进行个体化当量剂量值计算和(或)当量剂量率测量,获得一个标准,来评价¹³¹I治疗患者对周围人群的辐射危害是否在安全范围,以确定是采取住院治疗,进行有效的隔离,限制其正常的社会交往活动;还是允许其出院休养,恢复正常社会交往活动。

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