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类风湿关节炎患者抗 CCP, RF, AKA, ASO, RA33 的临床价值分析 *

李 钊 侯婷婷 赵万辉 王 英 索海燕

(山东大学附属省立医院 临床医学检验部 山东 济南 250021)

摘要 目的:分析抗环瓜氨酸肽(CCP)、类风湿因子(RF)、抗角蛋白抗体(AKA)、抗链球菌溶血素 "O"(ASO)、抗 RA33 抗体对类风湿关节炎诊断的临床价值。**方法:**选取 2015 年 3 月至 2016 年 2 月本院收治的 79 例类风湿关节炎患者视为观察组,另选取同期本院收治的 85 例非类风湿关节炎自身免疫性疾病者视为对照组。比较类风湿关节炎和非类风湿关节炎患者抗 CCP、RF、AKA、ASO、RA33 阳性情况,对抗 CCP、RF、AKA、ASO、RA33 的特异度和敏感度予以分析。**结果:**两组患者的 ASO 阳性率比较无显著性差异($P>0.05$),观察组的抗 CCP、RF、AKA、RA33 阳性率显著高于对照组($P<0.05$)。抗 CCP 抗体诊断类风湿关节炎患者的敏感度为 64.56%、特异度为 92.94%;RF 敏感度为 60.46%、特异度为 80.00%;AKA 敏感度为 51.90%、特异度为 96.47%;ASO 敏感度为 10.13%、特异度为 89.41%;抗 RA33 抗体敏感度为 30.38%、特异度为 95.29%。**结论:**抗 CCP、RF、AKA、RA33 对类风湿关节炎患者均具有较高的诊断价值,而 ASO 在类风湿关节炎患者中的诊断价值不明显。

关键词:类风湿关节炎;抗环瓜氨酸肽;类风湿因子;抗角蛋白抗体;抗链球菌溶血素 "O";抗 RA33 抗体

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Analysis of the Clinical Value of Anti - CCP, RF, AKA, ASO and RA33 in Patients with Rheumatoid Arthritis*

LI Tian, HOU Ting-ting, ZHAO Wan-hui, WANG Ying, SUO Hai-yan

(Department of clinical laboratory medicine, provincial hospital affiliated to Shandong University, Shandong, Ji'nan, 250021, China)

ABSTRACT Objective: To analyze the clinical value of anti-cyclic citrullinated peptide(CCP), rheumatoid factor(RF), anti-keratin antibodies (AKA), anti-streptolysin O (ASO), RA33 in diagnosis of rheumatoid arthritis. **Methods:** 79 patients with rheumatoid arthritis who were treated from March 2015 to February 2016 in our hospital were regarded as the observation group. 85 patients with autoimmune diseases of rheumatoid arthritis who were admitted in our hospital in the same period were selected as the control group. The anti RFA, AKA, ASO and RA33 in patients with rheumatoid arthritis and non-rheumatoid arthritis were detected to analyze the specificity and sensitivity. **Results:** There was no significant difference in the ASO positive rate between the two groups. The positive rates of anti-CCP, RF, AKA, RA33 in the observation group were significantly higher than those in the control group ($P<0.05$). The sensitivity of anti-CCP for rheumatoid arthritis patients was 64.56% and the specificity was 92.94%. The RF sensitivity was 60.46% and the specificity was 80.00%. The AKA sensitivity was 51.90% and the specificity was 96.47%. ASO sensitivity was 10.13% and specificity was 89.41%. The sensitivity of anti-RA33 antibody was 30.38% and the specificity was 95.29%. **Conclusion:** The anti-CCP, RF, AKA, RA33 had high diagnostic value for rheumatoid arthritis, while ASO was of little value in the diagnosis of rheumatoid arthritis.

Key words: Rheumatoid arthritis; Anti-cyclic citrullinated peptide; Rheumatoid factor; Anti-keratin antibody; Anti-streptolysin "O"; Anti-RA33 antibody

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前言

类风湿关节炎属于多系统、炎症性自身免疫疾病,会对周围关节造成累及性影响,多个周围关节呈现出慢性炎症病变是此病的主要特征,在临床中主要表现为关节功能降低、肿胀、疼痛,病变呈现出反复、持续发作的形式^[1]。慢性滑膜炎作为此病的主要病理特征,会对下层骨组织及软骨组织造成影响,破坏关节功能^[2]。类风湿性关节炎发病较为缓慢及隐匿,常常会使得

患者丧失劳动力,严重者可能会致残^[3]。在临床中主要依靠类风湿因子检测、X 线检查、临床表现对此病做出诊断。目前,抗环瓜氨酸肽 (Anti-cyclic citrullinated peptide, CCP)、类风湿因子 (Rheumatoid factor, RF)、抗角蛋白抗体(Anti-keratin antibodies, AKA) 及抗链球菌溶血素 "O" (Anti-streptolysin "O", ASO)、抗 RA33 抗体已逐渐成为了众多学者纳入研究的热点^[4]。为给临床在诊断类风湿关节炎中提供更多的参考依据,本文就类风湿关节炎患者抗 CCP、RF、AKA、ASO、RA33 的临床价值进行分

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作者简介:李钊(1984-),女,本科,检验师,研究方向:风湿免疫自身抗体研究,电话:15168886705

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析,现报道如下。

1 资料与方法

1.1 临床资料

选取 2015 年 3 月至 2016 年 2 月本院收治的 79 例类风湿关节炎患者视为观察组,纳入标准:① 患者的临床诊断均和类风湿关节炎诊治指南标准相符^[9];② 无精神疾病史;③ 依从性较好。排除标准:① 当前正在配合医护人员完成其他试验者;② 意识障碍者;③ 患者不愿加入本次试验。其中女性 52 例,男性 27 例;年龄 21~75 岁,平均(51.43±2.43)岁。另选取同期本院收治的 85 例非类风湿关节炎自身免疫疾病者视为对照组,其中 1 例伴有骨关节炎,2 例为贝切特氏综合征,2 例多肌炎,4 例特发性幼年性关节炎,4 例未分化结缔组织病,10 例狼疮性肾炎,12 例皮炎,15 例干燥综合征,17 例强直性脊柱炎,18 例系统性红斑狼疮;其中女性 57 例,男性 28 例;年龄 22~74 岁,平均(51.48±2.41)岁。两组患者的性别、年龄临床资料比较无显著性差异($P>0.05$),具有可比性。

1.2 方法

所有患者在入院后,收集所有研究对象 5 mL 的空腹静脉血,并放置一次性分离胶促凝试管中,在 1h 内对血清进行分离,放置在 5℃ 环境中保存,使用德国欧蒙医学实验公司提供的 CCP 抗体酶联免疫吸附试验试剂盒检测 CCP,均根据说明

书进行操作,根据 1:100 的标本进行稀释,若结果 >5 RU/mL 则为阳性。使用免疫比浊法检测 RF、ASO,全自动分析仪以及配套试剂型号均为 AU2700,其中 RF 值 >14 IU/mL 则为阳性,ASO 值 >200 IU/mL 则为阳性。采取间接免疫荧光法检测 AKA,由德国欧蒙医学实验诊断公司提供试剂,大鼠食管组织作为抗原基质,滴度 $\geq 1:10$ 则为阳性。使用酶联免疫吸附法检测抗 RA33 抗体试剂,由深圳亚辉龙生物科技公司提供抗 RA33 抗体试剂,若浓度 >30 AU/mL 则为阳性。上述步骤均根据说明书完成操作。

1.3 观察指标

比较类风湿关节炎和非类风湿关节炎患者抗 CCP、RF、AKA、ASO、RA33 阳性情况。对抗 CCP、RF、AKA、ASO、RA33 的特异度和敏感度予以分析。

1.4 统计学处理

本次实验数据处理选择 SPSS 11.5 软件包进行,计数资料用[n(%)]来表示,采取 χ^2 检验,其 $P<0.05$ 表明差异具有统计学意义。

2 结果

2.1 两组患者抗 CCP、RF、AKA、ASO、RA33 阳性率比较

两组患者 ASO 阳性率比较无显著性差异($P>0.05$),观察组抗 CCP、RF、AKA、RA33 阳性率显著高于对照组($P<0.05$),见表 1。

表 1 两组患者抗 CCP、RF、AKA、ASO、RA33 阳性率比较[例(%)]

Table 1 Comparison of the positive rates of CCP, RF, AKA, ASO and RA33 between the two groups[n(%)]

Groups	Case	Anti-CCP	RF	AKA	ASO	RA33
Observation group	79	51(64.56)*	48(60.76)*	41(51.90)*	8(10.13)	24(30.38)*
Control group	85	6(7.06)	17(20.00)	3(3.53)	9(10.59)	4(4.71)

Note: Anti-CCP: Anti-cyclic citrullinated peptide; RF: Rheumatoid factor; AKA: Anti-keratin antibodies; ASO: Anti-streptolysin "O". Compared with control group, * $P<0.05$.

2.2 五种单抗敏感度和特异度分析

抗 CCP 抗体对类风湿关节炎患者的敏感度为 64.56%、特异度为 92.94%;RF 敏感度为 60.46%、特异度为 80.00%;AKA 敏感度为 51.90%、特异度为 96.47%;ASO 敏感度为 10.13%、特异度为 89.41%;抗 RA33 抗体敏感度为 30.38%、特异度为 95.29%,见表 2。

表 2 五种单抗敏感度和特异度分析[例(%)]

Table 2 Analysis of the sensitivity and specificity of five kinds of monoclonal antibodies[n(%)]

Detection indicators	Sensitivity	Specificity
Anti-CCP	64.56%(51/79)	92.94%(79/85)
RF	60.46%(48/79)	80.00%(68/85)
AKA	51.90%(41/79)	96.47%(82/85)
ASO	10.13%(8/79)	89.41%(76/85)
RA33	30.38%(24/79)	95.29%(81/85)

Note: Anti-CCP: Anti-cyclic citrullinated peptide; RF: Rheumatoid factor; AKA: Anti-keratin antibodies; ASO: Anti-streptolysin "O".

3 讨论

类风湿关节炎属于临床较为常见的一种疾病,发病率较

高,存在着较为复杂的病因,难以在早期做出确切诊断^[6,7]。在诊断类风湿关节炎中,较为常见的临床指标 RF 有着较高的敏感性,但于狼疮性肾炎、皮炎、干燥综合征、系统性红斑狼疮等患者中均可能检测到 RF 的存在,甚至在某些正常人群中 also 呈现出阳性率,因此特异性欠佳,尤其对于早期类风湿关节炎的诊断^[8,9]。

近年来,实验室在诊断类风湿关节炎中逐渐将抗 CCP 抗体视为重点检测指标。相关研究者使用人工方法合成 CCP,在检测人工合成 CCP 中使用了酶联免疫吸附法,通过对类风湿关节炎患者的 CCP 抗体予以检测,发现此指标在类风湿关节炎患者中的特异度及敏感度分别为 98%、68%^[10-12]。目前也有越来越多的血脂使用酶联免疫吸附法检测 CCP 抗体,同样获取了较高的特异度和敏感度^[13,14]。本次研究中通过对 79 例类风湿关节炎患者和 85 例非类风湿关节炎患者采取欧蒙相对应的试剂予以检测发现,CCP 在类风湿关节炎患者中的特异度为 92.94%(79/85),敏感度为 64.56%(51/79)。相关研究者提出抗 CCP、RF 在类风湿关节炎患者中的阳性率分别为 53%、69%,明显比非类风湿关节炎患者高^[5]。本次研究结果显示抗 CCP、RF 在类风湿关节炎患者中的阳性率分别为 64.56%(51/79)、60.76%(48/79),明显比非类风湿关节炎患者的抗 CCP、RF 阳性

率高 7.06%(6/85)、20.00%(17/85),但类风湿关节炎患者的 ASO 阳性率和非类风湿关节炎患者的阳性率比较无明显差异性,提示可将 CCP、RF 作为类风湿关节炎的诊断指标,但 ASO 指标在类风湿关节炎中几乎无诊断价值。

AKA 作为不溶性纤维蛋白中的一种,是细胞骨架构建的主要部分^[10]。若在健康人群中发现此类抗体存在,其很有可能发展为典型的类风湿关节炎,因此在类风湿关节炎患者的早期中便可发现 AKA 的存在,在预测类风湿关节炎患者的进展情况中可将此指标视为主要检测标准^[17,18]。抗 RA33 抗体是在研究类风湿关节炎患者的外周血中所发现的指标,会和特定核酸蛋白相互作用发生反应,在诊断类风湿关节炎患者中 RA33 有着较好的特异度和敏感度^[19,20]。本次研究结果显示 AKA、RA33 在类风湿关节炎患者中的阳性率高达 51.90%(41/79)、30.38%(24/79),明显高于非类风湿关节炎患者,且 AKA、RA33 在类风湿关节炎患者中均存在较高的特异性和敏感性。

总之,临床检测类风湿关节炎患者抗 CCP、RF、AKA、RA33 均有着较高的诊断价值,而 ASO 在类风湿关节炎患者中的诊断价值不高。

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