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血清 BNP、h-FABP 对川崎病患儿的诊断价值分析 *

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摘要 目的：探讨与分析血清脑钠肽(Brain natriuretic peptide，BNP)、心肌型脂肪酸结合蛋白(heart type fatty acid binding protein，H-FABP)对川崎病(Kawasaki disease，KD)患儿的诊断价值。**方法**：采用病例对照的方法，选择 2018 年 1 月至 2019 年 7 月在本院诊治住院的川崎病患儿 78 例作为川崎病组，选取同期体检的健康儿童 78 例作为对照组。调查两组的临床资料，检测血清 BNP、h-FABP 水平并进行诊断价值判断。**结果**：两组的一般资料无统计学意义(P>0.05)。川崎病组的白细胞计数、血小板计数、淋巴细胞计数显著高于对照组，红细胞比容与血红蛋白值显著低于对照组(P<0.05)。川崎病组患儿的血清 BNP、h-FABP 含量都显著高于对照组(P<0.05)。在川崎病组中，Spearman 等级相关性分析显示 BNP 与 h-FABP 呈显著正相关性(r=0.782，P=0.000)。受试者工作特征曲线(receiver operating characteristic curve，ROC)显示 BNP 与 h-FABP 诊断川崎病的曲线下面积分别为 0.822、0.845，诊断灵敏性、特异性与准确性都在 70.0 %以上。**结论**：血清 BNP、h-FABP 在川崎病患儿中呈现高表达状况，对川崎病也有很好的诊断价值，可为临床诊治起到一定的指导作用。

关键词：脑钠肽；心肌型脂肪酸结合蛋白；川崎病；相关性；诊断价值

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Diagnostic Values of Serum BNP and h-FABP in Children with Kawereaki Disease*

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ABSTRACT Objective: To investigate and analysis the diagnostic values of brain natriuretic peptide (BNP) and heart type fatty acid binding protein (H-FABP) in children with Kawereaki disease (KD). **Methods:** Used a case-control method，78 children with Kawasaki disease who were hospitalized in our hospital from January 2018 to July 2019 were selected as Kawasaki disease group, and 78 healthy children with concurrent physical examination were selected as the control group. Investigate the clinical data of the two groups, detect serum BNP, h-FABP levels and make diagnostic value judgment. **Results:** The general data of the two groups were not statistically significant (P>0.05). The white blood cell count, platelet count and lymphocyte count of Kawasaki disease group were significantly higher than those of the control group, and the hematocrit and hemoglobin values were significantly lower than the control group (P<0.05). The serum BNP and h-FABP levels in the Kawereaki disease group were significantly higher than in the control group (P<0.05). In the Kawereaki disease group, Spearman rank correlation analysis showed there were significant positive correlation between BNP and h-FABP (r=0.782, P=0.000). The receiver operating characteristic curve (ROC) showed that the area under the curve of BNP and h-FABP for the diagnosis of Kawereaki disease were 0.822 and 0.845, respectively, and the diagnostic sensitivity, specificity and accuracy were above 70.0%. **Conclusion:** Serum BNP and h-FABP are highly expressed in children with Kawereaki disease, and have good diagnostic values for Kawereaki disease, which can play guiding roles in clinical diagnosis and treatment.

Key words: Brain natriuretic peptide; Myocardial fatty acid binding protein; Kawereaki disease; Correlation; Diagnostic value

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前言

川崎病(Kawasaki disease，KD)是一种好发于学龄前儿童的自身免疫性血管炎性疾病，为全身性血管炎[1,2]。已有研究显示在一定的遗传易感性基础上，细菌、病毒的感染可以以抗原或超抗原的形式引起机体的免疫激活，从而导致川崎病的发生，特别是 T、B 淋巴细胞介导的细胞因子、免疫应答相互作用的级联放大效应在川崎病的发生中发挥了重要作用[3,4]。川崎病在临床上主要表现为发热，伴有全身皮肤多形性皮疹、颈部淋巴结非化脓性肿大、口唇干红，部分患儿可形成冠状动脉巨大瘤，并发狭窄或血栓，严重影响患儿的身心健康与发育[5]。脑钠肽(Brain natriuretic peptide，BNP) 是从猪脑组织中发现的一种生

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物活性物质，在人体中主要来自心室肌细胞[6,7]。当心脏受到刺激或者心肌组织损伤时，可引起心肌张力和容量的改变，造成血液中 BNP 失访增加[8]。而 BNP 含量增加也能够减弱心肌收缩力、诱导凋亡和坏死、促进心室重构，从而形成恶性循环[9]。心肌型脂肪酸结合蛋白 (heart type fatty acid binding protein, H-FABP)是一种早期诊断心肌缺血的生化标志物，存在于心肌组织中的可溶性蛋白质中，由 132 个氨基酸组成，分子量约 15000[10,11]。可通过运输细胞内的长链脂肪酸进入人体的能量代谢体系，严重心肌缺血时可参与脂肪酸的代谢调节，从而对心肌细胞形成保护[12,13]。几年来，川崎病患儿逐年增加，该病已漏诊和误诊，错过最佳时间，心脏彩色多普勒超声用于判断川崎病，结果可靠，但费用较高，且技术要求过高，部分门诊无法使用，因此，寻找一种安全、准确的检测方式已成为临床研究重点。本文具体探讨与分析了血清 BNP、h-FABP 对川崎病患儿的诊断价值，以促进早期检出川崎病。

1 资料与方法

1.1 研究对象

采用病例对照的方法，研究时间为 2018 年 1 月至 2019 年 7 月，研究得到了本院伦理委员会的批准。选择在本院诊治住院的川崎病患儿 78 例作为川崎病组，明确诊断为川崎病(发热时间 >5 d；双眼结膜充血；颈部非化脓性淋巴结肿大；多形性红斑、皮疹；口唇绛红；足底及指趾末端潮红)或单纯发热，病程 5~10 d，平均病程 6.24±1.46 d。同时选取同期体检的健康儿童 78 例作为对照组。纳入标准：年龄均为 6 个月 -9 月；临床与随访资料完整；排除标准：临床与随访资料缺乏者；合并先天性心肝肾异常患儿。

1.2 血清 BNP、h-FABP 检测

患儿入院当天采集静脉血 2-3 mL，置于真空无菌采血管中，自凝后，3000 rpm 离心 10 min，分离上清分清，置于 -20℃以下冰箱中冷冻保存。采用酶联免疫法检测血清 BNP、h-FABP 含量，检测试剂盒购自上海生工公司。同时记录患者的常规血液学指标，包括白细胞计数、血小板计数、淋巴细胞计数、红细胞比容、血红蛋白等。

1.3 调查内容

调查所有患儿的性别、年龄、临床症状、发热病程、体重、身高等数据。

1.4 统计方法

采用 SPSS20.0，计量数据采用均数±标准差表示，对比为 t检验；计数数据采用%表示，对比为卡方 χ^2 分析，采用 Spearman 等级相关性进行相关性分析，采用 ROC 判断诊断价值，检验水准为 α=0.05。

2 结果

2.1 一般资料对比

两组的一般资料无统计学意义(P>0.05)。见表 1。

表 1 两组一般资料对比

Table 1 Comparison of general data between the two groups

Groups	n	Gender (Male /Female)	Age(olds)	Body weight (kg)	Height (cm)
Kawasaki disease group	78	40/38	4.86±0.32	15.69±2.55	99.82±5.11
Control group	78	39/39	4.91±0.44	15.20±1.85	99.89±4.62

Note: compared with the control group,*P<0.05.

2.2 常规血液学指标对比

川崎病组的白细胞计数、血小板计数、淋巴细胞计数显著高于对照组，红细胞比容 与血红蛋白值显著低于对照组(P<0.05)，见表 2。

表 2 两组常规血液学指标对比 ($\bar{x}\pm s$)

Table 2 Comparison of routine hematological indicators between the two groups ($\bar{x}\pm s$)

Groups	n	WBC ($\times10^9$/L)	PLT ($\times10^9$/L)	LC ($\times10^9$/L)	Hct (L/L)	Hemoglobin (g/L)
Kawasaki disease group	78	16.55±2.15*	401.44±56.39*	3.59±0.47*	0.21±0.02*	112.76±15.68*
Control group	78	6.58±1.21	241.52±72.54	2.24±0.14	0.35±0.05	143.27±14.01

2.3 血清 BNP、h-FABP 含量对比

川崎病组的血清 BNP、h-FABP 含量都显著高于对照组(P<0.05)。见表 3。

2.4 相关性与诊断价值分析

在川崎病组中，Spearman 等级相关性分析显示 BNP 与 h-FABP 呈显著正相关性 (r=0.782，P=0.000)。ROC 曲线显示

表 3 两组血清 BNP、h-FABP 含量对比 ($\bar{x}\pm s$)

Table 3 Comparison of serum BNP and h-FABP levels in two groups($\bar{x}\pm s$)

Groups	n	BNP(pg/mL)	h-FABP(ng/mL)
Kawasaki disease group	78	712.04±45.65*	45.30±5.20*
Control group	78	244.87±52.10	15.01±1.89

Note: compared with the control group, *P<0.05.

BNP 与 h-FABP 诊断川崎病的曲线下面积分别为 0.822、0.845，诊断灵敏性、特异性与准确性都在 70.0%以上。见表 4。

表 4 BNP、h-FABP 诊断川崎病的价值 (n=156)

Table 4 Value of BNP and h-FABP in the diagnosis of Kawasaki disease (n=156)

Index	Sensitivity	Specificity	Accuracy	Positive predictive value	Negative predictive value
BNP	70.88%	74.89%	72.94%	73.02%	74.92%
h-FABP	74.02%	72.99%	84.29%	83.42%	83.99%

3 讨论

川崎病和普通发热均为学龄前儿童常见疾病，两者在受累人群、发病机制、临床表现及并发症上存在关联[14]。该病的临床特征是持续发热、眼结膜充血、不同程度的口腔黏膜炎、手足硬性肿胀伴指尖脱屑等[15,16]。本研究显示两组患儿的性别、年龄、发热病程、体重、身高等对比差异无统计学意义；川崎病组的白细胞计数、血小板计数、淋巴细胞计数显著高于对照组，红细胞比容与血红蛋白值显著低于对照组，说明炎症因子在川崎病的患儿的发生发展发挥了重要的作用。川崎病具有一定的自限性，不过病理改变是全身中小血管非特异性炎症，以心血管系统损害最为严重，可形成冠脉扩张和冠脉瘤，甚至导致猝死[17]。流行病学调查显示，川崎病高发于≤ 5 岁以下小儿，具有区域流行特点，具有显著季节性[18,19]。

当前炎性细胞因子广泛参与免疫应答、介导炎症反应等，川崎病患儿外周血或者局部心肌中存在大量的炎症细胞因子能够促进心室重构，减弱心肌收缩力、诱导凋亡和坏死[20]。本研究显示治川崎病组患儿的血清 BNP、h-FABP 含量都显著高于对照组。BNP 基因定位于 1 号染色体的短臂末端，来自外界的刺激引起心室壁张力改变从而使心肌细胞分泌 BNP[21]。有研究显示 BNP 可作为反映左心室射血分数的独立指标，心肌坏死、损伤、缺血等均可刺激 BNP 的合成与释放，也是对心力衰竭进行综合评价的生物标记物[22]。缺血损伤能够增加心肌细胞膜的通透性。H-FABP 能够穿透细胞膜，升高其在血液中的浓度[23,24]，也能对抗氧自由基的损伤，保护膜磷脂，防止细胞器膜损伤[25]。

川崎病发生与机体免疫功能受抑制有关，尤其是细胞免疫在机体免疫应答中其非常重要的作用。此外，细胞因子作为促炎因子和抗炎因子在川崎病的发生和发展中也起到重要作用[26,27]。川崎病急性期反应是一种抗原介导的免疫反应，感染源通过呼吸道或消化道进入体内，也提示该病是一种感染而不是自身免疫性疾病[28]。川崎病急性期的相关炎症因子表达升高，有冠脉损害时更为明显，急性期后有所下降，也可认为其认为参与了川崎病冠脉损害的发生[29]。本研究 Spearman 等级相关性分析显示川崎病患儿的 BNP 与h-FABP 呈显著正相关性($r=0.782$，$P=0.000$)；ROC 曲线显示 BNP 与 h-FABP 诊断川崎病的曲线下面积分别为 0.822、0.845，诊断灵敏性、特异性与准确性都在 70.0 %以上。从机制上分析，和传统的炎症指标相比较，BNP、h-FABP 特异性更高，有较好的使用价值。特别是局部心肌炎症以及心肌损伤会导致心室肌的合成及分泌 BNP，进而会导致川崎病患儿 BNP 水平升高。而 H-FABP 分子量小，心肌损伤时迅速释放入血，因而血清 H-FABP 水平可以反应心肌细胞的损害程度[30,31]。本研究也有一定的不足，纳入调查的因素比较少，且随访时间短，可能在影响因素分析上存在偏倚，将在后续分析中深入研究。

总之，血清 BNP、h-FABP 在川崎病患儿中呈现高表达状况，对川崎病也有很好的诊断价值，可为临床诊治起到一定的指导作用。

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