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49 例儿童暴发性心肌炎的临床特点与预后

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摘要 目的:探讨儿童暴发性心肌炎的临床特点及与预后的关系。**方法:**回顾性分析患者病史、ECG、UCG、CMR、血清学检查资料及随访结果,得出影响预后的相关危险因素。**结果:**共收治 49 例暴发性心肌炎患者,平均年龄 8.89 ± 3.63 岁。死亡 9 例(18.37%),平均存活时间 4 天,无晚期死亡。以心外表现为首发症状者占 83.67%。初诊时血清 CK-MB 及 cTnI 异常检出率分别为 51.11% 和 81.39%,两者同时增高占 47.50%。49 例患者在疾病初期均存在明显的心电图异常,其中室性心律失常的发生率在恢复组与死亡组间存在明显差异($P=0.020$)。恢复组与死亡组 LVEF/LVFS 降低的发生率分别为 62.5% 和 100%($P=0.157$),恢复组 LVEF 恢复正常平均时间 10.22 天。恢复组中 10 例患者在急性期行 CMR 检查,其中 9 例符合路易斯湖。所有患者均使用大剂量激素及丙种球蛋白治疗。8 例患者安装临时心脏起搏器,4 例接受 ECOM 治疗。恢复组平均随访 19.28 月,100% 临床痊愈。多因素生存分析,最终与死亡有关的危险因素为年龄 ≤ 6 岁(RR40.215, 95%CI(1.285-1258.369))。**结论:**暴发性心肌炎起病急骤,以心外症状为首发者多见,经及时诊断、治疗的患者有望完全康复。所有患者均存在不同程度心电图异常。多因素生存分析发现年龄 ≤ 6 岁为死亡的危险因素。

关键词:暴发性心肌炎;预后;儿童

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Clinical Characteristics and Prognosis of 49 Children with Fulminant Myocarditis

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ABSTRACT Objective: To explore the clinical characteristics and outcomes predictors of fulminant myocarditis. **Methods:** The clinical finding and follow-up data, including medical history, ECG, UCG, CMR, serological examination were analyzed to get outcomes predictors of fulminant myocarditis. **Results:** 49 fulminant myocarditis patients were analyzed. The average age of 49 patients was 8.89 ± 3.63 years. Dead patients were 9 cases (18.37%) and the average survival time was 4 days, no late death. First symptom that outside the heart performance accounted for 83.67%. With serum CK-MB detection, the abnormal detection rate is 51.11%. With serum cTnI detection, the abnormal detection rate is 81.39%. Both abnormalities accounted for 47.50%. 49 patients in the early stages of the disease have obvious abnormal ECG. The incidence of ventricular arrhythmia was significantly different between the recovery group and the death group ($P=0.020$). The incidence of LVEF/LVFS reduction in the recovery group and death group was respectively 62.5% and 100% ($P=0.157$), and the LVEF recovered to normal average time of recovery group was 10.22 days. In the recovery group, 10 patients were examined by CMR in the acute phase, and 9 patients accorded with Lake Louise Consensus Criteria. In the recovery period. All the patients were given large doses of steroids and immunoglobulin. 8 cases were treated with temporary cardiac pacing, and 4 cases were treated with ECOM. The recovery group was followed up for 19.28 months, and all patients recured. By multivariate survival analysis, age ≤ 6 years (RR40.215, 95%CI (1.285-1258.369)) was the final risk factors associated with death. **Conclusions:** Fulminant myocarditis attacks abruptly, and the heart outside symptom is often the first to see. After timely diagnosis and treatment, patients are expected to make a full recovery. All patients had different degrees of abnormal ECG. Age ≤ 6 years was the final risk factors associated with death.

Key words: Fulminant myocarditis; Prognosis; Child

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前言

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暴发性心肌炎(fulminant myocarditis)是一种严重危害儿童健康的临床危重症。多项研究^[1,2]表明暴发性心肌炎具有起病急骤,死亡率高(约 10%-20%),及时治疗即可获得痊愈等特点。Pei 等^[3]总结了 24 例暴发性心肌炎患儿临床资料后指出暴发性心肌炎无特异性临床特点,左室射血分数(left ventricular

ejection fraction, LVEF)是影响预后的关键因素。Lee 等^[4]指出完全性房室传导阻滞、左室短轴缩短率(left ventricular short axis shortening, LVFS)减低提示患者病情严重,及时的机械辅助治疗对患者的预后有利。本文就我院近 16 年收治的暴发型心肌炎患儿临床资料进行回顾性总结分析,以加深对儿童暴发型心肌炎临床特点、诊治和预后的认识。

1 资料和方法

1.1 病例资料

收集 1999 年 1 月~2014 年 12 月上海儿童医学中心收治的 49 例暴发性心肌炎患者的住院病史及专科门诊随访资料。所有病例均符合 1999 年 9 月昆明全国小儿心血管年会修订的《小儿心肌炎诊断标准》(修订草案)^[5],且在发病 24 小时内病情急剧进展恶化,出现心源性休克、急性左心功能衰竭、严重室性心律失常或阿斯综合征。出院后至少在心脏专科门诊随访半年以上。

1.2 方法

收集患者病史、心电图(electrocardiogram, ECG)、24 小时动态心电图(24 h Holter)、二维超声心动图(ultrasonic echocardiography, UCG)、肌酸激酶(creatine kinase, CK)及同工酶(creatinine kinase MB isoenzyme, CK-MB)、血清脑钠肽前体(pro-brain natriuretic peptide, proBNP)、肌钙蛋白 I (cardiac troponin I, cTnI) 及心脏磁共振(cardiac magnetic resonance, CMR)检查资料。根据治疗结果分为恢复组和死亡组。

ST-T 变化:ST 段下移 ≥ 2 mm 或上抬 ≥ 2 mm, T 波倒置;传导阻滞:完全性左束支传导阻滞(Complete left bundle branch block, CLBBB)和完全性右束支传导阻滞(Complete right bundle branch block, CRBBB);室性心律失常:成对/联律室性早搏、多形性室性早搏、短阵室速。

1.3 统计方法

采用 SPSS21.0 软件统计,计量资料以均数 $\pm$ 标准差表示,发病年龄用中位数(M)表示。两组之间计量资料的比较采用 t 检验;计数资料的比较采用卡方检验, $P<0.05$ 表示差异具有统计学意义。生存分析采用寿命表法,先进行单因素生存分析,再引入多因素生存分析, $P<0.05$ 为具有统计学差异。

2 结果

2.1 一般资料

49 例患者中男性 22 例,年龄 1.25 岁~15 岁,平均年龄 8.89 ± 3.63 岁,中位年龄 9 岁。患者住院天数 0.5 天~74 天,平均 24.18 ± 15.58 天。49 例患者中临床恢复 40 例(占 81.63%),死亡 9 例(占 18.37%)。恢复组中位年龄 9 岁,平均年龄 9.27 ± 3.54 岁,死亡组中位年龄 6 岁,平均年龄 7.22 ± 3.77 岁($P=0.128$)。死亡组生存时间 1 天~10 天,平均 4 天,中位生存时间 2 天,有 3 例患者为入院当天死亡。

2.2 首发临床症状

初诊时以消化道症状(呕吐和/或腹痛)为首发症状 25 例,死亡 1 例;以呼吸道症状(咳嗽/流涕)为首发症状 7 例,死亡 2 例;同时有消化道及呼吸道症状 9 例,死亡 4 例;以胸闷胸痛为主要症状 8 例,死亡 2 例。

2.3 ECG, 24hHolter

49 例患者在疾病初期均存在明显的心电图异常:ST-T 变化 17 例;CRBBB 16 例;III 度房室传导阻滞(III degree atrioventricular block, III. AVB) 14 例;室上性心动过速 11 例;低电压 11 例;室性心律失常 7 例;CLBBB、QTc 延长及异常 Q 波各 6 例。

将患者的 ECG 异常归纳为 4 种类型:(1)全导联广泛 ST 段改变为主,死亡 2/17 例(11.76%);(2)III° AVB,死亡 1/14 例(7.14%);(3)室性心律失常为主,死亡 4/7 例(57.14%);(4)肢导联低电压为主,死亡 2/11 例(18.18%);经恢复组与死亡组间 4 种心电图异常发生率比较,室性心律失常的发生率在两组间存在明显差异($P=0.020$)(见表 1)。

2.4 UCG

49 例患者中 UCG 检查 46 例,3 例死亡患者无 UCG 检查资料。病初左室舒张末内径(left ventricular end diastolic diameter, LVDD)增大 23 例,其中死亡 1 例;LVEF $\geq 60\%$ 15 例,无死亡病例;LVEF 35%~59% 28 例,死亡 4 例;LVEF $<35\%$ 3 例,死亡 2 例。室间隔增厚 10 例,死亡 3 例。心包积液 25 例,死亡 4 例。

LVEF 与 LVFS 死亡组明显低于恢复组,两组组间差异有统计学意义($P=0.006$; $P=0.005$)。初诊时经体表面积标化的 LVDD 和左心房(left atrial, LA)内径,组间差异无统计学意义($P=0.362$; $P=0.900$)。心包积液例数两组之间差异无统计学意义($P=0.946$)(见表 1)。

2.5 血清学检查

恢复组与死亡组间 CK、CKMB、cTnI、NT-proBNP 的峰值比较均无统计学差异($P=0.65$, $P=0.33$, $P=0.51$, $P=0.57$)(见表 1)。急性期分别有 45 例和 43 例患者行血清 CK-MB 及 cTnI 检测,异常检出率分别为 51.11%和 81.39%,两者同时增高占 47.50%。

2.6 CMR

49 例患者中有 10 例(恢复组)患者在急性期(发病 2 周内 8 例,发病 4 周、12 周各 1 例)行 CMR 检查,其中 9 例符合路易斯湖 CMR 心肌炎诊断标准,该 9 例中 4 例于发病后 6 个月~16 个月复查均恢复正常,另 5 例于发病 18 个月首次做 CMR 检查,均未发现异常。

2.7 随访资料

恢复组 40 例,随访 6.0 月~104.0 月,平均随访 19.28 月,中位随访时间 12.33 月。恢复组急性期 LVEF $<60\%$ 25 例,经治疗均恢复正常,恢复至正常的平均时间 10.22 天。

14 例 III° AVB 患者中有 8 例安装临时心脏起搏器,其中 7 例为入院当天安装,1 例为入院第 2 天安装,8 例中有 1 例(12.5%)于安装起搏器后第 2 天出现呼吸、心跳骤停,抢救无效死亡。使用起搏器时间为 2~8 天,平均 4.75 天。49 例患者中接受体外膜肺氧合(extracorporeal membrane oxygenation, ECMO)治疗 4 例。其中有 3 例为入院当天安装 ECMO,1 例为入院后第 2 天安装,死亡 3 例(75%),平均使用 ECMO 时间为 4.5 天,恢复者使用 ECMO 时间为 5 天。安装 ECMO 者死亡原因分别是多脏器功能衰竭、严重心律失常及 ECMO 术并发症(出血)。单因素生存分析发现,与死亡有关的危险因素有:LVEF $<30\%$ 、LVFS $<15\%$ 、室性心律失常($P<0.05$)。年龄 ≤ 6 岁、心源性休克

对预后的影响虽无明显统计意义($P \leq 0.2$),但为了防止遗漏可能影响预后的因素,也将其归入 Cox 比例风险回归模型进行多因素分析。将以上危险因素引入多因素生存分析模型,最终与死亡相关的危险因素为年龄 ≤ 6 岁 (RR40.215,95% CI 1.285-1258.369, $P=0.035$)。(见表 2)。

表 1 恢复组与死亡组检查结果比较

Table 1 Comparison of the results between the recovery group and the death group

	Recovery group [n=40(81.63%)]	Death group [n=9(18.37%)]	P
ECG			
ST-T change	15	2	0.629
Ventricular arrhythmias	3	4	0.020*
III° AVB	13	1	0.382
Low voltage	9	2	1.000
UCG (Surface area standardization)			
LVDD(cm, $\bar{x} \pm s$)	3.59 $\pm$ 0.40	3.21 $\pm$ 0.92	0.362
LA(cm, $\bar{x} \pm s$)	1.99 $\pm$ 0.30	1.96 $\pm$ 0.54	0.900
LVEF(% , $\bar{x} \pm s$)	52.01 $\pm$ 11.14	36.90 $\pm$ 15.49	0.006**
LVFS(% , $\bar{x} \pm s$)	27.09 $\pm$ 7.23	17.61 $\pm$ 7.82	0.005**
Ventricular septal thickening	7	3	0.870
Pericardial effusion	21	4	0.946
Serological detection of myocardium			
CK	1068.72 $\pm$ 3017.56	845.25 $\pm$ 665.67	0.837
CK-MB	70.86 $\pm$ 125.85	171.50 $\pm$ 317.56	0.406
cTnI	7.08 $\pm$ 10.08	18.50 $\pm$ 37.22	0.450
BNP	7208.43 $\pm$ 6815.89	6537.67 $\pm$ 5987.76	0.828

Note: * $P < 0.05$; ** $P < 0.01$.

表 2 49 例爆发性心肌炎患者生存分析

Table 2 Survival analysis of patients with fulminant myocarditis in 49 cases

Variable	Single factor survival analysis		Multivariate survival analysis	
	RR(95%CI)	P	RR(95%CI)	P
Gender	0.660(0.177-2.460)	0.536		
Age ≤ 6 y	3.582(0.958-13.388)	0.058	40.215(1.285-1258.369)	0.035*
Cardiac shock	0.404(0.101-1.615)	0.200		
LVEF $\geq 30\%$ / $<30\%$	0.133(0.024-0.728)	0.020		
LVFS $\geq 15\%$ / $<15\%$	0.133(0.024-0.728)	0.020		
PE	0.867(0.159-4.734)	0.869		
ST-T change	2.037(0.423-9.810)	0.375		
Ventricular arrhythmias	0.140(0.037-0.528)	0.004		
Low voltage	1.060(0.220-5.103)	0.942		
III° AVB	3.373(0.422-26.977)	0.252		
CK $>500 \mu\text{L}$	0.334(0.080-1.400)	0.134		
CK-MB $>70 \mu\text{L}$	0.470(0.117-1.882)	0.286		
cTnI $\geq 7 \mu\text{L}$	0.784(0.175-3.506)	0.750		
BNP $\geq 5000 \text{ pg/mL}$	0.327(0.038-2.804)	0.308		

Note: * $P < 0.05$.

3 讨论

暴发性心肌炎多以心外症状为首表现,患者如能得到及时诊断、治疗,大于 90%可完全恢复,且并发症的发生率也降到最低^[1]。本文 49 例患者中以消化道或呼吸道症状为首发症状者占 83.67%。早期死亡率 18.37%,均于发病 10 天内死亡,无晚期死亡。未死亡者平均随访 19.28 月,100%临床痊愈,未见演变为扩张型心肌病。

心电图是暴发性心肌炎早期最有价值的诊断方法。本文中患者心电图异常以 ST-T 改变为多数。将心电图异常归类为 4 种类型,发现以室性心律失常为主要心电图变化的患者死亡率较高($P=0.020$)。心律失常可能与心肌细胞缺血、坏死等炎症性改变导致其自律性、和传导性改变有关^[6]。

多项研究表明^[7-10]低 LVEF 值与暴发性心肌炎患者的预后有关。本研究发现死亡组 LVEF 与 LVFS 值明显低于恢复组($P=0.006$, $P=0.005$)。恢复组有 62.5%的患者在病初有 LVEF 下降,随访中所有患者 LVEF 均恢复正常,说明能够度过急性期的暴发性心肌炎患者预后较好。

Gupta 等^[11]认为暴发性心肌炎急性期患者病情不稳定,绝大多数不能进行 CMR 检查,且用 CMR 来区别暴发性心肌炎和急性心肌炎是不可行的。Ryu 等^[12]提出 CMR 中表现的心肌水肿和 LGE 改变能反映暴发性心肌炎心肌病变程度,认为 CMR 在诊断暴发性心肌炎和预后评估中起一定的作用。本研究中 10 例在急性期行 CMR 检查,符合路易斯湖标准的 9 例(占 90%),说明 CMR 诊断急性心肌炎的阳性率较高。

Sachdeva 等^[13]对 58 例心肌炎患儿研究发现,cTnI>1 ng/mL 是患儿预后不良的危险因素之一。Lee 等^[14]对 17 例暴发性心肌炎患儿研究发现,死亡组患者 NT-proBNP 水平明显高于存活组患者,并认为 NT-proBNP 是可预测患儿预后的因素。本研究发现,CK-MB 及 cTnI 的异常检出率分别为 51.11%和 81.39%,说明血清学检测结果并不能作为排除心肌炎的依据。同时,本研究中未发现两组之间 cTnI、NT-proBNP 有差异。

暴发性心肌炎的治疗包括药物治疗和心脏机械辅助治疗^[15]。本研究中所有患者均使用糖皮质激素和丙种球蛋白治疗。多项研究^[16-19]表明采用心脏机械辅助治疗有助于患者度过危险期。Mody 等^[20]提出暴发性心肌炎合并心源性休克时心脏机械辅助治疗应该作为一线的治疗方法,能够有效延长患者的生存时间。本研究中采用 ECMO 治疗 4 例,3 例死亡。ECMO 死亡率考虑主要与 ECMO 术后并发症及多脏器功能衰竭有关。

暴发性心肌炎起病急骤,以心外症状为首发者多见,经及时、有效诊断、治疗的患者有望完全康复。所有患者均存在不同程度心电图异常。多因素生存分析发现年龄 ≤ 6 岁为死亡的危险因素。

本研究属于单中心的回顾性研究,因病例数有限,多因素生存分析结果存在一定局限性。今后拟扩大样本量,进一步完善研究设计。

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