

伴中央颞区棘波的儿童自限性癫痫临床特征及共病分析

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【摘要】目的 总结伴中央颞区棘波的儿童自限性癫痫(SeLECTS)的临床特征及共病注意缺陷多动障碍(ADHD)情况。**方法** 纳入2020年7月至2022年12月华中科技大学同济医学院附属同济医院收治的89例SeLECTS患儿,收集社会人口学资料、临床表现、视频脑电图资料、治疗与预后资料,采用SNAP-IV量表判断是否存在注意缺陷多动障碍。**结果** (1)临床特征:89例SeLECTS患儿男性49例,女性40例;首发年龄平均为(7.22 ± 2.04)岁。发作类型主要为局灶性运动性发作(36例,40.45%)和局灶性进展为双侧强直-阵挛发作(46例,51.69%),7例(7.87%)二者兼具。发作时主要表现为单侧阵挛或双侧强直-阵挛发作、流涎、双眼斜视或上翻、口角或下颌抽动、喉咙发声。(2)脑电图特征:56例患儿视频脑电图背景活动均正常,痫样放电波形主要为尖(棘)波、尖(棘)慢复合波、棘波簇,以及睡眠期癫痫性电持续状态;非快速眼动睡眠期棘波指数为 $33.00(19.25, 53.25)$ 。(3)治疗与预后:37例(41.57%)患儿控制至少6个月无发作,其中23例(25.84%)控制至少12个月无发作。(4)共病情况:44例(49.44%)共病注意缺陷多动障碍。与非ADHD组相比,ADHD组患儿首发年龄较小($t = 1.621, P = 0.002$)、棘波指数($Z = -2.134, P = 0.038$)和癫痫性电持续状态发生率($\chi^2 = 4.308, P = 0.038$)较高。**结论** SeLECTS是具有特征性临床和脑电图特征的儿童自限性癫痫综合征,对于年龄较小、棘波指数较高、存在睡眠期癫痫性电持续状态的患儿,应警惕共病注意缺陷多动障碍。

【关键词】 癫痫,罗兰多; 注意力缺陷障碍伴多动; 共病现象; 脑电描记术

Clinical features and comorbidity of self-limited epilepsy with centrot temporal spikes in children

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【Abstract】Objective To summarize and analyze the clinical features and comorbidity of attention deficit and hyperactive disorder (ADHD) with self-limited epilepsy with centrot temporal spikes (SeLECTS) in children. **Methods** A total of 89 SeLECTS patients diagnosed in Tongji Hospital, Tongji Medical College of Huazhong University of Science and Technology from July 2020 to December 2022 were selected. The social demographic data, clinical manifestation, video electroencephalography (VEEG) results, treatment and prognosis of the children were collected. Swanson, Nolan and Pelham-IV Rating Scale (SNAP-IV) was used to assess the comorbidity of ADHD. **Results** 1) Clinical features: there were 49 males and 40 females in 89 cases of SeLECTS. The age of onset was 3–12 years old, with an average of (7.22 ± 2.04) years old. The main seizure forms were motor seizures of focal origin (36 cases, 40.45%) and focal progression to bilateral tonic-clonic seizures (46 cases, 51.69%), and 7 cases (7.87%) had both. Main manifestations were unilateral clonic or tonic-clonic seizures, drooling, strabismus or upward movement of eyes, abnormal oral movement, and throat vocalization. 2) EEG characteristics: background activity of VEEG of 56 patients was

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normal, and epileptiform discharge waveforms were mainly sharp (spike) waves, sharp (spike) slow waves complex, spike clusters, and electrical status epilepticus during sleep (ESES). Spike wave index (SWI) during slow wave sleep was 33.00 (19.25, 53.25). 3) Treatment and prognosis: 37 cases (41.57%) were seizure-free at least 6 months, and 23 cases (25.84%) were seizure-free at least 12 months. 4) Comorbidity: 44 patients (49.44%) had comorbid ADHD. Compared with the non-ADHD group, the ADHD group had a younger age of onset ($t = 1.621, P = 0.002$), a higher SWI ($Z = -2.134, P = 0.038$) and a higher incidence of ESES ($\chi^2 = 4.308, P = 0.038$). **Conclusions** SeLECTS is a self-limited epilepsy syndrome in children with characteristic clinical and electroencephalographic features. For children with younger age, higher SWI and ESES, comorbid ADHD should be considered.

【Key words】 Epilepsy, Rolandic; Attention deficit disorder with hyperactivity; Comorbidity; Electroencephalography

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伴中央颞区棘波的儿童自限性癫痫(SeLECTS)是临床最常见的儿童癫痫综合征,占儿童癫痫的13%~23%^[1],男女比例约1.50:1^[2]。SeLECTS发病高峰年龄为7~8岁,通常于16岁前癫痫发作完全缓解且不遗留神经功能缺损,预后良好^[3]。然而,越来越多研究表明,SeLECTS患儿病程中易共病学习障碍、注意缺陷多动障碍(ADHD)、言语障碍、记忆力下降、偏头痛等,且即使癫痫发作完全缓解后上述共病仍可对患儿学习和生活产生不良影响,提示临床医师关注SeLECTS疾病特征的同时,还应关注疾病共病并尽早干预。本研究回顾总结89例SeLECTS患儿的临床和脑电图特征,并着重筛查注意缺陷多动障碍共病情况,以为SeLECTS的规范诊断及共病的早期发现提供临床依据。

对象与方法

一、观察对象

选择2020年7月至2022年12月在华中科技大学同济医学院附属同济医院门诊或住院治疗的SeLECTS患儿89例。SeLECTS的诊断符合2022年国际抗癫痫联盟(ILAE)推荐的癫痫和癫痫综合征分类中SeLECTS诊断标准^[4];年龄3~12岁;临床资料完整;无颞叶癫痫等其他类型癫痫,意识障碍及精神疾病病史;患儿父母或其他监护人对本研究知情同意并签署知情同意书;本研究经华中科技大学同济医学院附属同济医院道德伦理委员会审核批准(审批号:TJ-IRB20230387)。

二、研究方法

1. 临床资料采集 (1)一般资料:社会人口学资料(性别、年龄),既往史(高热惊厥史)和家族史(癫痫、偏头痛家族史)。(2)癫痫发作特征:根据患儿或家属回忆,记录发作时间、发作类型、发作表现、发作频率、持续时间。(3)脑电图特征:记录痫样放电部位、侧别、同步性,以及非快速眼动睡眠期(NREM)棘波指数(SWI)特征及特殊波形。(4)治疗及预后资料:抗癫痫发作药物(ASM)应用情况(药物种类、名称、剂量等),并追踪随访以记录癫痫发作情况。

2. 注意缺陷多动障碍的评价 采用SNAP-IV量表^[5](Swanson, Nolan and Pelham-IV Rating Scale)评估注意缺陷多动障碍,包括注意力缺陷和多动-冲动障碍两个维度共18项,每项根据相关表现发作频率分为0~3分,总评分为各项评分相加后除以18,评分≥1.60分为存在注意缺陷多动障碍;评分为1.10~1.50分且满足所有项目中至少5项为中度或重度,方可明确为存在注意缺陷多动障碍。

3. 统计分析方法 采用SPSS 22.0统计软件进行数据处理与分析。计数资料以相对数构成比(%)或率(%)表示,采用 χ^2 检验。正态性检验采用Shapiro-Wilk检验,呈正态分布的计量资料以均数±标准差($\bar{x} \pm s$)表示,采用两独立样本的t检验;呈非正态分布的计量资料以中位数和四分位数间距[$M(P_{25}, P_{75})$]表示,采用Mann-Whitney U检验。以 $P \leq 0.05$ 为差异具有统计学意义。

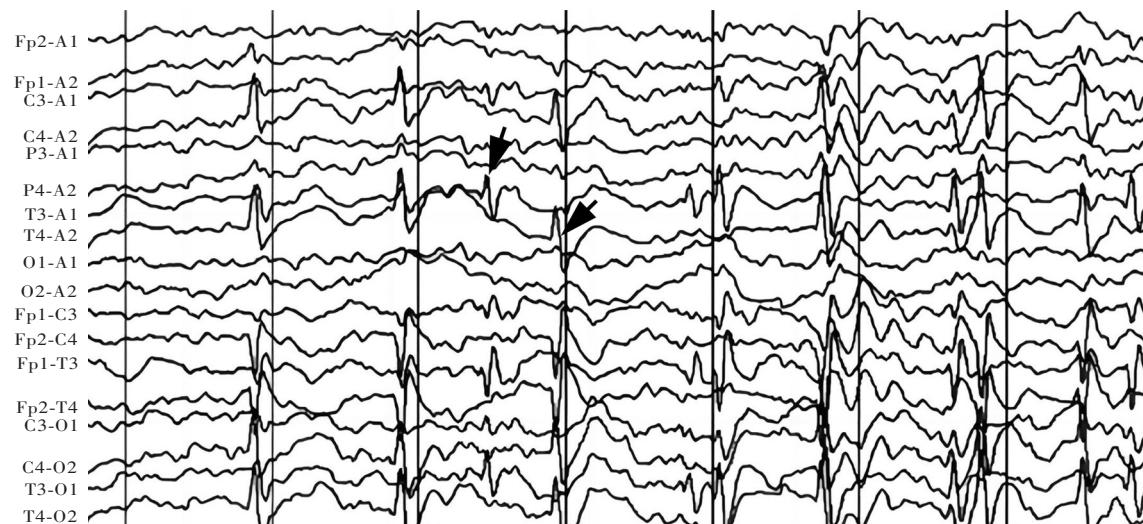


图1 女性SeLECTS患儿,9岁,视频脑电图可见发作间期背景活动正常,双侧颞区高波幅尖波,且左侧与右侧不同步(箭头所示)

Figure 1 A 9-year-old girl diagnosed with SeLECTS showed normal interictal background activity with asynchronous high-amplitude sharp waves in the bilateral temporal region (arrows indicate).

结 果

一、临床特征

1.一般资料 本组89例患儿,男性49例,女性40例;年龄4~12岁,平均(7.72 ± 2.36)岁;首发年龄3~12岁,平均(7.22 ± 2.04)岁, ≤ 6 岁32例(35.96%)、 >6 ~10岁者47例(52.81%)、 >10 ~12岁者10例(11.24%);既往有高热惊厥史11例(12.36%);有癫痫家族史13例(14.61%),偏头痛家族史21例(23.60%)。

2.癫痫发作特征 (1)发作时间:于夜晚入睡后1 h内发作66例(74.16%),清晨觉醒前1~2 h发作15例(16.85%),午休时发作8例(8.99%);(2)发作类型:36例(40.45%)为局灶性运动性发作,46例(51.69%)为局灶性进展为双侧强直-阵挛发作(FBTCS),7例(7.87%)二者兼具;(3)发作表现:主要表现为单侧阵挛或双侧强直-阵挛发作74例次(83.15%),流涎65例次(73.03%),双眼斜视或上翻54例次(60.67%),口角或下颌抽动49例次(55.06%),喉咙发声19例次(21.35%);(4)发作频率:近1年发作频率0~40次,中位数2(1,3)次,发作频率 ≤ 1 次者36例(40.45%)、 >1 ~ <5 次者46例(51.69%)、 ≥ 5 次者7例(7.87%);(5)持续时间:发作持续时间10 s至30 min,发作时间 ≤ 1 min 33例(37.08%), >1 ~5 min 48例(53.93%), >5 min者8例

(8.99%)。

二、脑电图特征

1.基本特征 (1)放电部位:89例患儿发作间期背景活动均正常,痫样放电位于中央颞区83例(93.26%),中央颞区以外区域6例(6.74%);(2)放电侧别:双侧放电43例(48.31%),单侧放电46例(51.69%),其中左侧放电27例(58.70%)、右侧放电19例(41.30%);(3)放电同步性:42例(47.19%)脑电图存在不同步放电(图1)。

2.非快速眼动睡眠期棘波指数及特殊波形

共采集到56例干扰小、波形清晰的视频脑电图(VEEG),用于分析非快速眼动睡眠期SWI指数特征及特殊波形。结果显示,痫样放电波形主要为尖(棘)波(100%,56/56)、尖(棘)慢复合波(76.79%,43/56)、棘波簇(37.50%,21/56;图2),及睡眠期癫痫性电持续状态(ESES;37.50%,21/56;图3)等。56例患儿非快速眼动睡眠期SWI指数为4.00~79.25,中位数为33.00(19.25,53.25)。

三、治疗及预后

本组89例患儿均予以抗癫痫发作药物,76例(85.39%)单药治疗,分别为丙戊酸27例(35.53%)、奥卡西平23例(30.26%)、拉科酰胺15例(19.74%)、左乙拉西坦11例(14.47%);余13例(14.61%)予以两种或以上药物联合治疗,其中5例奥卡西平+丙戊酸、4例拉莫三嗪+丙戊酸、2例左乙拉西坦+丙



图2 男性SeLECTS患儿,9岁,视频脑电图可见发作间期背景活动正常,右侧中央颞区棘波簇(箭头所示)

Figure 2 A 9-year-old boy diagnosed with SeLECTS showed normal interictal background activity with clusters of spikes in the right central temporal region (arrow indicates).



图3 男性SeLECTS患儿,8岁,视频脑电图记录一次ESES过程:发作间期背景活动正常,左侧颞顶区频繁高波幅尖波(箭头所示)

Figure 3 A 8-year-old boy diagnosed with SeLECTS showed normal interictal background activity with ESES phenomenon recorded by VEEG, which presented frequently occurred high-amplitude spikes in the left temporal and parietal regions (arrows indicate).

戊酸、1例拉莫三嗪+吡仑帕奈+丙戊酸、1例丙戊酸+托吡酯+左乙拉西坦。本组患者随访6~12个月,中位时间9(6,12)个月,无癫痫发作时间<6个月者52例(58.43%),6~12个月14例(15.73%),>12个月23例(25.84%)。

四、共病情况

本组89例患儿均完成SNAP-IV量表评估,44例

(49.44%)存在注意缺陷多动障碍(ADHD组),单纯表现为注意力缺陷者20例(45.45%),单纯表现为多动-冲动障碍6例(13.64%),二者兼具18例(40.91%);其余45例无注意缺陷多动障碍(非ADHD组)。与非ADHD组相比,ADHD组患儿首发年龄较小($P=0.002$),SWI指数($P=0.038$)和ESES发生率($P=0.038$)较高,其余指标组间差异无统计学意义。

观察指标	非ADHD组 (n=45)	ADHD组 (n=44)	统计量值	P值
性别[例(%)]			0.899	0.343
男性	27(60.00)	22(50.00)		
女性	18(40.00)	22(50.00)		
首发年龄($\bar{x} \pm s$,岁)	7.86±1.80	6.57±2.07	1.621	0.002
高热惊厥史[例(%)]	5(11.11)	6(13.64)	0.131	0.717
癫痫家族史[例(%)]	6(13.33)	7(15.91)	0.118	0.731
偏头痛家族史[例(%)]	7(15.56)	14(31.82)	3.264	0.071
发作频率 [M(P ₂₅ ,P ₇₅),次/年]	2.00 (0.00, 3.00)	2.00 (1.00, 4.00)	-1.928	0.054
持续时间 [M(P ₂₅ ,P ₇₅),min]	90.00 (60.00,150.00)	120.00 (60.00,180.00)	-1.537	0.124
脑电图特征	26	30		
尖(棘)慢复合波 [例(%)]	21(80.77)	22(73.33)	0.432	0.511
棘波簇[例(%)]	11(42.30)	10(33.33)	0.479	0.489
ESES发生率[例(%)]	6(23.08)	15(50.00)	4.308	0.038
SWI指数 [M(P ₂₅ ,P ₇₅),%]	25.50 (16.67, 48.69)	44.50 (27.25, 55.58)	-2.134	0.038
丙戊酸[例(%)]	16(35.56)	11(25.00)	1.173	0.279
奥卡西平[例(%)]	11(24.44)	12(27.27)	0.093	0.761
联合用药[例(%)]	4(8.89)	9(20.45)	2.386	0.122

Two - independent - sample t test for comparison of age of onset, Mann-Whitney U test for comparison of seizure frequency, seizure duration and SWI, and χ^2 test for comparison of others,首发年龄的比较采用两独立样本的t检验,发作频率、持续时间和SWI指数的比较采用Mann-Whitney U检验,其余各项指标的比较采用 χ^2 检验。ADHD, attention deficit and hyperactive disorder,注意缺陷多动障碍;ESES, electrical status epilepticus during sleep,睡眠期癫痫性电持续状态;SWI, spike wave index,棘波指数

学意义(均 $P > 0.05$, 表1)。因发作时间、发作类型及发作表现主观性较大,未进行统计分析。

讨 论

SeLECTS既往称为儿童良性癫痫伴中央颞部棘波(BECCCT),又称为儿童良性Rolandic癫痫,是儿童自限性癫痫的最常见类型。1989和2001年,国际抗癫痫联盟均将其归为特发性儿童局灶性癫痫^[6],2017年将其归为自限性局灶性癫痫^[4],至2022年,国际抗癫痫联盟将其更名为“伴中央颞区棘波的儿童自限性癫痫”,并归为儿童自限性癫痫综合征^[4]。目前,SeLECTS病因尚不明确,部分学者认为该病是一种常染色体显性遗传性年龄依赖性疾病^[7],更多学者则认为其是多基因突变所致^[4,8]。业已证实,GRIN2A、ELP4基因与SeLECTS的发生发展及预后

不良相关^[9]。此外,SeLECTS患儿既往史、围生期通常无异常,但有6.5%~13.0%的患儿有高热惊厥史,13%患儿有癫痫家族史^[9],进一步证实SeLECTS可能系遗传所致。本研究有11例(12.36%)首次发作前有高热惊厥史,13例(14.61%)有明确癫痫家族史,与上述研究基本一致。此外,偏头痛亦与SeLECTS及其他癫痫综合征相关^[10]。本研究21例(23.60%)有偏头痛家族史,但因纳入患儿年龄偏小,对偏头痛的症状无法准确描述,因此未记录共病偏头痛情况。

SeLECTS发作类型主要为局灶性发作,且具有特征性表现,78.60%患儿自口面部开始抽动或伴单侧阵挛,43.10%患儿呈双侧强直-阵挛发作,24.20%患儿发作过程中出现喉部发声,年龄稍大患儿可在发作后向家长描述口咽部感觉异常、言语障碍、面部不适等^[3,11]。在本研究中,SeLECTS患儿发作表现主要为单侧阵挛或双侧强直-阵挛(83.15%, 74/89),65例(73.03%)患儿发作时伴流涎,亦可见面部抽搐、双眼斜视或上翻,较少表现为喉部发声。除上述典型发作表现外,SeLECTS患儿发作时还可出现情感障碍(惊恐、自主神经功能紊乱和轻度意识障碍)、发作后Todd麻痹(TP)、癫痫持续状态(SE)、负性肌阵挛、局灶性感觉运动性发作、睡眠期局灶性强直性肌张力障碍发作^[9]。本研究有8例(8.99%)患儿发作持续时间超过5分钟,可以判定为癫痫持续状态;未见其他异常临床表现,可能与患儿多在夜间睡眠中发作,部分异常表现被忽视和误认有关。

脑电图是诊断SeLECTS的重要依据,患儿清醒和睡眠时脑电图背景活动正常;波形主要包括尖波、棘波、尖慢复合波和棘慢复合波^[12],通常表现为高波幅双相或三相尖波,有时伴后发慢波^[13]。典型特征为痫样放电分布于中央颞区^[14],90%以上SeLECTS患儿存在中央颞区痫样放电^[15];本研究中央颞区痫样放电比例高达93.26%(83/89)。痫样放电可见于清醒时,困倦和浅睡眠时明显增多^[16];可单侧,也可双侧,多局限于中央颞区,也可向额区、枕区、顶区扩散,约75%患者显示单侧放电,25%为双侧放电,可呈同步或非同步放电^[17],本研究也得出相似结论。注意力功能系前额皮质神经回路及其连接介导的一组认知过程^[18]。Deltour等^[19]发现,右侧大脑半球癫痫发作间期痫样放电可以引起持续性注意力功能损害,但Ay等^[20]在16例6~14岁

SeLECTS儿童队列中未发现注意缺陷多动障碍与癫痫灶单侧或双侧放电之间存在相关性。可能是由于脑部异常痫样放电并不局限于某一个脑区,而是可以沿一条或多条神经回路扩散至其他脑区,甚至波及至对侧大脑半球。

ESES是一种年龄依赖性和自限性癫痫综合征,其特征为非快速眼动睡眠期持续性弥漫性棘波,伴或不伴临床发作,可能与认知功能障碍和精神行为异常有关^[21],SWI指数≥85%是较公认的ESES诊断标准,亦有学者提出不同标准,如SWI指数≥90%、85%、60%、50%等^[22]。本研究有35.71%(20/56)患儿SWI指数≥50%,较Beydoun等^[23]报告的14.6%稍高,在共病注意缺陷多动障碍的患儿中这一比例升至50%(15/30),与非ADHD组患儿相比,ADHD组患儿ESES发生率较高。Massa等^[24]认为,ESES发生率较高可能是SeLECTS共病注意缺陷多动障碍的相关危险因素。本研究并未选择较公认的SWI指数≥85%诊断标准,主要考虑以SWI指数≥50%作为ESES诊断标准有助于SeLECTS共病的早期诊断与管理,诊断标准过高致阴性结果可能导致临床医师忽视注意缺陷多动障碍的诊断。

既往认为,约90%的SeLECTS患儿12~15岁可终止发作,预后良好,远期随访患儿智力基本不受影响,不存在明显学习、记忆障碍等^[3]。但近年发现,SeLECTS患儿与健康同龄儿童相比,存在学习、记忆力下降,突出表现为语言表达、读写能力、视空间能力、拼写计算力等功能下降,有1/4患儿共病注意缺陷多动障碍^[25]。本研究结果显示,合并注意缺陷多动障碍的SeLECTS患儿占49.44%(44/89),较Huang等^[26]报告的24.58%(29/118)稍高,可能与本研究采用SNAP-IV量表家长版评估时家长对患儿过度关注有关,可以进行多次评估以校正结果。引起共病的机制可能与神经元异常电活动破坏神经网络功能和发育有关^[27]。研究显示,首发年龄较早(<6岁)患儿共病注意缺陷多动障碍的比例高于首发年龄较晚患儿^[25]。本研究ADHD组患儿首发年龄亦较小,与上述研究结果相一致。亦有研究显示,中央颞区棘波放电频率增加可使共病注意缺陷多动障碍及言语障碍比例增加^[17],本研究ADHD组与非ADHD组棘波簇(2~3个连续出现的棘波)无明显差异,可能与样本量较小有关。另有研究表明,共病可能与抗癫痫发作药物初始不良反应相关^[28]。本研究应用拉科酰胺及左乙拉西坦的患儿较少,故

未进行深入对比,但未发现丙戊酸、奥卡西平或联合用药在注意缺陷多动障碍患儿之间存在统计学差异,可能与丙戊酸、奥卡西平相对安全、疗效较好、应用剂量较小有关,且所纳入患儿均未应用对注意力和认知功能影响较大的苯巴比妥类药物。提示临床医师应规范应用抗癫痫发作药物,可以有效减少发作间期痫样放电并控制临床发作,降低SeLECTS患儿共病注意缺陷多动障碍的风险^[29]。

综上所述,SeLECTS是具有特征性临床和脑电图特征的儿童自限性癫痫综合征,对于年龄较小、SWI指数较高、存在ESES的患儿,应警惕其共病注意缺陷多动障碍,早期干预,改善预后。

利益冲突 无

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下期内容预告 本刊2023年第6期报道专题为神经重症医学,重点内容包括:神经外科重症医学规范化诊断与治疗;大剂量舒巴坦治疗神经外科重症患者鲍曼不动杆菌感染专家共识;神经重症目标温度管理研究进展;继发性脑积水发病机制及研究进展;第二代测序技术在重症神经系统感染中应用进展;重症结核性脑膜炎预后影响因素分析;重型颅脑创伤患者颅内感染影响因素分析及风险预测模型建立;脑电双频指数和颅内压监测与自发性脑出血患者预后相关分析;直视下经皮气管切开术在神经重症患者中的应用;长程皮下通道脑室外引流术在神经外科应用探讨;抗CD38单抗达雷妥尤单抗治疗重症抗N-甲基-D-天冬氨酸受体脑炎一例