

选择性脊神经后根切断术在单纯型遗传性痉挛性截瘫相关下肢痉挛中的应用

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【摘要】目的 探讨选择性脊神经后根切断术治疗单纯型遗传性痉挛性截瘫相关下肢痉挛的有效性和安全性。**方法** 纳入 2021 年 1 月至 2023 年 2 月在华中科技大学同济医学院附属协和医院行选择性脊神经后根切断术的 9 例单纯型遗传性痉挛性截瘫患者, 评价手术前后髋内收肌、股四头肌、小腿三头肌和胭绳肌肌张力[Ashworth 量表(AS)], 股角、胭窝角和足背屈角角度, 下肢粗大运动功能[粗大运动功能分级系统(GMFCS)], 并记录术后并发症。**结果** 共 9 例患者均顺利完成手术, 术后均未发生严重并发症。手术前后髋内收肌($F = 43.568, P = 0.000$)、股四头肌($F = 43.000, P = 0.000$)、小腿三头肌($F = 59.200, P = 0.000$)和胭绳肌($F = 116.138, P = 0.000$)AS 评分差异有统计学意义, 其中术后 1 d 和 12 个月髋内收肌($P = 0.000, 0.000$)、股四头肌($P = 0.000, 0.000$)、小腿三头肌($P = 0.000, 0.000$)和胭绳肌($P = 0.000, 0.000$)AS 评分低于术前。与术前相比, 术后 5 d 股角($t = -17.812, P = 0.000$)和胭窝角($t = -12.791, P = 0.000$)增大, 足背屈角缩小($t = 14.050, P = 0.000$)。术前与术后 12 个月 GMFCS 评分差异无统计学意义($t = 1.000, P = 0.347$)。**结论** 对于处于稳定期的单纯型遗传性痉挛性截瘫患者, 选择性脊神经后根切断术可以作为缓解下肢痉挛的一种安全、有效方法。

【关键词】 痉挛性截瘫, 遗传性; 痉挛; 下肢; 脊神经根切断术; 神经电生理监测

Selective posterior rhizotomy for the treatment of pure hereditary spastic paraplegia-associated lower limb spasticity

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【Abstract】Objective To evaluate the efficacy and safety of selective posterior rhizotomy (SPR) for the treatment of pure hereditary spastic paraplegia (PHSP)-associated lower limb spasticity. **Methods** Nine patients with PHSP were admitted to Union Hospital, Tongji Medical College, Huazhong University of Science and Technology from January 2021 to February 2023. The Ashworth Scale (AS) score of hip adductors, quadriceps femoris, triceps surae and hamstring, femoral angle, popliteal fossa angle and dorsiflexion angle of foot, and Gross Motor Function Classification System (GMFCS) score before and after surgery were analyzed. Postoperative complications were recorded. **Results** All 9 patients completed SPR. No serious complication was observed. The AS score before and after surgery were significantly different of hip adductors ($F = 43.568, P = 0.000$), quadriceps femoris ($F = 43.000, P = 0.000$), triceps surae ($F = 59.200, P = 0.000$) and hamstring ($F = 116.138, P = 0.000$). The AS score of hip adductors ($P = 0.000, 0.000$), quadriceps femoris ($P = 0.000, 0.000$), triceps surae ($P = 0.000, 0.000$) and hamstring ($P = 0.000, 0.000$) 1 d and 12 months after surgery were significantly decreased comparing with those before surgery. The femoral angle ($t = -17.812, P = 0.000$) and popliteal angle ($t = -12.791, P = 0.000$) 5 d after the surgery were significantly increased comparing with those before surgery, while the dorsiflexion angle of foot 5 d after surgery was significantly decreased comparing with that before surgery ($t = 14.050, P = 0.000$). The GMFCS score before and 12 months after surgery were no significantly different ($t = 1.000, P = 0.347$). **Conclusions** SPR has good efficacy and safety for the treatment of PHSP-associated lower limb spasticity.

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【Key words】 Spastic paraplegia, hereditary; Spasm; Lower extremity; Rhizotomy; Neurophysiological monitoring

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遗传性痉挛性截瘫(HSP)亦称Stompell-Lorrain病,是一组具有高度遗传异质性的单基因遗传病,根据遗传方式分为常染色体显性遗传、常染色体隐性遗传和X连锁隐性遗传^[1]。目前已发现致病基因80余种,通过神经系统炎症^[2-3]、脂质代谢障碍、细胞器功能障碍、髓鞘形成障碍、轴浆运输障碍等机制导致皮质脊髓束、脊髓后柱细胞等退行性变,临床表现为进行性双下肢痉挛、僵硬、肌力下降、腱反射亢进等^[4-6]。除膀胱功能障碍外,根据是否伴共济失调、震颤、癫痫发作、视神经萎缩、肌萎缩、构音障碍等神经功能障碍可分为单纯型和复杂型^[7]。遗传性痉挛性截瘫发病率为(1~5)/10万^[8-9],于2018年5月纳入我国《第一批罕见病目录》,常见的常染色体显性遗传基因型为SPG4型、常染色体隐性遗传基因型为SPG11型^[10]。治疗方面尚无有效方法,根据不同基因型病理生理学特点设计的药物和基因治疗正在研发中。目前以药物治疗和康复治疗为主,因疾病导致的下肢痉挛严重影响患者日常生活,药物和康复治疗效果欠佳^[11],部分患者采取选择性脊神经后根切断术(SPR)缓解下肢痉挛,但疾病较罕见,手术经验报道有限。本研究以近3年在华中科技大学同济医学院附属协和医院行选择性脊神经后根切断术的单纯型遗传性痉挛性截瘫(PHSP)患者为研究对象,对比手术前后下肢肌张力和运动功能变化以评价该术式对下肢痉挛的改善作用及其安全性。

对象与方法

一、研究对象

1. 纳入标准 (1)符合单纯型遗传性痉挛性截瘫的诊断标准,临床表现为进行性双下肢无力、肌张力增高,排除其他原因,并检出相关致病基因^[12]。(2)年龄≥18岁。(3)Ashworth量表(AS)评分≥3分。(4)病程>2年。(5)近1年无明显下肢肌力下降或肌张力增高。(6)粗大运动功能分级系统(GMFCS)<Ⅲ级。(7)头部和脊髓MRI未见中枢神经系统占位性病变及脑积水、脊髓拴系、脊髓空洞、脊柱不稳、

脊柱畸形等。(8)随访时间>12个月。(9)本研究经华中科技大学同济医学院附属协和医院伦理委员会审核批准(审批号:UHCT-IEC-SOP-016-03-01)。(10)所有患者及其家属均对手术方案和手术风险知情并签署知情同意书。

2. 排除标准 (1)存在上肢肌力和肌张力异常。(2)合并除痉挛性截瘫和膀胱功能障碍外的其他神经功能缺损,如共济失调、震颤、癫痫发作、视神经萎缩、肌萎缩、构音障碍等。(3)智力障碍。(4)合并其他脏器疾病。(5)临床资料不完整。

3. 一般资料 选择2021年1月至2023年2月在我院神经外科行选择性脊神经后根切断术的单纯型遗传性痉挛性截瘫患者9例,男性8例,女性1例;手术年龄20~58岁,平均为(33.67±13.35)岁;病程3~31年,中位病程12.00(3.00,19.50)年;基因型分别为SPG4型5例,SPG11型1例,SPG15型1例,SPG5型1例,REEP型1例。

二、研究方法

1. 选择性脊神经后根切断术 患者仰卧位,参照文献[13]方法,安置双下肢前侧肌电图监测电极,再改为俯卧位,安置双下肢后侧电极,共16对(双侧髓内收肌、股直肌、半膜肌、胫骨前肌、腓肠肌外侧头、腓骨长肌、腓肠肌内侧头、肛门括约肌;图1a,1b)。手术取俯卧位,气管插管全身麻醉,术中先行X线透视定位,以L₂和L₅对应皮肤作为手术切口,采取后正中入路,切开椎板前再行X线透视定位,限制性切除L₂和L₅椎板并保留双侧关节突和椎板峡部,保留L₃和L₄后柱结构,切开硬脊膜,显露双侧L₂、L₃、L₅和S₁神经根(图1c~1e)。术中根据解剖位置和电生理监测鉴别脊神经前根与后根,将后根分为3~5束神经小束,采用肖波教授团队提出的选择性脊神经后根切断术中电生理监测方案^[13]判定所刺激的神经小束是否为责任神经小束,切断责任神经小束50%或75%,常规水密缝合硬脊膜,还纳L₂和L₅椎板,逐层缝合。患者术后卧床3d,可翻身侧卧;3d后可起床和离床活动,并开始规范化康复训练。

2. 疗效及安全性评价 (1)疗效:包括下肢主要

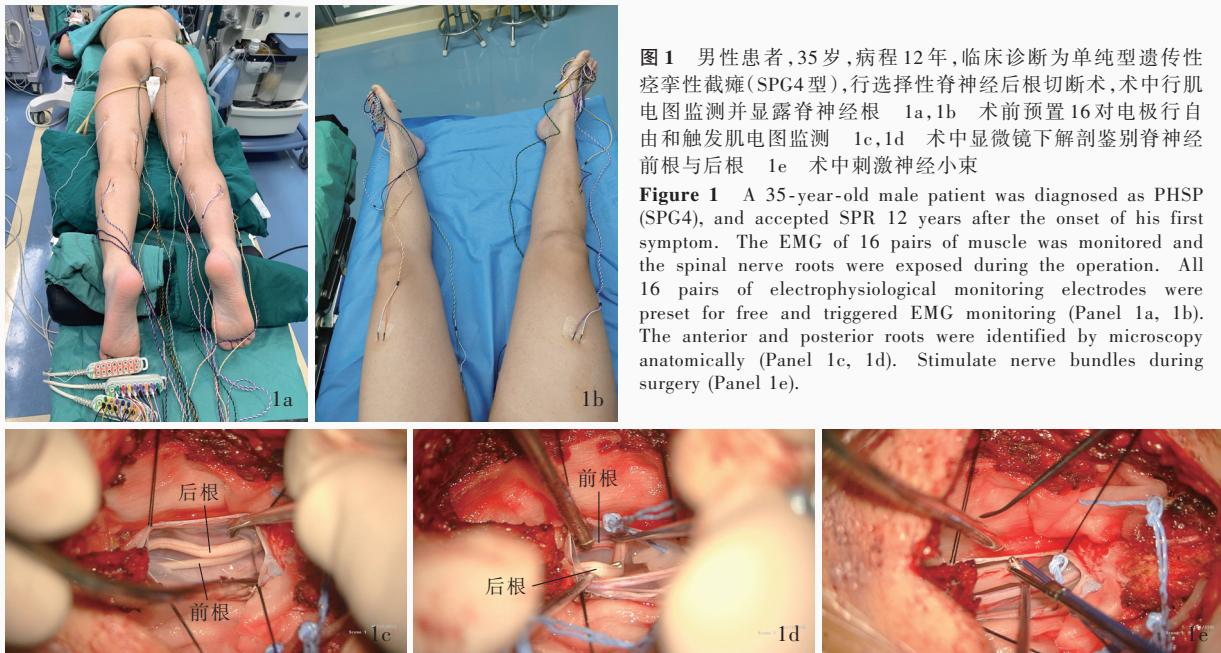


图 1 男性患者,35岁,病程12年,临床诊断为单纯型遗传性痉挛性截瘫(SPG4型),行选择性脊神经后根切断术,术中行肌电图监测并显露脊神经根 1a,1b 术中预置16对电极行自由和触发肌电图监测 1c,1d 术中显微镜下解剖鉴别脊神经前根与后根 1e 术中刺激神经小束

Figure 1 A 35-year-old male patient was diagnosed as PHSP (SPG4), and accepted SPR 12 years after the onset of his first symptom. The EMG of 16 pairs of muscle was monitored and the spinal nerve roots were exposed during the operation. All 16 pairs of electrophysiological monitoring electrodes were preset for free and triggered EMG monitoring (Panel 1a, 1b). The anterior and posterior roots were identified by microscopy anatomically (Panel 1c, 1d). Stimulate nerve bundles during surgery (Panel 1e).

肌群肌张力、关节角度和粗大运动功能。①肌张力,分别于术前、术后1 d 和12个月采用AS量表评价髋内收肌、股四头肌、小腿三头肌和腘绳肌肌张力,分为1~5级,1级,1分,肌张力正常;2级,2分,肌张力轻度增高;3级,3分,肌张力中度增高,受累关节较易被动屈伸;4级,4分,肌张力明显增高,受累关节被动活动困难;5级,5分,受累关节固定、僵直。②关节角度,分别于术前和术后5 d 记录股角、腘窝角和足背屈角角度。③粗大运动功能,分别于术前和术后12个月采用GMFCS分级系统评价粗大运动功能,分为I~V级,I级,1分,行走不受限,但完成更高级运动技巧受限;II级,2分,行走无需移动器械辅助,但在室外和社区内行走受限;III级,3分,可在移动器械辅助下行走,室外和社区内行走受限;IV级,4分,自身移动受限,被转运或室外和社区行走时需移动器械辅助;V级,5分,即使应用移动器械辅助,自身移动仍严重受限。(2)安全性:记录术后切口感染、脑脊液漏、新发或加重的大小便困难或失禁、下肢麻木无力等并发症发生率。

3. 统计分析方法 采用SPSS 27.0统计软件进行数据处理与分析。呈正态分布的计量资料以均数±标准差($\bar{x} \pm s$)表示,手术前后下肢主要肌群肌张力AS评分的比较采用随机区组设计的方差分析,两两比较行LSD-t检验;手术前后各关节角度和GMFCS评分的比较采用配对t检验。以 $P \leq 0.05$ 为

差异具有统计学意义。

结 果

本组9例患者均顺利完成选择性脊神经后根切断术。术后无切口感染、脑脊液漏、新发或加重的大小便困难或失禁以及下肢麻木等并发症,2例术后即刻出现下肢肌力下降,3~4周后恢复至术前肌力;1例术后12个月病情进展,下肢痉挛复发。手术前后髋内收肌($P = 0.000$)、股四头肌($P = 0.000$)、小腿三头肌($P = 0.000$)和腘绳肌($P = 0.000$)AS评分差异有统计学意义(表1,2),与术前相比,术后1 d 和12个月髋内收肌($P = 0.000, 0.000$)、股四头肌($P = 0.000, 0.000$)、小腿三头肌($P = 0.000, 0.000$)和腘绳肌($P = 0.000, 0.000$)AS评分均减少,而术后1 d 与术后12个月髋内收肌($P = 0.432$)、股四头肌($P = 0.238$)、小腿三头肌($P = 0.384$)和腘绳肌($P = 0.529$)AS评分差异无统计学意义。与术前相比,术后5 d 股角($P = 0.000$)和腘窝角($P = 0.000$)增大,足背屈角缩小($P = 0.000$),而术前与术后12个月GMFCS评分差异无统计学意义($P = 0.347$,表3)。

讨 论

遗传性痉挛性截瘫的罕见性、遗传异质性、致病基因多样性、病理生理学机制复杂性均导致其治疗具有挑战性。疾病初期常表现为下肢僵硬,患者

表1 单纯型遗传性痉挛性截瘫患者手术前后下肢主要肌群AS评分的比较($n=9, \bar{x} \pm s$, 评分)

Table 1. Comparison of AS score of the lower limbs muscles before and after SPR in PHSP patients ($n=9, \bar{x} \pm s$, score)

检测项目	术前	术后1 d	术后12个月
髋内收肌	3.56 ± 0.53	1.22 ± 0.44	1.44 ± 0.73
股四头肌	3.56 ± 0.53	1.22 ± 0.44	1.56 ± 0.73
小腿三头肌	3.44 ± 0.53	1.00 ± 0.00	1.22 ± 0.67
胭绳肌	3.33 ± 0.50	1.00 ± 0.00	1.11 ± 0.33

表2 单纯型遗传性痉挛性截瘫患者手术前后下肢主要肌群AS评分的随机区组设计的方差分析表

Table 2. Variance analysis of randomized block design data on AS score of the lower limbs muscles before and after SPR in PHSP patients

变异来源	SS	df	MS	F值	P值
髋内收肌					
处理	29.852	2	14.926	43.568	0.000
区组	2.519	8	0.315	0.919	0.526
误差	5.481	16	0.343		
总变异	154.000	26			
股四头肌					
处理	28.667	2	14.333	43.000	0.000
区组	2.667	8	0.333	1.000	0.473
误差	5.333	16	0.333		
总变异	157.000	26			
小腿三头肌					
处理	32.889	2	16.444	59.200	0.000
区组	1.333	8	0.167	0.600	0.765
误差	4.444	16	0.278		
总变异	135.000	26			
胭绳肌					
处理	31.185	2	15.593	116.138	0.000
区组	0.741	8	0.093	0.690	0.696
误差	2.148	16	0.134		
总变异	123.000	26			

因不适感或害怕跌倒而活动减少,导致肢体废用;随着病程延长,肌力下降和肌肉痉挛进一步导致肌肉关节挛缩,平衡障碍和步态障碍加重^[12,14]。疾病发生和进展无规律,同一家族中相同基因型个体的发病时间可能不同(可发生于婴儿期或成年期),疾病进展速度也不尽相同^[15]。治疗方面主要通过药物治疗、康复训练和外科手术等缓解下肢痉挛状态、改善下肢肌张力,并在神经康复科医师指导下进行拉伸和平衡训练,以维持或改善运动功能,延缓瘫痪进程^[11,16-18]。

表3 单纯型遗传性痉挛性截瘫患者手术前后各关节角度和GMFCS评分的比较($n=9, \bar{x} \pm s$)

Table 3. Comparison of the joint angles and GMFCS score before and after SPR in PHSP patients ($n=9, \bar{x} \pm s$)

检测项目	术前	术后	t值	P值
股角(°)	61.82 ± 3.55	75.56 ± 4.61	-17.812	0.000
胭窝角(°)	112.06 ± 14.46	124.36 ± 11.51	-12.791	0.000
足背屈角(°)	119.01 ± 15.40	112.73 ± 15.56	14.050	0.000
GMFCS(评分)	2.22 ± 0.44	2.11 ± 0.33	1.000	0.347

GMFCS, Gross Motor Function Classification System,粗大运动功能分级系统

选择性脊神经后根切断术是公认的可显著降低脑瘫患者下肢肌张力的有效方法,对上运动神经元损伤如脑卒中、脊髓损伤导致的下肢痉挛也有一定改善作用^[19-20]。目前关于选择性脊神经后根切断术用于遗传性痉挛性截瘫下肢痉挛的报道较少,2014年首都医科大学宣武医院报道4例单纯型遗传性痉挛性截瘫患者行选择性脊神经后根切断术^[21],2016年Sharma等^[22]报告4例儿童期行选择性脊神经后根切断术的单纯型遗传性痉挛性截瘫患儿,2021年Park等^[23]报告37例单纯型遗传性痉挛性截瘫患者行选择性脊神经后根切断术,上述研究表明对于处于稳定期的单纯型遗传性痉挛性截瘫患者,选择性脊神经后根切断术可以有效降低下肢肌张力,且手术安全性较高,未发现其与疾病恶化或进展有明确关系。本研究9例患者均顺利完成选择性脊神经后根切断术,无严重手术相关并发症,手术前后髋内收肌、股四头肌、小腿三头肌和胭绳肌AS评分差异具有统计学意义,术后1天和12个月上述下肢主要肌群AS评分均减少,提示术后下肢肌张力明显改善;术后5天股角和胭窝角增大,足背屈角缩小,提示术后下肢关节活动度明显改善;而手术前后GMFCS评分无明显变化,推测可能与病例数较少、GMFCS评分不够细化或个别患者疾病进展有关,表明选择性脊神经后根切断术治疗单纯型遗传性痉挛性截瘫以缓解下肢痉挛安全、有效。

单纯型遗传性痉挛性截瘫患者可选择的选择性脊神经后根切断术方式不尽相同,包括经典Peacock术式、Park术式和扩大的Park术式,神经切断比例亦不同。本研究9例患者均采用跳跃性限制性椎板切开的Peacock术式,术中监测及肌电判读及神经根切断比例采用肖波教授团队的选择性脊神经后根切断术中电生理监测方案^[13],术中仅切开

L_2 和 L_5 椎板，通过少量切除下位椎板上缘及调整显微镜角度精准定位马尾神经，并在显微镜下根据解剖位置结合电生理监测双重鉴别脊神经前根与后根，神经小束的切断比例根据术前责任肌肉判定、术中肌电图监测及判读，予以保留、切断 50% 或 75%，并还纳椎板以减少对脊柱后柱的影响，有利于患者术后恢复和维持脊柱稳定性。

综上所述，选择性脊神经后根切断术对单纯型遗传性痉挛性截瘫患者下肢痉挛具有明显缓解作用，且未发现明显手术相关并发症及导致病情进展或恶化的证据。因此认为，对于处于稳定期的单纯型遗传性痉挛性截瘫患者，药物和康复治疗效果有限的情况下，选择性脊神经后根切断术可以作为缓解下肢痉挛的有效方法。然而，受限于疾病散发，发病率较低，本研究所纳入病例数较少，随访时间较短，后续将逐步纳入更多病例，并进行多中心随机对照试验，延长随访时间，进一步明确选择性脊神经后根切断术在单纯型遗传性痉挛性截瘫患者中的适用性。

利益冲突 无

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