·综　　述·

无骨折脱位型颈脊髓损伤的病理机制与治疗进展

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【摘要】无骨折脱位型颈脊髓损伤(CSCIWFD)是一种特殊类型的脊髓损伤,在临床中并不少见。病人虽然具有颈脊髓损伤的临床症状,但X线、CT检查却没有骨折脱位等影像学表现,很容易被临床医生误诊,从而影响后续诊疗。本文就CSCIWFD的损伤机制、临床表现、病理生理特点、分型及目前治疗进展进行综述,为临床提供参考,以使CSCIWFD病人可以得到早期准确的诊断,降低漏诊率,早期得到有效的治疗,改善病人的预后。

【关键词】脊髓损伤;无骨折脱位型颈脊髓损伤;发病机制;治疗进展

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Progress in pathological mechanism and treatment of cervical spinal cord iniury without fracture and dislocation

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【**Abstract**】Cervical spinal cord injury without fracture and dislocation (CSCIWFD) is a distinct type of spinal cord injury that is not uncommon in clinic. Although patients with CSCIWFD exhibit clinical symptoms of cervical spinal cord injury, imaging manifestations such as fracture and dislocation are absent on X-ray and CT scans, making it easy for clinicians to misdiagnose the condition, which can impact subsequent diagnosis and treatment. This article provides an overview of the injury mechanism, clinical manifestations, pathophysiological characteristics, classification, and current treatment progress of CSCWFD to serve as a reference for clinical practice. The aim is to enable early accurate diagnosis of CSCWFD patients while reducing missed diagnoses rates so that effective treatment can be administered promptly thereby improving patient prognosis.

【**Key words**】Spinal cord injury; Cervical spinal cord injury without fracture and dislocation; Pathogenesis; Treatment progress

急性脊髓损伤(spinal cord injury,SCI)可导致严重的、永久性感觉、运动和自主神经功能障碍[1]。无骨折脱位型颈脊髓损伤(cervical spinal cord iniury without fracture and dislocation,CSCIWFD)是一种特殊类型的SCI,在临床中并不少见。研究报道,SCI占全身损伤的0.2%~0.5%,而CSCIWFD占SCI的9%~16%[2]。CSCIWFD病人具有颈脊髓损伤的临床症状,但X线、CT检查却没有骨折脱位等影像学表现,又称为无放射影像学异常的SCI[3,4]。CSCIWFD病人很容易被临床医生误诊,从而影响后续诊疗。本文就CSCIWFD的损伤机制、临床表现、病理生理特点、分型及目前治疗进展进行综述,为临床提供参考。

1 发病机制及临床表现

CSCIWFD是一种低能量的颈脊髓损伤,50岁以上病人多见,常见于摔倒、碰伤等轻微损伤,以后伸损伤多见,亦可发生于交通事故伤或高处坠落伤等。损伤机制主要是病人既往存在颈脊髓受压的病理基础,如伴多节段颈椎后纵韧带骨化、多节段颈椎间盘突出或黄韧带肥厚钙化导致继发性椎管狭窄,还有一部分病人存在发育性椎管狭窄,早期并未出现明显颈脊髓压迫症状,未予重视或诊治,但颈髓缓冲空间明显减少,一旦发生颈部外伤,特别是颈椎过伸,极易造成SCI,被认为是CSCIWFD的一个重要机制。另外,老年严重SCI可能与年龄相关的脊髓血管变化有关,导致脊髓缺血、脊髓前角细胞和皮质脊髓束减少[5,6],从而导致感觉、运动及自主神经功能障碍,严重时可伴有脊髓休克及呼吸肌麻痹等。CSCIWFD主要表现为上肢运动神经功能损伤重于下肢,直肠、膀胱功能受累以及损伤平面以下感觉神经功能的障碍,颈脊髓的损伤程度由轻至重依次出现上肢运动功能受累、直肠和膀胱功能受累以及下肢运动神经功能受累。因其X线或CT检查无明显的骨折、脱位,所以在临床上常有误诊或漏诊[7]。此时,MRI检查是极其重要的,不但可以明确是否存在持续的脊髓压迫(如椎间盘退变、血肿、后纵韧带骨化和椎管狭窄),还可以检测在脊柱节段椎旁复合体是否稳定,进而指导临床治疗[8]。虽然静态MRI可以评估椎体前或椎旁出血或水肿、前后纵韧带损伤、创

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伤性椎间盘突出、脊髓压迫及损伤，但不能显示不同颈椎位置的真实病理解剖变化、颈椎在屈伸运动中的后纵韧带和椎间盘的变化，因此，在大多数情况下，静态MRI诊断CSCIWFD的价值有限[9]。Lao等[10]发现动态MRI伸展位发现颈椎间盘突出明显增加。大约16.4%的中立位椎间盘无膨出或膨出<3 mm的病人在伸展时出现≥3 mm的膨出，11.6%的中立位椎间盘膨出3~5 mm的病人在伸展位膨出≥5 mm[11]。最近的研究显示，动态MRI扫描前后美国脊髓损伤协会（American Spinal Injury Association，ASIA）分级和日本矫形外科协会（Japanese Orthopaedic Association，JOA）评分无显著差异，提示动态MRI是一种安全可行的诊断CSCIWFD的技术，可降低误诊率和漏诊率。Liu等[12]通过动态MRI对CSCIWFD病人的颈椎和脊髓进行影像学评估发现，脊髓直径/椎管直径的比值越高是发生颈脊髓压迫症的危险因素。

2 病理生理学特点

CSCIWFD包括原发性损伤和继发性损伤。脊髓本身最初的物理损伤被称为原发性损伤，之后，脊髓发生一系列复杂的生物反应，导致进一步损伤，称为继发性损伤，是损伤从几小时发展到几天甚至几个月的原因[13]。在大多数情况下，继发性损伤更为重要，是防止损伤扩散的治疗靶点[14]。根据脊髓损伤后时间和病理机制，继发性损伤过程可分为几个阶段：急性、亚急性（或中度）和慢性期。急性期是在最初的物理损伤后持续48 h，主要表现为脊髓内血管破裂、出血和由此引起的局部缺血。当微循环中断后，随之而来的病理变化，如离子失调、兴奋毒性、自由基的过量产生和炎症反应，与神经元和神经胶质细胞的进一步损伤有关[15,16]。亚急性期持续到受伤后数周，其特征是吞噬反应、星形胶质细胞反应性增生。这种反应性增殖导致神经细胞内神经胶质瘢痕的形成，为轴突再生的关键屏障，是中枢神经系统损伤后再生受限的主要原因[17,18]。慢性期的定义存在争议，但普遍认为持续时间超过6个月即为慢性期，包括疤痕形成和瘘管形成是其特征[19]。

3 分型

目前，CSCIWFD有几种分型。第一种分型根据病人颈髓MRI信号改变分型：水肿型、出血型、水肿+出血型。水肿型MRI T_1像为低信号，T_2像为高信号；出血型伤后72 h内MRI T_1、T_2像均为低信号，伤后72 h~7 d内T_1像为高信号、T_2像为低信号，7 d后T_1、T_2像均为高信号；水肿+出血型MRI T_1、T_2像均为高信号[20]。第二种分型根据病人颈脊髓MRI长度范围分型：轻度（损伤信号<1.5 cm）、中度（1.5~4.0 cm）、重度（≥4.0cm）[21]。第三种分型根据病人的影像学特征、外伤类型及病理基础分为3种类型：1型以急性颈椎间盘突出或脱出为主要表现，单节段或多节段突出，受压部位为脊髓前方，受压节段T_2高信号改变；2型伤前已患有中度及以上颈椎退变性疾病，如后纵韧带骨化、发育性椎管狭窄等，各种病因致椎管储备空间进行性减少，使脊髓腹背侧均受压迫；3型既往无或仅有轻微颈椎基础疾病，颈椎管储备空间充足，脊髓无压迫，呈“挥鞭样”损伤，MRI见脊髓信号明显改变，相应节段的前纵韧带损伤或断裂，伴前方椎间盘破裂、血肿，可见完全或重度不完全SCI，遗留功能少，常有合并伤、多发伤[22]。

4 治疗方法

CSCIWFD的临床管理一直存在许多争议，其中神经保护概念一直是研究和争论的主题。本文从保守治疗、手术减压、细胞治疗、社会康复等进行阐述。

4.1 *药物治疗* Kawano等[23]认为手术治疗与保守治疗相比没有明显优势。目前，许多药物可以减少原发性损伤和最小化继发性损伤，包括甲泼尼龙冲击治疗，联合脱水、神经营养药物治疗，可以减轻脊髓损伤。

4.2 *手术治疗* 近年来，研究发现在SCI后24 h内进行早期手术减压会有更好的预后。多中心、国际性、前瞻性队列研究STASCIS表明伤后24 h内进行手术减压可显著改善病人6个月随访结果，显著改善神经功能[1,24]。Chen等[27]荟萃分析显示，与保守治疗相比，手术治疗可提高成人CSCIWFD的有效率和JOA评分，原因可能是手术减轻了脊髓的水肿和其内部压力，改善血液循环，减轻或避免脊髓二次损伤，从而加速脊髓功能的早期恢复。

目前，颈脊髓损伤手术方式的选择，一般取决于损伤节段，其中3个节段以下选择前路手术，3个节段以上选择后路手术，甚至部分病人需要前后路联合手术[25,26]。前路手术包括颈前路椎间盘切除椎间融合术、颈前路椎体次全切除钛笼植入融合术、颈椎前路可控前移融合术，后路手术包括颈后路单开门椎管扩大椎板成形术、颈后路双开门椎管扩大椎板成形术、后路全椎板减压侧块螺钉内固定术[28-30]。由于缺乏具体的标准，最佳手术入路的选择主要基于

脊柱外科医生的个人经验及病人的影像学结果和临床表现[31]。前路手术减压可以稳定韧带复合体损伤引起的不稳定节段，但通常需要融合更多的椎体节段，这可能会牺牲更多的运动节段。后路椎板成形术具有更宽的范围减压，比前路手术更能保留运动节段，但后期可出现颈椎不稳。后路椎板切除术可以提供所需的稳定性，但也牺牲了需要减压的运动节段的功能。因此，最佳手术入路的选择不仅受脊髓受压程度的影响，还受脊髓受压节段的影响。另外还要考虑颈椎的矢状位平衡[32,33]。

4.3 细胞治疗 有学者提出干细胞再生医学的发展有望成为SCI的新型治疗手段。临床试验发现，通过髓内移植的方法将胎儿神经干细胞直接注射于完全性胸段SCI的损伤部位周边，部分病人感觉、运动功能有显著改善，细胞移植后长期随访未发现肿瘤生长，验证了其安全性[34]。虽然干细胞治疗SCI已引起越来越多的关注，但不同学者、机构和国家在该领域的合作强度需要加强，更重要的是，干细胞修复SCI的关键靶点、分子机制、移植策略（剂量、时机、途径、来源、频率）、干细胞的临床转化、安全性、组织工程策略以及外来体的治疗潜力尚未得到明确阐述，这些方面是该领域应该重点关注和亟待解决的关键问题[35]。

4.4 电刺激治疗 脑干深部电刺激（deep brain stimulation，DBS）可“盘活”损伤的脊髓。DBS的基本原理是首先利用立体定向技术将电极导管精准放置在特定的核团内，随后利用高频电进行刺激，使相应核团兴奋或抑制，以达到治疗的目的。有学者提前2周在正常大鼠楔形核（Cuneiform Nucleus，CNF）区植入DBS设备并进行运动训练，使大鼠适应植入的设备；随后利用显微剪刀剪断部分脊髓，仅留下双侧腹内侧纤维束，以造出“脊髓不完全损伤模型”，从多种步态分析层面证明CNF-DBS植入后的大鼠具有康复优势；该方案在SCI慢性期同样能够起到显著效果[36]。以往，我们都认为SCI慢性期，内部瘢痕已经形成，或许多数疗法的效果都要打折扣，但本研究恰是针对SCI慢性期，具有重要意义。

4.5 NT3壳聚糖治疗 NT3壳聚糖可在清除瘢痕后修复慢性SCI。有学者在将NT3-壳聚糖支架移植入切除5 mm脊髓的大鼠和切除10 mm脊髓的猴可以很好地促进其神经再生。这种壳聚糖支架可以缓慢释放NT3达14周，同时促进长距离轴突生长、促进神经干细胞分化为神经元及神经回路重建，从而促进了运动和感觉功能恢复[37]。这表明陈旧性瘢痕对神经再生的阻碍作用，临床上可通过彻底清除陈旧性瘢痕以促进内源神经再生，对于临床治疗慢性SCI具有重要参考价值。

4.6 高压氧（hyperbaric oxygen，HBO）治疗 研究表明HBO可能具有缓解缺氧、保护周围组织、通过控制caspase-3表达抑制凋亡、减少SCI区域线粒体功能障碍、减少出血面积和水肿等多种功能。HBO治疗可抑制炎症因子的产生，促进神经元的修复和再生，可以改善SCI病人术后功能障碍[38,39]。有学者对78例外伤性不完全性颈脊髓损伤病人的临床资料进行回顾性分析，结果发现HBO组受试者比非HBO组的受试者有更好的疗效，其中治疗1个月的效果最显著；此外，治疗1个月，两组Barthel指数以及ASIA感觉和运动功能评分均有显著改善，HBO组明显优于非HBO组（$P<0.01$）；正确的HBO治疗可在术后第一个3个月内达到恢复期，可有效促进脊髓功能恢复，减少残疾，提高病人的生活质量[40]。

5 总结与展望

随着医学的进步，越来越多的神经脊柱外科医生主张对CSCIWFD病人进行早期手术治疗，因为持续压迫下的脊髓在狭窄的椎管内难以恢复。术后疗效受到损伤类型、损伤长度、Pavlov比值、ASIA分级、后纵韧带骨化及椎间盘突出等多种因素的影响，因此术前MRI对手术疗效的预测极其关键。年轻病人、早期手术、术前较好的ASIA分级及术前MRI髓内损伤长度越短是预后较好的关键因素。术前MRI显示水肿+出血型损伤或损伤长度≥45 mm的病人，手术疗效欠佳的风险更高，术前需与病人及家属充分沟通。早期手术是治疗CSCIWFD的重要方法，可减轻脊髓水肿，降低脊髓内压力，改善脊髓血液循环，避免或者减轻脊髓的继发性损害。手术可以使颈椎获得坚固的稳定，恢复脊柱生理弯曲和椎体高度，有利于脊髓功能恢复。损伤慢性期可进行细胞治疗、壳聚糖支架移植以及联合HBO治疗，促进脊髓功能恢复。总之，CSCIWFD是一个复杂且具有潜在破坏性的疾病，需要进行深入研究，最终能为病人提供一种有效的治疗方法。

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