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·综 述·

颈椎后纵韧带骨化的发病机制及治疗研究进展

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[摘 要] 颈椎后纵韧带骨化(OPLL)是脊柱外科常见且治疗具有挑战性的疾病,其可能导致严重的脊髓神经损伤。OPLL是由多因素导致的一种疾病,遗传及环境因素参与其发生及发展过程。该病治疗方式繁多,目前尚无统一的治疗标准。本文结合国内外文献,就OPLL的发病机制、影像学表现及治疗作一综述,以期为其临床治疗提供一定的参考。

[关键词] 颈椎;后纵韧带骨化;病理生理解剖;颈椎手术;椎板成形术;椎板切除术

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Advances in pathogenesis and treatment of ossification of the posterior longitudinal ligament of cervical spine

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Abstract: Ossification of the posterior longitudinal ligament (OPLL) of cervical spine is a common and challenging disease in spine surgery, which can cause a severe spinal nerve injury. OPLL is a multifactorial disease in which many genetic and environmental factors are involved in its occurrence and development. There are many treatment methods for OPLL, but there is no unified treatment standard at present. This paper reviews the pathogenesis, imaging manifestations and treatments of OPLL based on domestic and foreign literatures, in order to provide some references for its clinical treatment.

Keywords: cervical spine; ossification of the posterior longitudinal ligament; pathophysiological anatomy; cervical surgery; laminoplasty; laminectomy

颈椎后纵韧带骨化(ossification of the posterior longitudinal ligament,OPLL)是指脊柱后纵韧带出现病理性增生并骨化的现象[1-2]。OPLL早期不易发现,晚期治疗难度较大,是东亚地区的常见病,其在日本的患病率最高,达1.9%~4.3%[3],在欧美的患病率为0.1%~1.7%[4-6]。OPLL多见于40~60岁的人群,男女比例为2∶1[7]。多数患者无明显临床症状,仅在影像学上可见OPLL。随着OPLL逐渐加重,脊髓或神经

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压迫症状亦加重[8-9],从而导致肢体感觉和运动障碍及大小便功能等自主神经功能受损。因此,早期干预对OPLL患者的预后有极大意义。目前医疗技术逐渐发展成熟,但仍难以阻止OPLL的进展,亦不能降低其发生率,后期仍需手术治疗,然而其治疗标准尚未统一。故本文对OPLL的发病机制及治疗进展作一综述,以期为其临床治疗提供参考。

1 OPLL的发病机制

1.1 病理生理学

OPLL的发生是多种因素共同作用的结果,后纵韧带内局部血管组织及梭形细胞浸润、软骨样或成纤维细胞增生、后纵韧带退化或肥厚等使韧带组织转变为骨组织,形成板状骨。有研究发现OPLL与遗传和环境因素相关[10]。目前OPLL的病理生理尚不明确,其可能与弥漫性特发性骨肥厚症相似[11-13]。

1.2 基因组学及分子生物学

OPLL有明显的遗传倾向,有研究报道,IL17RC基因的rs199772854A位点是OPLL的潜在致病基因,可能与OPLL的发生有关[14]。此外,COL6A1、COL6A6、COL9A1、COL11A2、TLR1、FGFRI和BMP2等基因亦与OPLL有关[15-18]。OPLL还与部分代谢性疾病相关,如高胰岛素血症、低磷血症性佝偻病等[19-21]。超过30种骨形态形成蛋白及其亚型被发现参与OPLL的形成[22-28]。

1.3 机械力学

脊柱慢性退变过程中,机械力学因素进一步加速了OPLL的进展。Chen等[29]研究发现,日常生活中进行脊柱屈伸等活动时,若存在节段不稳定,则可能导致脊柱机械应力的分布异常,从而刺激骨化通路激活。机械应力的异常分布与OPLL的形成密切相关[1,30-31]。机械应力异常分布会诱导后纵韧带成纤维细胞成骨分化,其通过激活细胞内部机制,上调碱性磷酸酶、骨钙素和Ⅰ型胶原等成骨标志物的表达[32-35]。有研究认为,脊柱稳定性的下降会促进韧带结构的骨化,骨化的韧带又会对脊髓产生静态压迫及动态撞击摩擦,这是OPLL神经症状产生及进展的重要原因[36-38]。

1.4 其他因素

长期不良的颈部姿势、劳累、颈部剧烈运动等可能是导致OPLL发生的危险因素。体内激素(如胰岛素、生长激素、雌激素、雄激素、甲状旁腺激素等)水平变化也可能与OPLL的形成相关[39-40]。因此,OPLL是一种涉及多个基因,存在多种致病因素,并受环境因素影响的慢性疾病。

2 OPLL的影像学诊断

可通过X射线片测量颈椎的矢状位参数,了解颈椎曲度及颈椎是否稳定[13]。有学者提出,在颈椎X射线侧位片上测量K线可预测后路减压的效果,进一步指导手术入路的选择[41]。

CT可对病灶的位置、形状、大小进行判断,其中CT平扫可了解后纵韧带与硬膜囊是否存在骨化粘连,若存在骨化粘连,选择前路手术出现脑脊液漏的可能性较大[42]。此外,CT还可在OPLL治疗过程中监测骨化灶进展情况[43]。

MRI对软组织成像有较高的优势,其可以较好地显示脊髓神经受压情况,其中T2像脊髓出现局部高信号,提示脊髓不可逆损伤的可能,手术效果改善有限[44]。

3D重建有助于观察病灶,了解患者解剖结构及其与病灶的关系,为选择安全有效的手术方式提供一定参考,并指导临床制定手术方案[45]。

3 OPLL的治疗

3.1 保守治疗

对于无症状或症状较轻且CT及MRI检查无明显脊髓神经受压或脊髓变性的患者,可先行保守治疗,嘱患者卧床休息,日常生活中可佩戴颈托,并辅以颈椎牵引治疗,配合使用营养神经药物。但有研究指出,约17%的无症状患者最终仍会出现脊髓症状[37]。此外,保守治疗的OPLL患者仍存在发生脊髓损伤的风险[46]。因此,对于保守治疗的OPLL患者应动态评估其发生颈椎创伤时出现脊髓损伤的风险,若脊髓损伤风险极大,则建议行手术治疗。

3.2 手术治疗

当OPLL患者出现进行性或者突发性加重的脊髓压迫症状,或保守治疗无效时,则应进行手术治疗[40]。在脊髓型颈椎病患者中,OPLL是脊髓损伤的危险因素,手术治疗可以降低脊髓损伤的风险[13,38]。出现脊髓压迫症状的OPLL患者瘫痪风险明显升高,而手术治疗可以取得良好的神经功能恢复并降低瘫痪风险。因此,患者具有明确的手术指征时应该尽早手术。脊髓减压、重建颈椎稳定性是OPLL患者手术的核心思路,但目前对于手术方式的选择尚无统一标准,需要根据患者骨化的严重程度及类型、椎管内占位程度等因素来选择。

3.2.1 前路手术 前路手术适应证:①前方脊髓压迫导致单节段或多节段椎管占位<50%,且无颈椎管狭窄;②脊髓型颈椎病后方压迫不严重,前方不超过2个节

段的脊髓压迫,且椎管占位≥50%[47]。前路手术具有创伤较小、直接减压、便于维持或重建颈椎前凸的优势,但由于颈椎前方特殊的解剖结构,颈椎前路手术依旧存在食管损伤、吞咽困难、声音嘶哑、硬膜撕裂、植骨沉降、硬膜外血肿、假关节形成等并发症发生风险[48]。

颈椎前路椎间盘切除融合术及颈椎前路椎体次全切除融合术作为颈椎前路手术的经典术式,可直接去除骨化的后纵韧带,治疗 OPLL 的效果确切,但对于压迫严重的 OPLL 患者,前路手术操作时仍存在脊髓损伤的风险[6,8-9]。

Yamaura 等[49]于 1999 年首次报道了颈椎前路骨化病灶漂浮减压融合术,若后纵韧带骨化物同硬膜粘连,可在术中将骨化物打磨至厚度 <5 mm,使其随硬脊膜游离,从而达到减压效果,该术式适用于 OPLL 或硬脊膜粘连严重的患者,但存在骨化物去除不完全的风险,且对于压迫严重的 OPLL 患者亦存在脊髓损伤的风险。

上海长征医院史建刚教授团队率先开展了前路椎体骨化物复合体前移融合术,通过在椎体两侧开槽,使椎体后壁及与之相连的骨化后纵韧带向前游离,利用螺钉与钛板拉力使椎体骨化物复合体前移,以达到扩大椎管容积的目的[50]。该术式具有诸多优点:①手术为前路减压,其操作主要在椎体两侧的钩椎关节,而非直接对椎体后方的骨化后纵韧带进行操作,减压直接彻底,故降低了术中脊髓损伤的风险;②减压范围大,对宽基底型 OPLL 减压效果良好;③避免直接在骨化灶上操作,明显降低了手术风险及操作难度;④对脑脊液漏等并发症处理较为简便。但该术式也有其局限性,如难以处理偏向椎管一侧的骨化灶[51];此外,受累范围超过 5 个节段是前路椎体骨化物复合体前移融合术的相对禁忌证[51]。

Lee 等[52]报道的前路椎体滑移截骨术类似于史建刚教授的前路椎体骨化物复合体前移融合术,其通过前移受压节段椎体,达到扩大椎管容积的效果,治疗效果较好,但存在手术创伤大、操作难度高等问题。

3.2.2 后路手术 后路手术适应证:①受累节段超过 3 个;②受累范围上至 C_1、C_2,下至胸椎;③脊髓后方压迫;④前路减压风险及难度较大;⑤需广泛减压;⑥K 线阳性[41]。

后路椎板切除术通过切除对应节段椎板并辅以螺钉内固定,可实现大范围间接减压,明显扩大椎管容积,但椎板切除后仍存在颈椎后凸风险增加等问题。Lee 等[38]对 25 例颈椎 OPLL 患者行单纯椎板切除术后进行了平均 3.7 年的随访,患者均取得满意的远期临床效果和影像学结果。

后路椎板成形术最早由日本学者 Hirabayashi 等[53]提出,现逐步发展为单开门椎板成形术。该术式在打开椎板后,通过钛板固定开门侧,脊髓向后漂移,避开前方骨化韧带,从而达到间接减压的目的。相较于单纯椎板切除术,后路椎板成形术后颈椎后凸畸形的发生率更低[54]。Liu 等[54]对 67 例颈椎 OPLL 患者进行研究发现,椎板成形术后颈椎后凸畸形的发生率较椎板切除术低。经过多年的发展,后路椎板成形术已十分成熟,且操作简单,减压效果确切,但其对于 K 线阴性患者存在疗效不佳的可能。

对于少数特殊病例,需进行后路杂交手术(联合后路椎板成形术、椎板切除术、后路固定融合术)才能达到治疗效果。后路杂交手术既能完美减压又能提高颈椎的稳定性,可联合椎板成形术及椎板切除术,必要时辅以椎间孔切开减压减轻根性症状[55];固定方案可选择自体骨移植融合、钛板固定、侧块及椎弓根钉固定。后路杂交手术的优点:减压范围大且彻底;后路固定系统可提高颈椎的稳定性,延缓骨化的进展;可预防颈椎后凸畸形的发生。

后路手术减压为间接减压,无法直接切除 OPLL 形成的骨化物,对于椎管狭窄严重的患者可能减压效果不理想,故不推荐用于 K 线阴性患者[41]。有研究发现,行后路手术的 OPLL 患者术后随访 CT 提示 OPLL 长度、宽度和厚度均有不同程度增加[45],若患者术后出现神经症状缓解不佳或加重,则可二期行前路手术切除骨化物。单纯后路椎板切除术存在术后颈椎后凸畸形的风险,为了解决该问题,目前后路椎板切除术普遍采用钉棒内固定,通过钉棒系统塑形,可以改善颈椎曲度,提供长期的颈椎稳定性,并可延缓 OPLL 进展[38]。

颈椎后前联合手术可根据患者具体病情选择一期或者分期完成,先行广泛的后路减压,扩大椎管容积,增加脊髓活动空间,再行前路减压进一步直接解除压迫[49]。联合入路手术虽然可以较好地减压以及恢复颈椎稳定性,但其兼具前路及后路手术优点的同时亦存在两种入路相关的缺点,且治疗费用高。因此,选择颈椎后前联合手术则应更加谨慎。

4 总结

OPLL 是一种罕见且具有挑战性的颈椎疾病,目前其相关的基础及临床研究较多。无症状的 OPLL 患者可采取保守治疗,而存在神经根或脊髓压迫症状的患者应考虑手术减压。手术方式的选择应综合评估手术风险、术后疗效、治疗费用等,以患者快速康复为原则,制定个性化方案。

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