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Pathophysiology of cervical myelopathy

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Abstract

BACKGROUND CONTENT: Cervical myelopathy is a group of closely related disorders usually caused by spondylosis or by ossification of the posterior longitudinal ligament and is characterized by compression of the cervical spinal cord or nerve roots by varying degrees and number of levels. The decrease in diameter of the vertebral canal secondary to disc degeneration and osteophytic spurs compresses the spinal cord and nerve roots at one or several levels, producing direct damage and often secondary ischemic changes.

PURPOSE: Clinicians who treat cervical myelopathy cord injuries should have a basic understanding of the pathophysiology and the processes that are initiated after the spinal cord has been injured.

STUDY DESIGN/SETTING: Literature review.

METHODS: Literature review of human cervical myelopathy and clinically relevant animal models to further our understanding of the pathological mechanisms involved.

RESULTS: The pathophysiology of cervical myelopathy involves static factors, which result in acquired or developmental stenosis of the cervical canal and dynamic factors, which involve repetitive injury to the cervical cord. These mechanical factors in turn result in direct injury to neurons and glia as well as a secondary cascade of events including ischemia, excitotoxicity, and apoptosis; a pathobiology similar to that occurring in traumatic spinal cord injury.

CONCLUSIONS: This review summarizes some of the significant pathophysiological processes involved in cervical myelopathy. © 2006 Elsevier Inc. All rights reserved.

Keywords: Cervical myelopathy; Ossification of the longitudinal ligament; Spinal cord injury; Spondylosis; Stenosis; Ischemia; Apoptosis

Introduction

Cervical myelopathy is the most serious condition of cervical spondylosis and is the most commonly acquired cause of spinal cord dysfunction among those aged over 55 years [1]. This disorder was originally described by Stookey in 1928 and was attributed to compression of the cord by cartilaginous nodules of degenerated disc material [2]. The symptoms and signs with which myelopathy patients present are dependent on the relative degree to which the posterior, dorsolateral and ventrolateral columns, the ventral horns, and the cervical nerve root of the spinal cord are involved [3]. In most cases, patients present with more than one of the aforementioned structures being affected [4].

Although the exact pathophysiology underlying cervical myelopathy remains uncertain, it is largely accepted to be a disorder that involves compressive forces on the spine, likely due to multiple factors. Cervical cord compression can occur as a result of a disc herniation alone; degenerative changes that occur in the spine such as degeneration of the joints, intervertebral discs, ligaments, and connective tissue of the cervical vertebrae; and bone spur growth in the spinal canal (spondylosis). Posteriorly, infolding of the ligamentum flavum and facet joint capsule can create decreased space within the spinal canal and foraminal dimensions [5]. Conversely one is placed at increased risk for developing cervical cord compression and myelopathy as the space within the spinal canal narrows (stenosis).

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Pathogenesis of cervical myelopathy

The pathophysiology of cervical myelopathy involves static factors, which result in acquired or developmental stenosis of the cervical canal, and dynamic factors, which involve repetitive injury to the cervical cord. These mechanical factors in turn result in direct injury to neurons and glia as well as a secondary cascade of events including ischemia, excitotoxicity, and apoptosis (Table 1). Indeed, the pathobiology of cervical myelopathy bears many similarities to traumatic spinal cord injury [1,6].

Static mechanical factors contributing to cervical myelopathy

Acquired spinal stenosis—Spondylosis and disc degeneration

In healthy adults, the intervertebral discs in the cervical spine have a structure analogous to that of the discs of the lumbar spine, consisting of the annulus fibrosis and nucleus pulposus [7]. The chemical composition of the nucleus pulposus and annulus fibrosis deteriorates with age [5]. This results in a progressive loss of viscoelastic properties of the spinal cord and disc bulging. However, it has been observed that in the first and second decades of life, before complete ossification occurs, lateral tears do occur in the annulus fibrosis [8]. The tears in the lateral part of the disc tend to enlarge towards the medial aspect of the intervertebral disc. These anatomical characteristics demonstrate that, with increased age, the disc cannot bear or transfer load due to ongoing dehydration, medial splitting of the disc, and the disappearance of the nucleus pulposus. With the increased load on the uncovertebral processes, these uncovertebral processes become flattened, which alters the load-bearing function of the intervertebral joint. This process puts greater stress on the articular cartilage of the vertebrae and their respective end plates. Osteophytic spurs develop at the margins of these end plates. Osteophytes stabilize adjacent vertebrae whose hypermobility is caused by the degeneration of the disc [3]. The disc also calcifies, further stabilizing the vertebrae. Osteophytes increase the weight-bearing surface of the end plates and, therefore, decrease the effective force being placed on them. In addition to osteophytic overgrowth, the ligamentum flavum may stiffen and buckle into the spinal cord dorsally [9]. Osteophytic overgrowth ventrally and, in some cases, buckling of the ligamentum flavum dorsally can cause direct compression of the spinal cord, resulting in myelopathy. Furthermore, such transformation of bony structures can lead to compression of the spinal nerve and the vertebral artery, which can cause intermittent or chronic pain, as well as demyelination of ascending and descending spinal pathways, possibly due to deficient blood supply to the spinal cord itself.

Kuhlman reported that the elderly had less mobility in the cervical spine compared with that of the younger generation in a survey of a healthy population [10]. A more recent report from Mihara et al. showed that elderly patients with cervical spondylotic myelopathy have increased segmental mobility at C3–C4, which was the level at which their myelopathy developed [11]. Conversely, elderly patients showed significantly less mobility at C4–C5 and caudal motion segments. Consequently, the hypermobility in conjunction with the static spinal stenosis causes neurologic impairment in the elderly population. Significantly greater angulation at the C3–C4 level, associated with age-related postural change, was noted in the elderly patients with a C3–C4 disorder [11]. Additionally, hypermobility at the C3–C4 segment to compensate for decreased mobility at the lower segments was identified as a potential contributor to the high incidence of pathology at C3–C4 in the elderly patients with cervical spondylotic myelopathy [11].

Table 1
Pathophysiological factors involved in cervical myelopathy

Static factors
Spondylosis
Disc degeneration
Ossification of the posterior longitudinal ligament
Ossification of the ligamentum flavum
Congenital stenosis
Other acquired compressive pathology (eg, tumors and calcification)
Dynamic factors
Changes in neck flexion/extension, which narrow the cervical spinal canal dynamically and place increased strain and shear forces on the spinal cord
Biomolecular factors
Ischemic injury due to chronic compression of spinal cord vasculature
Glutamate-mediated excitotoxicity
Oligodendrocyte and neuronal apoptosis

Ossification of the posterior longitudinal ligament

Ossification of the posterior longitudinal ligament (OPLL) is a common multifactorial disease, having a prevalence of 1.9–4.3% among Japanese as well as present in other ethnic groups. [12,13]. This disorder can result in a progressive cervical myelopathy caused by compression of the spinal cord from ectopic ossification of spinal ligaments (Figs. 1 and 2). Patients with OPLL frequently present with a severe myelopathy that potentially can lead to quadriparesis. The natural course of OPLL suggests progression with age, implying the contribution of environmental factors such as accumulated mechanical stress on the spine, and genetic factors.

Utilization of the naturally occurring mutant Tiptoe Walking Yoshimura mouse, which spontaneously develops ossification of posterior ligaments about the atlantoaxial membrane of C1–C2 similar to human OPLL, that has a characteristic tip-toe walking, has allowed researchers to deduce the genetic basis responsible for ectopic OPLL

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