Pathobiology of Degenerative Cervical Myelopathy

Farhana Akter, MBBS, BSc, MSc, MRCS*,
Mark Kotter, MD, MPhil, PhD

KEYWORDS

• Degenerative cervical myelopathy • Pathobiology • Chronic spinal cord compression • Cell loss
• Axon degeneration • Myelin changes

KEY POINTS

- Degenerative cervical myelopathy (DCM) is caused by mechanical stress.
- The pathobiology of DCM includes inflammation, apoptosis and vascular changes.
- A full understanding of the mechanisms of injury is currently lacking.

INTRODUCTION

Degenerative cervical myelopathy (DCM) is caused by mechanical compression of the spinal cord. However, the mechanism by which mechanical stress results in spinal cord injury is poorly understood. Furthermore, there is a poor correlation between disease severity and degree of compression measured by static MRI scanning[1,2] DCM is thought to be composed of a static and dynamic component. Static factors include developmental canal stenosis, bulging of the intervertebral disc posterior margin, and hypertrophy of the ligamentum flavum. Dynamic factors include invagination of the ligamentum flavum[3] and shearing and tethering of the spinal cord as a result of neck movements. The most common mechanisms involved in the pathobiology of DCM include apoptosis of cells, an inflammatory response, and vascular changes leading to axon degeneration, myelin changes, and cell loss. However, the exact pathophysiologic mechanisms of DCM are unclear. As a result, surgery is the only available treatment of DCM. Surgery can halt disease progression and enable a degree of recovery[4,5]; however, most patients have long-term disability. A better understanding of the pathogenesis of DCM is required for the development of treatments to improve outcomes. In this article, the authors discuss the pathophysiology of DCM and recent advances in our understanding of the disease.

PATHOBIOLOGY OF DEGENERATIVE CERVICAL MYELOPATHY

Human Studies

Histopathologic studies of human DCM suggest that the disease is progressive in nature and mainly affects white matter tracts. Wallerian degeneration of motor axons in the lateral corticospinal tract is one of the major signs of early disease.[6] Clinically, patients present with signs of corticospinal tract damage, including spastic gait. DCM also affects the central gray matter and posterior column leading to symptoms of impaired sensation, proprioception, and sphincter disturbance.[7]

Disclosure Statement: The authors confirm that they have no commercial or financial conflicts of interest.
Department of Clinical Neurosciences, Ann McLaren Laboratory of Regenerative Medicine, University of Cambridge, Addenbrooke's Hospital, West Forvie Building, Forvie Site Box 213, Hills Road, Cambridge CB2 0SZ, UK
* Corresponding author.
E-mail address: farhanaakter@doctors.org.uk

Neurosurg Clin N Am ■ (2017) ■–■
https://doi.org/10.1016/j.nec.2017.09.015

Animal Studies

Preclinical animal studies have highlighted that a range of mechanisms of injury are involved in the pathogenesis of DCM following compression (Fig. 1). The most common pathogenesis observed is loss of neurons following compression. Other cells affected include oligodendrocytes, astrocytes, and microglia. Mechanisms of injury include apoptosis of cells, inflammation, and vascular changes.

Cellular Changes

Neuron loss

Neurons are vulnerable to spinal cord compression. Degeneration of neurons and axons are a prominent feature in human postmortem studies and can cause significant atrophy of the spinal cord. Studies have shown loss of neurons in patients with DCM, particularly in the anterior horn.[8] In addition, segmental loss of interneurons occurs[9] as well as loss of lower motor neurons in the anterior horns.[8,9] These findings have been echoed in animal studies, with the greatest cell loss in the gray matter of the ventral horns at the focus of the lesion.[10–14]

Oligodendrocyte loss

Oligodendrocytes make and maintain myelin sheaths. The loss of oligodendrocytes results in demyelination and impaired axon function and survival.[15] Several studies have demonstrated the loss of oligodendrocytes in chronic compression models. Most published studies were performed in the Tiptoe-walking-Yoshimura (Twy/Twy) mice model, and these studies demonstrated apoptosis of oligodendrocytes in the compressed group. Studies in rats have also shown evidence of oligodendrocyte apoptosis using Terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) staining[16] More importantly, postmortem samples of human individuals affected by DCM demonstrated clear evidence of demyelination.[17]

Astrogliosis

Astrogliosis (also known as astrocytosis or reactive astrocytosis) is an abnormal increase in the number of astrocytes. Reactive astrocytes are characterized by high-level expression of glial fibrillary acidic protein (GFAP), an intermediate filament protein. Several articles have demonstrated increased expression of GFAP in compressed groups compared with control Twy/Twy mice[8,18] This finding has also been reported in rats,[19]

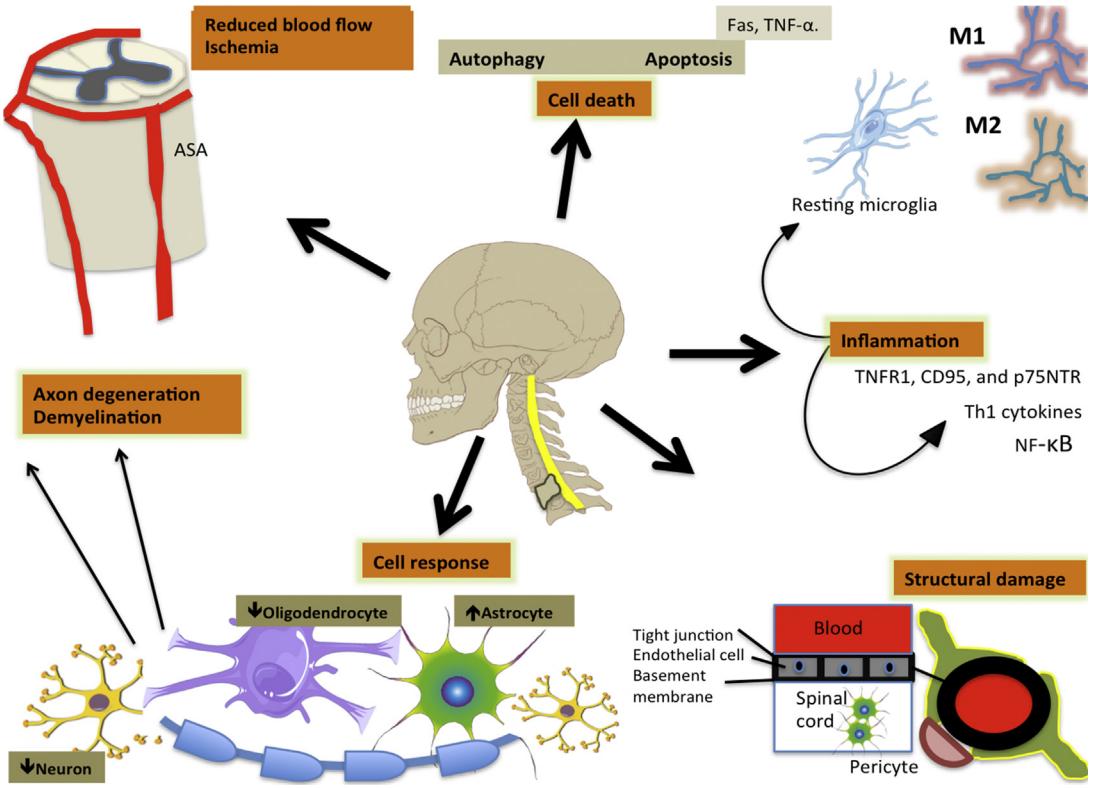

Fig. 1. Pathophysiologic changes observed in DCM. ASA, anterior spinal artery; NF-κB, nuclear factor–κB; Th1, T-helper 1; TNF-α, tumor necrosis factor–α; TNFR1, tumor necrosis factor receptor 1.