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REVIEW ARTICLE

Spinal cord ischemia and atherosclerosis: a review of the literature

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Abstract

Introduction. A paucity of literature exists regarding spinal cord ischemia and atherosclerosis. Therefore, the present study aimed to review this literature in hopes of better understanding this pathology.

Methods. Various search engines and databases were accessed using the following terms ''atherosclerosis and spinal cord ischemia'', ''atherosclerosis and vascular myelopathy'', ''spinal cord ischemia'' and ''arteriosclerosis of spinal arteries''.

Results. Twenty publications were found to be relevant to the present review. However, very few studies were identified that dealt specifically with atherosclerosis and spinal cord ischemia. The more valid cross-sectional studies indicated that local atherosclerosis in the spinal arterial network is minimal in comparison with the rest of the body. The anterior spinal artery appears to be one of the few arteries affected by atherosclerotic plaque formation. A greater propensity to affect the lower cervical spinal cord and a correlation with advancing age appears to exist. Systemic atherosclerosis may or may not have an effect on ischemia of the spinal cord.

Conclusions. Much of the current literature regarding atherosclerosis and spinal cord ischemia is vague and conflicting. Future studies aimed at, for example, imaging of the spinal cord in patients with ischemic-like symptoms are warranted.

Key words: *Spinal cord, pathogenesis, atherosclerosis, ischemia, vascular myelopathy.*

Introduction

With such a lack of data regarding atherosclerosis and spinal cord ischemia, the present study aims to review the relevant literature. The focus of this study was, more specifically, to investigate the effects of the chronic nature of systemic atherosclerosis, not a single acute event, even though it may be a result of atherosclerosis.

Heart disease attributable to atherosclerosis presents as a primary cause of death for all men and women in the United States.[1,2] Data from 2004 estimated the total number of Americans suffering from atherosclerotic-related heart disease to be approximately 80 million, with roughly half of these being more than 65 years old.[1] In 2004, the prevalence of mortality due to atherosclerosis was 1 of every 2.75 deaths, or 36.3% of all deaths in the United States.[1,3] The American Heart Association estimated that more than $400 billion from direct and indirect costs can be attributed to atherosclerosis.[1]

There is paucity of data regarding ischemic pathology of the spinal cord secondary to vascular occlusion. This is despite the fact that areas of the spinal cord ''softening'' because of atherosclerosis were first described as early as the late 19th century.[4–7] Spinal cord infarctions are responsible for less than 1% of all strokes.[8] Hughes[9] postulated that the spinal cord is much less susceptible to atherosclerosis than the brain because of its complex blood supply and tendency toward developing collateral flow. However, the morbidity and mortality related to ischemia of the spinal cord may be overlooked because of the difficulty of diagnosis.[10] Also, a condition such as atherosclerosis may not be acutely fatal, but is capable of leading to a myriad of other conditions that are more likely to be diagnosed at post-mortem dissection, such as thrombosis, embolus, aneurysm or anterior spinal artery syndrome (Spiller syndrome).[11–13]

Like atherosclerosis, myelopathies from focal necrosis, Wallerian degeneration and neuronal atrophy increase in incidence and severity with age.[4,11,14] These neural degradations can manifest as unexplained local and generalised paresthesia, paresis, muscular atrophy, incontinence, diminished proprioception and balance, hyper-reflexa or diminished tendon reflexes, or any number of symptoms that are commonly attributed to ''old age''.[4,7,11,15]

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Near the turn of the 20th century, Adamkiewicz and Kadyi began to study the arterial vasculature of the human spinal cord and the tributaries that stem from the aorta to supply it (Fig. 1).[16–18] Other studies emerged throughout the 20th century that continued to map the spinal vasculature using evolving technology to view even the smallest arterioles and capillaries.[16,17,19,20] During this time, sporadic case studies posited the idea that atheroma in the spinal arteries leads to various neural deficits.[4,15,21–24]

Our current knowledge and understanding of atherosclerosis has provided support to the hypothesis that atheromatous plaque formation tends to occur more frequently near arterial bifurcations.[25–27] Because of the numerous bifurcations through which blood must pass to perfuse the spinal cord and its ''looped and tortuous''[16] vessels, this information adds substance to the theory that atherosclerosis is correlated with degenerative changes of spinal neurons.

Methods

The articles used for this research review came from a search of PubMed, CINAHL, Cochrane and OVID electronic databases using the keywords: ''atherosclerosis and spinal cord ischemia'', ''atherosclerosis and vascular myelopathy'', ''spinal cord ischemia'' and ''arteriosclerosis of spinal arteries''. The primary searches of these databases produced 278 articles. This body of literature was narrowed to articles published in peer-reviewed journals, printed in the English language, and involving human subjects, which resulted in 141 articles. The titles of these articles were reviewed and 69 were felt to be relevant. Additional searches of relevant articles, cited studies and authors' names produced an additional 10 articles for review that met the aforementioned criteria. The abstracts of these 79 articles were reviewed for relevance to the present research, of which 37 were felt to have significant relevance to the scope of the study. Full-text articles of the 37 were reviewed, and 17 were excluded on the basis of relevance or because they appeared to be outside the focus of the study. Of the final 20 articles used for the present research, 7 articles provided background information regarding pertinent anatomy and physiology of the spinal arterial network. Another 9 articles provided the foundation of pathophysiology of ischemic myelopathy, etiologies of spinal cord ischemia and infarction, and related information regarding anterior spinal artery syndrome. Five additional articles were reviewed and included studies that analysed the occurrence of anterior spinal artery syndrome since this can be caused by atherosclerosis of this specific spinal artery. Finally, five articles were selected for their pertinent data and used for the main portion of this review. In addition to the articles researched, statistics from the Centers for Disease Control and the American Heart Association were used for epidemiologic data. Exclusion criteria were minimal due to the rather scarce amount of research involving this topic. However, several articles regarding spinal cord ischemia were excluded from the main review if ischemia was caused by atheromatous emboli.

Results

Hughes and Brownell[4] presented five cases of elderly patients whose main presenting abnormality was paresis (four with quadriparesis and one with paraparesis), which could not be accounted for by any other motor neuron or neurological disorder. Weakness was found to be asymmetrical and accompanied by hyperreflexia or areflexia, as well as muscle wasting.[4] At necropsy, cerebral and spinal cord atrophy were visible, and cerebral arteries displayed

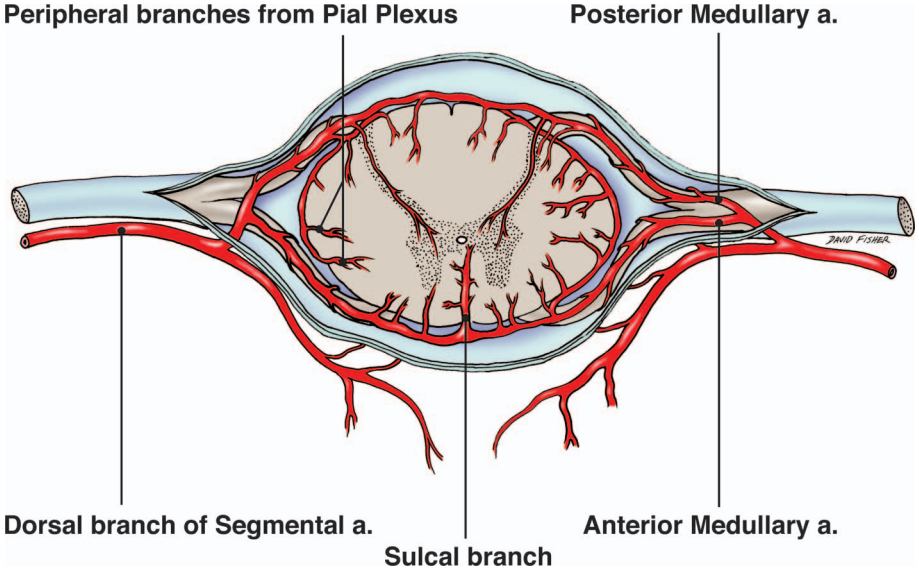

FIG. 1. Schematic drawing illustrating the blood supply to the spinal cord.

signs of atheromatous plaques.[4] Microscopy revealed focal necrosis of both the grey and white matter; degenerative softening of white matter; Wallerian degeneration of long tracts; gliosis and death of neurons and ischemic changes in living neurons.[4] These neurologic findings were accompanied with severe, systemic atherosclerosis and hyaline thickening and mural changes of the capillaries and small vessels within the grey and white matter.[4] These findings prompted the authors to hypothesise the existence of a neurologic syndrome caused by spinal cord ischemia from atherosclerosis.[4]

Fieschi *et al.*[5] attempted to look at ischemic lesions of the spinal cord and the degree of atherosclerosis present in undamaged segments of the spinal cord from 10 elderly subjects who died of acute cerebrovascular pathology. A single lesion was found in four of the subjects and another subject was found to have two lesions.[5] Of the six lesions, two were found at the level of C8, two were found at the level of T5, one at the level of L2 and one at the terminal conus.[5] Three of the lesions were located at the base of the anterior and lateral horns, one was at the base of the posterior horn, and one in the centre of the anterior horn.[5] All of the lesions showed gross necrosis of neurons.[5] Nine of the subjects were found to have gross atherosclerosis of the aorta and other extraspinal vessels.[5] The authors concluded that their findings indirectly supported the theory of vascular myelopathy caused by ischemia of the spinal cord in the elderly.[5]

Jellinger[11] investigated spinal cord atherosclerosis and vascular myelopathy in a large sample of cadavers. The study included 961 cadavers without vascular disorders of the spinal cord and 76 cadavers with cases of vascular myelopathy.[11] Atherosclerotic changes of major spinal vessels were found in 12.7% of the total number of subjects, and in 27.1% of subjects >61 years old.[11] Unlike findings from previous case studies, atherosclerotic plaques were rarely seen in the intramedullary network and radicular arteries, yet diffuse fibrosis was found throughout the spinal arteries at all levels of the spinal arterial network.[11] However, this fibrosis rarely was associated with vessel stenosis, and was correlated with advancing age.[11] Within the spinal arterial system, the anterior spinal artery was found to be affected most frequently.[11] From these data, this author hypothesised that the smaller lumen of the intramedullary vessels produced less space for turbulent flow to occur, thus reducing shear stress and preventing atherosclerotic plaque formation.[11] The author concluded that although spinal cord atherosclerosis may not be as prevalent as other areas of the cardiovascular system, it is still far more common than previously supposed, and was noted in well over a quarter of the total population sampled.[11] Atherosclerosis of the aorta was found to be more prevalent than atherosclerosis in the spinal arteries and displayed the greatest correlation with the observed myelopathy.[11] This led the author to also theorise about the impact of atherosclerosis of the larger, extraspinal vessels on spinal cord degeneration.[11] Likewise, Turnbull *et al.*[16] found no evidence of arterial narrowing due to atherosclerosis in the capillary or central arterial network of the spinal cord. The authors suggested that the numerous extraspinal vessels and hemodynamic factors protected these vessels from the effects of atherosclerosis.[16]

The findings of Jellinger[14] are contrasted by a more recent study by Wang *et al.*,[28] in which the pathologic changes in spinal cords of 19 centenarians were studied. Although Wang *et al.*[28] found microscopic evidence of atherosclerosis in 13 subjects, they found no neuronal degradation due to vascular disturbances. The study did identify areas of myelin loss, neuronal damage, and Wallerian degeneration, but the majority of these proved to be a result of degeneration/disorders of the spinal canal.[28] It was concluded that further research was merited into the effect of atherosclerosis in extraspinal vessels (vertebral, lumbar and intercostals arteries) on spinal lesions.[28]

Discussion

Anterior spinal artery syndrome

Systemic and spinal cord atherosclerosis play a role in the development of anterior spinal artery syndrome.[12,13,23,29,30] In addition to atherosclerosis, anterior spinal artery syndrome can be caused by syphilis, trauma, cross-clamping of the aorta during surgery, intervertebral disc disease, osteophytes, spondylosis, aneurysm, compression by neoplasm or congenital malformation.[12,13,23,29,30] It commonly presents with acute neck pain, paresthesia, flaccid paralysis that may progress to spastic paralysis, loss of bowel and bladder control, loss of temperature sensation and loss of pain sensation.[12,13,23,29,30] These symptoms are accompanied by glial scarring and necrosis of the grey matter supplied by the anterior spinal artery.[12,13,23,29,30]

Atherosclerosis has always been one of the more common aetiologies of anterior spinal artery syndrome, especially with insidious onset, but early case studies and research illustrated the impact of systemic atherosclerosis on hypoperfusion of the spinal cord.[12,13,23,29,30] Skinhoj[23] presented three cases of pure anterior spinal artery syndrome with insidious onset that could be explained by no other aetiology. Upon further investigation, the patients were found to have extensive aortic calcification from atherosclerosis.[23] Similar cases were published by O'Moore[29] and Laguna and Cravioto[30] demonstrating aortic calcification in patients with unexplainable cases of anterior spinal artery syndrome. More recent studies by Nedeltchev *et al.*[12] and de la Barrera *et al.*[13] also confirmed that atherosclerosis and its sequelae are the most common cause of anterior

spinal artery syndrome, and cause more than a third of all cases.[12,13]

Hemodynamic factors associated with the spinal cord blood flow

The direction of blood flow through the spinal arterial network plays a crucial role in the maintenance of tissue perfusion and the prevention of ischemia. Di Chiro *et al.*[10,31] used angiography to demonstrate that both ascending and descending flow exists in the anterior and posterior spinal artery pathways, and that further watershed zones are created where opposing currents meet. These converging currents allow for ample collateral flow in the event of arterial occlusion.[10,31]

Conclusions

The more valid cross-sectional studies indicate that local atherosclerosis in the spinal arterial network is minimal in comparison with the rest of the body. The anterior spinal artery appears to be one of the few arteries affected by atherosclerotic plaque formation. Other vessels have been shown to undergo fibrosis and thickening, but these too are not to the degree observed in other vessels commonly plagued with plaque formation.

Many theories have been suggested as to why the spinal arterial network itself is only minimally affected by atherosclerosis. Reason would suggest that because of the vast number of bifurcations in the spinal vasculatures, it would have diffuse plaque formation and arterial narrowing caused by the turbulent flow of blood and the resultant shear stress that is seen in other areas of the circulatory system. However, this is not so. Some researchers theorise that the minute luminal diameter limits turbulent flow, and that a lower pressure environment is less conducive to the genesis of large plaque formation. Other theories suggest that the expansive nature of the spinal cord vasculature provides more than ample collateral circulation, despite any fibrosis that may exist. The consensus in the literature is that further research is needed to assess the impact that atherosclerosis of the extraspinal arteries has on the spinal cord. Such research might be aimed at new methods or technologies for imaging of the spinal cord.

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