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Spinal Cord Ischemia: A review of clinical and imaging features, risk factors and long-term prognosis

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ABSTRACT

Spinal cord ischemia is a rare disorder carrying a high rate of morbidity. However, only a few case series concerning it have been published in the literature. The aim of this study was to determine the causes, the clinical characteristics, the functional outcomes and the prognostic indicators of spinal cord ischemia. For this reason, a review of the current literature was performed by following the PRISMA guidelines and by using the online PubMed database and the keywords "Spinal cord ischemia" and "Spinal cord infarction". Fourteen studies with a substantial total number of patients (526 patients) were finally included in this review, providing accurate and conductive results regarding spinal cord ischemia. The clinical presentation is nonspecific and characterized by rapid decline of function with a severe neurologic deficit. The cause remains unknown for half of the patients although multiple traditional cardiovascular risk factors are recognized. MRI is the imaging modality of choice for suspected spinal cord ischemia and a variety of characteristic MRI signs have been described such as the "pencil-like" zone and "owl's eye" sign. In contrast to cerebral ischemic infarction, in which guidelines for management are well-established, no consensus guidelines exist for the management of acute spinal cord ischemia.

Keywords: Spinal Cord Ischemia, Spinal Cord Vascular Diseases, Anterior Spinal Artery Syndrome, Posterior Spinal Artery Syndrome

Introduction

Spinal cord infarction (SCI) is an uncommon disorder that is considered a diagnostic challenge due to the variety of its clinical presentation. Its clinical signs are nonspecific, thus providing a challenging differential diagnoses and there is no consensus upon its management.

Before delving into the characteristics of spinal cord infarction, it is important to acknowledge the spinal cord's blood supply. The spinal cord is supplied by 3 longitudinal arteries: a single anterior spinal artery, which supplies the anterior two-thirds of the spinal cord and two, paired posterior spinal arteries, which are the primary blood supply to the posterior columns, dorsal grey matter and dorsal sensory columns. The entire blood supply to the cord is reinforced by numerous radiculomedullary or segmental medullary arteries. Segmental medullary arteries are the remnants of the multiple fetal segmental arteries and originate from the spinal branches of the ascending cervical,

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deep cervical, posterior intercostal and lumbosacral arteries. They penetrate the spinal canal through the intervertebral foramina and accompany the roots. The dominant and clinically most important segmental medullary/radiculomedullary artery is the artery of Adamkiewicz, also known as the great anterior radiculomedullary artery. [1] The artery of Adamkiewicz typically arises from the left posterior intercostal artery and is the only significant arterial supply feeding the anterior spinal artery along the lower thoracic, lumbar and sacral spinal cord (from T8 to the conus medullaris). [2] Injury to this artery can cause neurologic damage manifesting as fecal and urinary incontinence, impaired motor function and preserved sensory function. [3]

Considering this blood supply, spinal cord infarcts can occur in the territories of the anterior spinal artery (ASA) or posterior spinal artery (PSA), or both. [4] The most common clinical presentation of a spinal cord infarction is anterior spinal artery syndrome. The clinical manifestation includes bilateral loss of motor function and pain/temperature sensation, with relative sparing of proprioception and vibratory sense below the level of the lesion. The neurological deficits will manifest below the level of infarction due to the anatomical distribution of the spinal cord tracts affected. If the injury is at a high cervical level, dysfunction of the phrenic nerve may lead to respiratory failure. Clinical findings are usually bilateral due to the spinal cord supply by the anterior spinal artery. [5] In the case of incomplete spinal artery syndrome, when ischemia is localized at the level of the anterior horns, there is acute paraplegia without sensory abnormalities and without sphincter dysfunction. The ischemia of the spinal cord coming from infarction of the posterior spinal artery invokes loss of proprioception and vibratory senses below the level of the injury and total anesthesia at the level of the injury.

Spinal cord ischemia could be the result of low flow due to arterial hypotension, surgical injury to spinal arteries or embolic events. Thus it is useful to classify etiologies as spontaneous or periprocedural. However, in a significant share of patients the causative source cannot be identified.

Spontaneous causes of spinal cord ischemia include aortic pathology, atherosclerotic disease and degenerative spine disease[6] Other less common causes include embolic strokes from aortic atheroma, myxoma or infectious valvular vegetation. An abrupt motion when paired with large osteophytes and spinal stenosis can lead to acute cord ischemia. [7]

Iatrogenic causes of spinal cord ischemia account for at least 45% of all reported cord infarctions. [8] Aortic surgery is recognized as the highest risk factor, where spinal cord ischemia can occur during both cross-clamping and de-clamping. [9] The duration of cross-clamp time, pre-existing vascular risk factors and length of the repaired aortic segment contribute to the risk. Other less common causes of perioprocedural spinal cord infarction include orthopedic lumbar surgery, epidural steroid injection, intra-aortic balloon pump and lumbar epidural catheter placement.

Materials and Methods

The aim of this study was to determine the causes, the clinical characteristics, the functional outcomes and the prognostic indicators of spinal cord ischemia. For this reason, a review of the current literature was performed by following the PRISMA guidelines and by using the online PubMed database and the keywords "Spinal cord ischemia" and "Spinal cord infarction". Studies that were written in English related to SCI with the full text available were screened. Furthermore, the search was narrowed to studies published after 2000 to provide the most recent data and to case series studies. Case reports were excluded from the study. Finally, 14 papers were selected and included in the current study.

Inclusion criteria to the review were case studies written in English language. The primary search included 6474 articles. By excluding the articles prior to 2000, 5826 articles were found to contain the key words "spinal cord ischemia" and "spinal cord infarction". Furthermore, 5781 records were excluded for not being relevant with the topic of spinal cord ischemia or not having spinal cord ischemia as their main research theme. Subsequently, a scan of the articles' reference list was performed to check for more eligible articles to be included in the review. Case reports, reviews and animal studies were excluded. Following the above procedure, 14 articles were finally included in this review. (Table 1).

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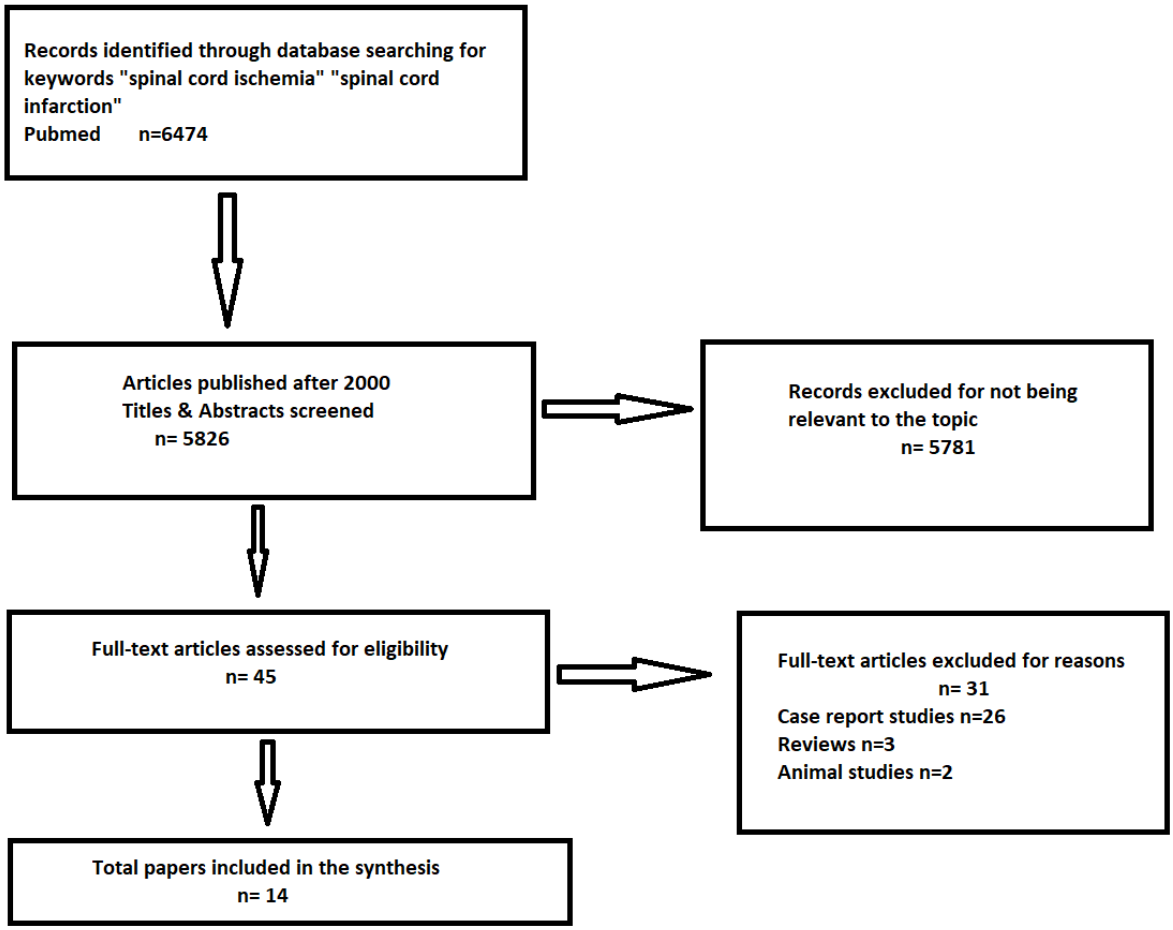

Table 1. Flowchart of the review

Results

Patient characteristics

Demographic data from the 14 studies included in this review were collected and averaged. There were a total of 526 patients suffering from SCI with an average age of 53.1 years (range 9-89 years). One study didn't specify the ratio between male and female patients. As a result, in a total of 444 patients (283 male and 161 female) the male to female ratio was 1.7.

Clinical Presentation

The clinical features of spinal cord ischemia include muscle weakness, sensory loss, pain, absent reflexes and hypotonia. Based on the results of 3 studies ([8], [10], [11]) including the larger number of patients and the most detailed clinical evaluation, it appears that at the initial examination muscle weakness was present at 87-99% of patients, sensory loss at 86-93% of patients and pain at 15-62% of patients. In the study of Cheng et al, [12] it was noted that pain was adjacent to the SCI level, ranging from back pain to neck pain. In a study by Zalewski et al [10], including 133 patients, the maximum neurologic deficit was observed in less than 4 hours at 55% of the patients, while 81% of them required a wheelchair for mobility and 86% had to be catheterized. Motor deficits were the most serious and prominent characteristics of spinal cord ischemia, affecting almost 100% of patients. Paraparesis was the most frequent presentation, followed by paraplegia and quadriplegia. Absent reflexes and hypotonia in the lower extremities occurred in 31-64% of patients.

Etiology

It is quite obvious that spinal cord ischemia re-

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mains without identifiable cause in almost half the cases. In 24-74% of patients included in the studies of this review the cause of infarction remained unknown. Studies that were conducted in centers where spinal and aortic surgeries were performed included more postprocedural SCI cases. Data collected mainly in neurological departments depicted factors such as aortic dissection, hypertension and diabetes mellitus as contributing risk factors. In a recent study by Zalewski et al [10], including 133 patients, a history of one or more vascular risk factors was present in 101 patients (76%). The results of the study by Cheng et al [12], further reinforced this finding by identifying at least 1 vascular risk factor in 81% of patients and at least 3 vascular risk factors in 45,5% of patients. The risk factors for spinal cord ischemia as gathered from the 14 studies included in this review include hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, smoking, peripheral artery disease, previous stroke, and previous myocardial infarction.

Interestingly enough, the study of Novy et al, [13] showed that ischemic symptoms appeared immediately after a movement in 48% of patients (13 patients out of 27). In 7 patients this was a movement of the back, in 3 it was an arm movement and in the remaining 3 patients it was a Valsalva movement or a gait initiation. In all cases, the level of the spinal cord lesion corresponded to the level of mechanical stress in the spine.

MRI Findings

MRI is the examination of choice for the diagnosis of spinal cord ischemia [14]. In the acute phase, the use of intravenous contrast media can aid in the differential diagnosis between ischemia and inflammatory, tumoral or infectious diseases because usually enhancement is absent at this stage of ischemia. Nevertheless, in a study by Zalewski et al, 43% of spinal MRIs showed enhancement within the spinal cord parenchyma, after the administration of gadolinium[15] .

Another point to be noticed regarding MRI and spinal cord ischemia, is that 10% of patients with SCI may have a normal initial MRI despite a severe deficit.[15] Patients with severe impairments (ASIA A or B) are more likely to have a positive MRI for infarction than patients with less severe deficits. Indeed, 78% of the negative MRIs performed in the initial phase corresponded to patients whose deficits were mild to moderate (ASIA C and D). The ideal time for performing an MRI seems to be 3 to 4 hours after the onset of symptoms.

In the acute phase, ischemia presents as a restriction in diffusion-weighted imaging of the spinal cord. Classic findings of owl eyes (T2-hyperintensity restricted to anterior horns on axial views) or anterior pencil-like hyperintensity were found in 40,5-100% of cases. The cause for these findings is that the grey matter of the anterior horns exhibits the highest vulnerability to ischemia due to its high metabolic demands.

The posterior one-third of the spinal cord is more rarely involved. In the study of Novy et al, [13] including 27 patients, 37% of patients had anterior spinal artery patterns, 15% had anterior and 15% posterior unilateral patterns, 11% had central patterns and 7% had posterior spinal artery patterns. The most frequent location of infarction is the thoracic region. However, this is highly affected by the cause of spinal cord ischemia. If the infarction is postprocedural (after aortic or spinal surgery) the highest MRI abnormality will be most definitely located in the thoracic region followed by cervical and lumbar/conus regions.

Cerebrospinal fluid examination

The articles of Cheng et al, Zalewski et al, Novy et al, and Robertson et al, provided data regarding the evaluation of cerebrospinal fluid (CSF). In the study of Cheng et al, [12] including 22 patients, 7 patients were tested and 5 of them were found having elevated CSF protein concentrations without pleocytosis. Similarly, in the study of Novy et al, [13] 12 patients had an increased CSF protein concentration but no pleocytosis. In two studies by Zalewski et al, [10,15] 74% of the patients underwent a CSF examination and all demonstrated elevated protein levels. Only 8% had elevated nucleated cell count and 2% had supernumerary oligonuclonal bands. Finally, in the study of Robertson et al [8], including 27 patients, 44% of patients demonstrated elevated protein levels but normal cell count and only 7% demonstrated both elevated protein levels and cell counts.

Treatment

No treatment has been proven to reverse or treat ischemic spinal cord injury outside the surgical realm. Accordingly, there are no guidelines regarding spe-

cific therapeutic regimens in patients who have suffered spinal cord ischemia. Preventive measures, such as avoiding prolonged and profound hypotension during aortic surgery or the use of spinal somatosensory evoked potentials during aneurysm surgery have shown to be effective in preventing cord ischemia. Correction of underlying risk factors such as hypertension, smoking, heart disease and diabetes mellitus is very important. Regarding the studies included in this review, only 5 out of 14 provided data upon treatment of spinal cord infarction. In the largest study included in this review, conducted by Zalewski et al [10], immunotherapy for a suspected immune-mediated condition was given to 56% of patients, blood pressure augmentation to 6% and lumbar drain to 6%. Anticoagulation was initiated in 8% of 135 patients and at least one antiplatelet agent was used in 68% of patients. Antiplatelet and anticoagulation therapies have proven to be the most used treatments, for cerebral infarction. The perioperative role of CSF drainage is recognized in thoracic and abdominal aortic surgery; however, its role in the treatment of spinal cord infarction has not been studied.

Outcomes

Based on the case series included in this review, the percentage of favorable functional outcome is around 40-50%. As stated, predictors of poor outcome include severe neurological impairment (ASIA A or B) on initial examination, absence of Babinski sign, presence of sensory level and longitudinally extensive MRI lesions [8]. In general, motor deficits showed a higher frequency of recovery than sensory or sphincter deficits. In the study of Qureshi et al [11], through studying the long-term follow-up data of 89 survivors, it was shown that 42% of patients were using a wheelchair, 26% were using a gait aid, 33% walked unaided, 54% needed a bladder catheter and 29% still had significant pain. The long-term mortality after spinal cord infarction can range from 9% to 23%, as shown in different studies and it varies depending on etiology. Mortality is higher for patients with spinal cord infarction related to surgery or aortic aneurysm and dissection with poor prognosis. [16]

Discussion

Spinal cord ischemia can cause a great diagnostic confusion, making this entity underrecognized and frequently misdiagnosed as transverse myelitis. Zalewski et al, after studying most of SCI cases included in the published literature, proposed some diagnostic criteria. Based on these, spinal cord infarction has 3 major criteria. [10] The first criterion is a clinical one, and is no other than the rapid development of severe neurologic deficits within the first 12 hours after the onset of symptoms. The second criterion is the MRI findings supporting the infarction and excluding the spinal cord compression and the third criterion is the non-inflammatory cerebrospinal fluid profile that differentiates SCI from infectious and inflammatory disorders. Based on these three parameters, patients were classified as having definite, probable, or possible spinal cord ischemia. To further validate these criteria, the authors applied them in a cohort of 280 patients with non-ischemic diagnoses. Only 3.2% of patients met the criteria for possible spinal cord ischemia and none for definite ischemia, suggesting that the presented criteria are highly specific. [10]

The symptoms of spinal cord infarction develop quickly and usually reach a maximum within 12 hours in 50% of patients and within 72 hours in almost all patients. The clinical presentation depends on the vascular territory involved and the severity of the impairment varies widely from paraplegia to minor weakness.[4] Different clinical subtypes have been recognized: anterior and posterior spinal artery syndrome due to radicular territory infarction, and central and transverse infarctions due to general spinal cord hypoperfusion. Consistent with its functional neuroanatomy, ASA syndrome typically presents with abrupt onset of bilateral weakness, sudden back pain, flaccid paraplegia, loss of pain and temperature sensation below the level of the lesion, and autonomic dysfunction involving the bowel and the bladder. In ASA syndrome there is a sparing of proprioception and vibration sense. The posterior spinal artery syndrome leads to ipsilateral loss of light touch, vibration and proprioception while mostly sparing motor function. The PSA syndrome is usually unilateral and less severe, due to the presence of two posterior spinal arteries. Moreover, the central spinal infarction includes bilateral spinothalamic sensory deficit with sparing of the posterior columns. Motor deficits and sphincter

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dysfunction are usually absent. The transverse medullary infarction provides a rare presentation of sudden paraplegia/paraparesis, with complete sensory loss and autonomic dysfunction.

Diffusion-weighted magnetic resonance imaging seems to be the most reliable diagnostic tool for spinal cord ischemia. [17]However, it is technically challenging due to important limitations. The bone enclosing the spine causes magnetic field distortions and also the motion distortion caused by respiration, CSF, and arterial pulsation, as well as swallowing can result in distorted images.[18] The classical MRI findings in spinal cord ischemia are pencil-like hyperintensities from the involvement of anterior horn cells and on axial imaging this appears as two bright dots, the so-called owl eyes' sign. However, these changes are not specific and it is often difficult to distinguish SCI from other causes of acute non-compressive myelopathies based on MRI alone.

In their study, including 24 patients, Mawad et a,l [19] suggested that MRI lesions start in the anterior horns of the gray matter and progress to the posterior horns. They made a correlation between the presence of owl's eyes signs and motor deficit outcome. Patients with owl's eye signs usually retained partial motor function and had better outcomes than those with diffuse lesions involving the adjacent white matter. However, in the early stages the extent of the infarct can be difficult to be defined and this correlation hasn't been proven by other studies in this review.

Nonetheless, the absence of proprioceptive impairment at onset was associated with a better outcome. In anterior spinal artery syndrome, when there is proprioceptive impairment, it is suggestive of a more extensive infarct which involves the inner part of the dorsal columns and the posterolateral part of the lateral columns. The long-term outcome can remain poor in patients with complete or nearly complete syndromes, but the optimistic finding is that delayed functional recovery is possible and not infrequent. Half of surviving patients unable to walk after the onset of spinal infarction were able to walk on follow-up and even in patients with severe deficits, substantial functional recovery may occur over time. [20]

Regarding the treatment of spinal stroke, there are no clear guidelines. Immunotherapy, anticoagulant and antiplatelet therapy, and lumbar drain have been used. However, Seze et al, [21] in their retrospective study, found no difference in the clinical course of patients who all received antiplatelet therapy and some were additionally treated with corticosteroids or anticoagulation therapy. The use of agents such as prostaglandins, nimodipine, naloxone hydrochloride, adenosine, thiopental sodium, and magnesium has yielded some promising results in animal investigations; however, their effect in SCI needs further investigation. [22] The value of the modification of the risk factors of spinal cord ischemia, which are similar to many common vascular disorders such as stroke, myocardial infarction and renal failure, cannot be overestimated. Moreover, because this serious condition can occur in a wide variety of iatrogenic settings, special attention should be given during aortic and spinal surgery[23].

The current review has several limitations mostly inherent to the retrospective design of the studies included. In addition, the search was conducted by using one search engine (PubMed). Moreover, regarding the case series, not all of them shared the same characteristics or number of details. The timing of MRI scanning was variable and diffusion-weighted sequences were not routinely obtained. The value of therapeutic interventions could not be evaluated because of the lack of treatment standardization and the timing and duration of follow-up were not uniform.

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