Spinal cord trauma: pathophysiology, classification of spinal cord injury syndromes, treatment principles and controversies

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Abstract

Acute spinal cord trauma is a devastating injury which often leads to severe disability. The tissue response following the initial insult extends the cord damage, while there is limited repair potential with regards to axon regeneration resulting in permanent neurological deficits. Management of acute cord injury is an area of active research in order to stabilize the spine in a timely manner, minimize the secondary insult and promote regeneration. Methyl-prednisolone administration for limitation of the secondary injury phase and acute versus late operative treatment are areas of current debate among several authors. This article is an overview of all aspects of early and long term spinal cord injury management. It focuses on the patho-physiological mechanisms of the acute injury phase and the different clinical types of cord injury syndromes. The treatment principles are described along with an updated view on the controversial issues.

Keywords cord syndromes; methyl-prednisolone; neuro-plasticity; neuro-protection; spinal cord trauma

Introduction

The neural tissues forming the spinal cord are highly susceptible to injury and have little capacity for self-repair. Reversal of spinal cord injury continues to be one of the greatest challenges in medicine. Knowledge of patho-biology is rapidly evolving and components once thought to be detrimental such as glial scarring and inflammation are now believed to have beneficial effects.[1,2] Traumatic spinal cord injury (SCI) is typically caused by a contusive force to the spinal cord leading to activation of numerous mechanisms that both extend and limit the injury.[3]

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Neurons are especially vulnerable to injury because of the length, complexity and specificity of their connection. In addition, the receptor and membrane specializations that enable chemical and electrical neuronal transmission cause a high capacity for and vulnerability to major ionic shifts. The spinal cord components are rarely exposed to inflammatory cells and there is a specialized barrier between endothelial cells supported by astroglia that restricts movement of proteins and other molecules.[1]

Spinal cord salvage and repair are two primary goals of therapy.[2] Traditionally, the role of the Spinal Surgeon is in post-traumatic spinal cord salvage focussing on acute care, surgical decompression, vertebral stabilization and management of chronic complications, such as syringomyelia, tethering and deformity.[2,4] Neuro-protective and repair strategies are based on understanding of the temporal evolution of injury mechanisms. Spinal teams with surgical and scientific expertise will translate new advances from experimental studies into clinical studies aiming to design and apply new treatments.[1–3]

Epidemiology

The estimated annual incidence of acute SCI in the United States among those who survive a traumatic event is 40 per million population or approx. 12 500 per year.[1,5] The distribution of age at injury is bimodal; the first peak (approximately 50% new injuries) involves young adults and the second peak involves adults older than 60 years.[5,6] The average age of young adults has increased from 28.7 to 42 years.[5] Adults older than 60 are vulnerable to SCI due to age related bony changes, such as cervical spondylosis and stenosis, the effects of medication and sensory loss.[5] The clinical outcome in patients >60 years is considerably worse than that in younger patients. Approximately 50% of patients have cervical, 35% thoracic or thoracolumbar and 11% lumbar injury; the location of the remaining 4% is unknown or unreported. The single most commonly affected level is C5. The most frequently reported post-SCI neurologic category is incomplete tetraplegia (39.5%); complete paraplegia accounts for 22.1%, complete tetraplegia for 21.7% and incomplete paraplegia for 16.3%.[5] At least 20% of patients with SCI have other major injuries such as cerebral contusions or flail chest.[5]

Mechanisms of cord injury

The spinal cord may be injured by compression, contusion, laceration or vascular insult.[3] The impact of injury depends on the magnitude of initial insult and the underlying condition of the spinal cord. The difference between compression and contusion is in the rate of deformation.[1] In cord contusion, the compressive force exceeds the tissue components tolerance leading to disruption of axons and damage of neuron cell bodies, myelinating cells and vascular endothelium.

Mechanical failure of the osseo-ligamentous spinal column structure may lead to SCI by abrupt physical deformation of the cord substance (contusion) and/or by direct laceration/compression by bone fragments.[6] Gunshot injuries may cause direct laceration of the cord by the projectile or indirect injury by the bone/disc fragments.[6–8] Abrupt distortion and shearing by the blast cavitation of the projectiles' kinetic energy may also

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cause injury to the cord.[7] Knife injuries may cause direct complete or partial laceration of the cord.[9]

Based on the macroscopic findings, SCI can be classified into four groups: (a) *solid cord injury*, the least common type, is associated with normal appearance of the cord after injury; (b) *contusion*, the most common type, is associated with areas of haemorrhage and expanding necrosis/cavitation but with no disruption of the surface of the cord; (c) *laceration*, where is a clear-cut disruption of the surface anatomy; and (d) *massive compression*, where the cord is macerated to varying degrees.[10] In most instances, the anatomic degree of spinal cord damage does not correlate with the degree of functional loss.

Pathophysiology-neurological insult

The predominantly lipid structure of the spinal cord partially accounts for its vulnerability to injury. Aside from the pia matter there is very little connective tissue in the spinal cord in comparison with the peripheral nerves, which are much more resilient.

Primary injury

After the SCI the spinal cord is contused, may be partially lacerated but is rarely transected. The maximal neurologic deficit is observed immediately after a SCI because axonal transmission is disrupted or blocked by abrupt neuronal cellular damage, endothelial and blood vessel damage, haemorrhage and massive shifts in membrane potential and ionic concentrations.[1] This is mostly irreversible.[6]

Secondary injury

The secondary injury phase begins immediately and may extend for several days. The tissue damage continues during that phase substantially extending the size of the injury. Oedema and haemorrhage within the cord may spread from the primary site of impact over several rostral and caudal levels. Haemorrhage is more evident in the gray matter because of its rich vascularity. Endothelial damage leading to increased permeability and intracellular oedema, is a key factor in the recruitment of inflammatory cells.[6]

The secondary injury response can be divided into acute, intermediate and chronic phases. The intermediate phase starts a few days after injury and lasts for several weeks. The events of each phase are summarized in Table 1; however there is close interrelation among all phases without distinct borders between them.

Vascular injury/inflammatory response

The spinal cord is not exposed to inflammation like tissues as skin, bone, lungs, which frequently undergo healing process. Endothelial cells normally form a barrier that excludes the active blood components from the Central Nervous system (CNS).[1,17] This blood-CNS barrier is characterized by tight junctions between endothelial cells and strong interactions between the surrounding astrocyte foot processes and basal lamina.[1,17] Thus macrophages, lymphocytes and poly-morpho-nuclears are seldom observed in the normal spinal cord and the intrinsic microglia is quiescent. Also, CNS cells are rarely exposed to inflammatory cytokines (Table 2).

Key-stages of the spinal cord response to closed trauma[1,6,11–16]

Acute phase (up to 72 hours)	• Cord oedema, intracellular swelling • Haemorrhage • Regional cord perfusion shifts • Inflammatory response: free radical production, lipid peroxidation and cytokine release • Membrane instability: shifts in electrolytes and accumulation of neurotransmitters • Demyelination • Cell necrosis and apoptosis
Intermediate phase (days to weeks)	• Proximal and distal extension of oedema, necrosis and apoptosis • Continued inflammatory response • Vascular angiopathy • Peak levels of astrocyte and macrophage activity • Initial scar formation • Neuroplasticity • Spasticity
Chronic phase (months to years)	• Formation of fluid – filled cavity • Wallerian degeneration • Glial scar formation • Demyelination • Schwann cell proliferation • Syringomyelia • Tethered cord • Neurite sprouting, altered neurocircuits and chronic pain syndromes

Table 1

Endothelial damage is the primary event that initiates the cascade of SCI inflammation. Mechanical gaps between endothelial cells develop within 1.5 minutes of injury leading to damage of perivascular basement membrane, red blood cell extravasation, platelet aggregation and fibrin deposition. Platelet aggregates occlude vessels leading to ischaemia. Endothelial gaps promote influx of fluid and proteins thus producing oedema. Subsequent events promote microglial activation and leucocyte infiltration. The basal laminae are further degraded due to increased endothelial expression of vascular cell adhesion molecule. These events further exacerbate the loss of endothelial integrity, increasing vascular permeability and leucocyte influx.

The prominent cytokines present at SCI include IL-1, IL6, TNF-α, and TGF-1. Early expression of TNFα and IL1 by microglia enhances the recruitment of inflammatory cells to the injury site. IL1β is upregulated within one hour of injury, peaks at eight hours after injury and persists at least seven days.[1,11,17]

The four general classes of inflammatory cells that respond to SCI are microglia, neutrophils, macrophages and lymphocytes. Microglia, neutrophils, macrophages offer innate immunity and lymphocytes offer adaptive immunity.[6] Neutrophils enter the damaged spinal cord immediately after injury and reach peak

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