Pathophysiology of adult tethered cord syndrome: review of the literature

WILLIAM R. STETLER JR., M.D., PAUL PARK, M.D., AND STEPHEN SULLIVAN, M.D.

Department of Neurosurgery, University of Michigan Health System, Ann Arbor, Michigan

Object. Tethering of the spinal cord has been a recognized cause of neurological symptoms in pediatric patients and is increasingly being recognized as a cause of symptoms in adults as well. The pathophysiology surrounding spinal cord tethering has begun to be understood in the pediatric population but is still unclear in adult patients.

Methods. Using a PubMed database literature search, the authors reviewed the pathology and pathophysiology surrounding the tethered spinal cord, focusing particularly on the pathophysiology of adult tethered cord syndrome (TCS).

Results. Experimental data obtained in pediatric patients at surgery and in animal models indicate that spinal cord tethering causes a reduction in spinal cord blood flow and dysfunction of neuronal mitochondrial terminal oxidase. Retrospective analyses of patients undergoing surgery for adult TCS show that many adults developed symptoms following an event that could stretch the spinal cord, while others did not. Many patients also were found to have structural lesions in addition to a tethered spinal cord at diagnosis.

Conclusions. Both adult and pediatric TCSs are likely the result of a relative lack of blood flow to the spinal cord, causing dysfunction in mitochondrial oxidative phosphorylation. The likely reason the syndrome present later and differently in adults is that a secondary threshold of tension or a cumulative effect of repetitive, transient tension is placed on the cord before symptoms are recognized. (10.3171/2010.3.FOCUS1080)

KEY WORDS • adult tethered cord syndrome • pathophysiology • ischemia • spine surgery

Tethered cord syndrome was originally described in 1976 by Hoffman et al.7 after observing that the conus medullaris was affixed via an enlarged filum terminale to the sacrum in 31 children and that there was noticeable neurological improvement following release of the cord. Since that time, the term has encompassed many forms of occult spinal dysraphism in children who present with a constellation of neurological symptoms including motor, sensory, and urological complaints, as well as imaging findings of an affixed conus with a variety of structural pathologies including lipoma, tumor, fibrous tissue, and myelomeningocele, to name a few.1,2,4,12,15,22

Recently, it has become recognized that adults may also present with a variety of neurological complaints secondary to a tethered spinal cord.1,6,9,15 Unlike children, adult symptomatology is slightly different, with pain being the most common presenting symptom (rare in children3), and this is followed by sensory disturbances, motor dysfunction and weakness, and urinary dysfunction.1,2,13,15,18,20 Similar to the pediatric population, surgical intervention to release the adult tethered cord has proven to be successful in preventing further deterioration as well as sometimes improving symptoms and deficits. Thus, cord release has increasingly been accepted as a necessary intervention in symptomatic patients.2,6,9,10,15

The question as to what causes neurological dysfunction in patients with TCS has long been only theorized. Over the last 2 decades, there have been multiple advances in the understanding of the basic science and pathology behind the tethered spinal cord in animal models and in humans. These insights have begun to elucidate the pathophysiology behind this disorder.16,21–23 However, what is still not clear is whether the adult tethered spinal cord and the pediatric tethered spinal cord share the same disease process and pathophysiology, or if they represent 2 different pathological processes, which could explain the different ages at presentation and different presenting symptoms.

Methods

A comprehensive literature search was performed using the PubMed database for all journal articles published until March 2010. Key words used in the search included “adult tethered cord syndrome,” “pathophysiology,” “pediatric,” “outcomes,” and “surgery”; terms were searched individually or in combination. The appropriate articles for our review were selected based on the scientific investigations surrounding the pathology and physi-
ology of TCS in humans and animal models. In total, we found 4 papers addressing the basic science pathophysiology behind TCS, as well as many retrospective surgical analyses and reviews addressing the issue.

Results

Acute Model of Tethered Spinal Cord

Yamada et al.22 examined the redox ratio of cytochrome a,a, using dual-wavelength reflection spectrophotometry as a surrogate marker for the metabolic function of neurons in human spinal cords at surgery and animal tethered cord models. Changes in the ability of a cell to undergo oxidative metabolism can be identified by changes in the redox ratio of this (cytochrome a,a,) terminal oxidase of the mitochondrial electron transport chain used in oxidative phosphorylation of adenosine diphosphate to adenosine triphosphate. During a period of hypoxia, cytochrome a,a, becomes reduced and thus the redox ratio is increased and easily measured.

At the time of surgery in 7 pediatric patients with TCS, there was an abnormal unresponsiveness (no or only mild change in redox ratio) to transient induced hypoxia (via decreasing concentration of \( \text{FiO}_2 \)) prior to tethered cord release. However, after the release, there was a trend toward normal redox changes of cytochrome a,a, following transient hypoxia (increase in redox ratio). This change suggested that mitochondria prior to release were highly reduced, and thus, hypoxic changes did not produce significant further reduction of cytochrome a,a,, suggesting that there is a chronic inability of mitochondria to efficiently produce adenosine triphosphate in the tethered cord. The trend toward normal redox ratio changes following release suggests that there is potential for normal mitochondrial function following surgery.

These effects were further studied in an experimental cat model, in which a progressive amount of traction was placed on the filum terminale in a controlled setting, and reduction of cytochrome a,a, was determined. It was found that with the application of low and moderate amounts of traction, there was a marked trend toward cytochrome a,a, existing in the reduced state (thus indicating a state of relative ischemia), which was completely reversible after the traction was removed. When a large amount of traction was implemented, there was again significant reduction of cytochrome a,a,; however, after removal of the traction there was incomplete resolution of the oxidative state of cytochrome a,a,. This suggested that with a large degree of traction, irreversible damage to the spinal cord might occur secondary to the traction-induced mitochondrial dysfunction.

Chronic Model of Tethered Spinal Cord

Yamada et al.23 performed additional experimentation using the cat model to measure redox ratio changes and observe behavior changes at various time points up to 9 months following the imposition of chronic, isometric traction on the filum terminale. They observed that the cats’ hind limbs were weakened immediately following experimental tethering and that this weakness was worse in cats that had more traction applied to create the tethering. However, after several months’ time, the cats adapted to the tethering and were then able to use their hind limbs naturally. This process took longer in the group in which more traction was applied than in the group with less traction. The redox ratios were measured at the time of sacrifice (9 months)—when all subjects were noted to have normal observed hind limb function—and were noted to be no different than controls. Light and electron microscopy of spinal cord specimens obtained in these animals were also noted to be no different than those acquired in controls.

Blood Flow Studies in Tethered Spinal Cord

Schneider et al.18 used LDF to measure microcirculation of the spinal cord in 10 pediatric patients undergoing surgical tethered cord release. With detethering, it was noted that in all patients there was an increase in spinal cord blood flow as measured using LDF. In fact, on average, the spinal cord blood flow more than doubled. As a control, LDF was used to measure spinal cord blood flow in 5 patients undergoing dorsal rhizotomy. Blood flow to the spinal cord measured by LDF did not change in any of these patients at any point during the procedure and was similar to parameters measured in patients following tethered cord release.

Reduction of cytochrome a,a, through dual-wavelength reflectance spectrophotometry has also been examined by Yamada et al.9,25 following aortic occlusion in cat models. They found that as blood pressure and oxygen tension declined, there was a marked increase in the level of reduced cytochrome a,a, (redox ratio increased). Additionally, interneuron potentials measured on the surface of the dorsolateral surface of the cord were markedly decreased after aortic occlusion. Both redox ratio and interneuron potentials recovered after blood flow was restored. However, if blood flow was interrupted for a longer period of time (15 minutes), there was only a partial recovery. This data provided a link between Yamada and colleagues’ prior work with redox state of cytochrome a,a, and blood flow to the spinal cord.

Theorized Pathophysiology Based on Retrospective Analysis

The pathophysiology of adult TCS has been theorized by many groups based on their retrospective analyses of patients undergoing untethering surgery. Many of these theories take into account the aforementioned experimental data and extrapolate hypotheses as to how and why patients with adult TCS present in adulthood as opposed to childhood.

When Pang et al.15 first described adult TCS, they theorized the pathophysiology behind it based on a variety of precipitating factors that led to a patient’s presentation in 61% of their series. Three mechanisms were noted: 1) transient stretching of the spine, 2) mechanical constriction/narrowing of the spinal canal, and 3) spinal trauma, all in the presence of an already tightly tethered conus medullaris. In their series, examples of transient stretching included the lithotomy position during child-
Pathophysiology of adult tethered cord syndrome

birth, forced flexion of the hips following motor vehicle collision, prolonged sitting, and “missionary position” intercourse. Mechanisms causing spinal canal narrowing included heavy lifting, lumbar spondylosis/spondylolisthesis, and intervertebral disc herniation. Mechanisms of trauma included direct trauma to the lumbar spine as well as falling on the buttocks. Pang et al. theorized, based on the majority of their patients’ presentations following such a precipitating factor, that the amount of traction determines age of symptom onset. Thus, the degree of tethering on the conus in many adult patients may not be enough to cause symptoms until there is a precipitating factor that increases traction directed to the conus. Following Pang and colleagues’ initial description, many groups have noted similar precipitating factors in their patients with adult TCS, even up to 70% of patients.6

Long before Pang and colleagues’ description of symptom onset in ATCS,15 Breig1 demonstrated that flexion of the neck could cause sudden movement of the spinal cord. Repetitive tension resulting from various movements placed on a cord that is already tethered could, in theory, cause cumulative damage leading to adult-onset TCS.5,13,15,20 Yamada and Losner18 further categorized such movements that cause straightening of the lumbar spine and thus could potentially stretch a tethered spinal cord as the “three ‘B’ signs:” 1) difficulty sitting with legs crossed (“like Buddha”), 2) difficulty bending, and 3) difficulty holding a small amount of weight at the waist level (similar to the weight of a “baby”).

Additionally, many patients who present with adult TCS have structural lesions that are tethering the cord and causing symptoms. These lesions include tumor, myelomeningocele, lipomyelomeningocele, fibrous tissue and arachnoid adhesion surrounding the filum terminale, and scar tissue from prior operation, to name a few.5,9,10,14,17,18 Thus, it has been proposed that the adult patient with such an underlying pathology may present only after such pathology slowly progresses to the point that it significantly tethers (and therefore places traction upon) the cord.19,20

Adults may also present because of retethering from scar tissue formation following an initial operation for spinal dysraphism.1,6,31 Retethering is considered a relatively common postoperative complication following correction of pediatric spinal dysraphism.3 No studies were found analyzing the pathophysiology of retethering following operative intervention of pediatric TCS and spinal dysraphism.

Discussion

Since its first description nearly 2 decades ago,15 adult TCS has become an increasingly recognized pathological entity encountered by neurosurgeons. Multiple retrospective analyses have been performed, suggesting that this disorder is perhaps more common than previously thought, may cause significant neurological dysfunction, and may be treated adequately with surgical cord release.1,2,5,8,14,17 Common presenting symptoms,1,2,5,6,8,9,14,16,17,20 indications for surgery,5,6,8,10,13,15,17,18,20 outcomes following surgery,1,2,5,6,8,10,13,15,17,18,20 and complications after surgery5,8,10,14,17 have been well described in the adult TCS literature. However, the pathophysiology of adult-onset TCS is less clear. While there have been many advancements over the last 20 years to help explain the basic science physiology behind TCS, we do not know why a minority of patients with TCS do not present until adulthood. Furthermore, because both adult and pediatric TCS often present with different symptomatologies, it begs the question of whether the underlying pathology behind the 2 syndromes is different.

After the excellent work that Yamada et al.21–23 have performed over the last 20 years, it seems that in both human and experimental animal models of TCS there is dysfunction in neuronal mitochondrial terminal oxidase in the electron transport chain. Such inability to use oxidative methods to efficiently produce adenosine triphosphate via oxidative phosphorylation likely causes cellular dysfunction that ultimately leads to cell death. Similar experiments proved that similar mitochondrial redox dysfunction was observed in experimental models in both an acute and chronic model of spinal cord tethering; however, the dysfunction eventually improved in the chronic model.23 Although it was clear that this change in terminal oxidase redox state was caused by hypoxia, the cause of hypoxia in TCS could not be elucidated from the original experiments.22 It was later shown that alteration in cytochrome oxidase redox state could be caused by experimental cessation of blood flow.19 Furthermore, it has been shown by Schneider et al.,19 using LDF, that there was a relative decrease in spinal cord blood flow in vivo in patients with pediatric TCS. Following cord release, blood flow normalized to control levels.

Thus, it seems that in children and animal models alike, tethering of the filum terminale causes a reduction in blood flow to the spinal cord, causing local tissue hypoxia that ultimately causes dysfunction of neuronal mitochondria, which can lead to cellular dysfunction and death. Furthermore, it seems apparent that the degree of traction on the spinal cord 1) correlates with cellular dysfunction, and 2) determines the permanence of this dysfunction after traction is released. One can extrapolate that if the filum is under too much tension, blood flow to the cord is not only reduced but is cut off altogether, causing neuronal cell death and permanent dysfunction that will not reverse after blood flow is restored following cord release. This also seems to explain how a patient who has had symptoms for a longer period of time may have a less likely chance of regaining neurological function following filum terminale release.

Following the observations made during retrospective analysis of adults with TCS, it seems that despite differences in presenting symptomatology, adults with a tethered cord have many of the same findings as children intraoperatively and radiologically. Thus, does adult-onset TCS represent the same pathophysiological process that is seen in pediatric TCS, or does the delayed presentation indicate a different underlying pathological process altogether?

Many authors argue that what determines when symptoms begin is actually how much tension is on the filum terminale.1,5,18 This theory is consistent with the experimental data summarized above. Thus, adults who
are found to have TCS likely have always had a tethered spinal cord that has not been under significant tension. In children, symptoms develop as the child grows and the inflexible tethering of the filum is stretched and placed under tension. In this case, the degree of tethering is likely much greater than in adult patients with a tethered cord, and thus the necessary amount of tension placed on the cord is realized earlier in life when the child’s spinal column reaches a certain size. This also would explain why adults with TCS often present after a precipitating event.\(^1,2,6,8,15\) If the adult tethered cord is under just enough tension to not cause symptoms, any movement or lengthening of the spinal canal that would place slightly more traction on the already tethered cord may exceed the amount of tension that blood flow may overcome, thus producing hypoxia and symptoms. Thus, the patient with a tethered cord with only slight tension on the filum would be thrown over the “threshold” level of tension to reduce blood flow and cause symptoms if there was a precipitating event such as an acute disc herniation, for example.

This theory does not explain the existence of adult patients with TCS who do not present after a precipitating event. Rather, in these patients, it seems most likely that either 1) the underlying tethering process, such as fibrous tissue, scar tissue, tumor, or lipomyelomeningocele,\(^5,10,14,15,17,18\) progresses to the point that it places enough tension on the cord to overcome blood flow, or 2) the normal daily movements of the neck (as Breig described\(^3\)) and back place enough transient tension on the already tethered cord that they cumulatively produce enough ischemia periodically over the course of many years to begin to slowly cause symptoms.\(^6,13,15,20\) In the first case, the underlying pathology progresses until the tension it is placing on the tethered cord exceeds the threshold limit to cause symptoms. In reality, adult TCS is likely explained by both the “threshold” tension model and the repetitive, cumulative-effect model described above.

Thus, it seems logical that adult-onset TCS is also caused by a reduction of blood flow to the spinal cord, as implicated in children with TCS and animal models, because such a reduction in blood flow is likely related to the degree of tension the cord is under. The overall, underlying pathophysiology in adult TCS appears to be the same as that in pediatric TCS. However, the presentation of adult TCS is different because the reduction of blood flow to the cord occurs over differing periods of time in adult TCS and pediatric TCS. This may very well explain some of the different presenting symptoms in adults and children with a tethered cord (namely, that adults are more likely than children to present with chronic pain).

Conclusions

Both adult and pediatric TCSs are likely caused by tension placed upon the filum terminale, causing a reduction in blood flow to the spinal cord that, in turn, affects cellular respiration and function. The delayed presentation of adult TCS is most likely the result of the following: 1) the fact that there is a threshold level of tension required for symptoms that is not reached until events later in life precipitate further tension on the cord in some patients, whereas in other patients 2) the low level of transient tension that is placed on the tethered cord with movement does not cause neuronal dysfunction until years of cumulative, repetitive movement reduce blood flow. Despite the similar underlying pathophysiology, such variations to achieve reduction in blood flow may explain some of the different presenting symptoms among adults and children with tethered spinal cords.

Disclosure

Dr. Park is a consultant for Medtronic and DePuy Spine.

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following: Concept and design: all authors. Acquisition of data: Park, Stetler. Analysis and interpretation of data: Park, Stetler. Drafting the article: Stetler. Critically revising the article: Park. Reviewed final version of the manuscript and approved it for submission: Park, Sullivan. Study supervision: Park, Sullivan.

References


16. Schneider S, Rosenthal AD, Greenberg B, Danio J: A prelimi-
Pathophysiology of adult tethered cord syndrome

- 214–218, 1993
- Neurol Res 26:741–744, 2004
- Neurosurg Focus 16(2):E6, 2004
- Neurosurg Focus 23(2):E6, 2007

Accepted March 24, 2010.
Address correspondence to: Paul Park, M.D., Department of Neurosurgery, University of Michigan Health System, 1500 East Medical Center Drive, Room 3552, Taubman Center, Ann Arbor, Michigan 48109-5338. email: ppark@umich.edu.