Tethered Cord Syndrome

To the Editor: The recent article by Lee and colleagues (Lee GYF, Paradiso G, Tator CH, et al: Surgical management of tethered cord syndrome in adults: indications, techniques, and long-term outcome in 60 patients. *J Neurosurg Spine* 4:123–131, February, 2006) well presented the diagnosis and treatment of patients with true tethered cord syndrome (TCS). Symptoms and outcomes from half of these patients were similar to those of our Group 2 adult patients with TCS16,20 and to those described by Hoffman et al.4 in children. Of concern is that certain statements and discussions in the article may conflict with and lead to confusion about known information on TCS.

For example, the statement that the clinicopathophysiology of TCS “is poorly understood” is not consistent with several reports on the biochemical and physiological basis of this syndrome. Among these reports are studies by Yamada and colleagues who demonstrated a link between oxidative metabolic functioning, electrophysiology, and TCS, with impairments observed prior to TCS surgery and improvements noted after the release of cord stretching by surgery. Such studies support the theory that TCS is linked to (and likely is caused by) compromised energy metabolism and electrophysiology in the stretched spinal cord.12,13,22

To explain further the putative link between dysfunction of metabolism and electrophysiology in the stretched spinal cord, one should refer to 2 concepts. The first concept is that adenosine triphosphate (ATP) serves as the free energy source in the CNS. As a result, CNS function is exclusively dependent upon adequacy of ATP supply and CNS turnover of ATP is very high. Conditions that contribute to ATP limitations are quickly accompanied by physiological dysfunction. The second concept is that shifts in the reduction/oxidation ratio of the electron carriers of the mitochondrial respiratory chain (cytochromes) are indicative of changes in the metabolic activities that produce ATP. Many studies in isolated mitochondria and in CNS tissues, including the spinal cord, have shown that there is a shift toward reduction of the mitochondrial cytochromes under conditions of hypoxemia17 or ischemia.18

When the spinal cord is stretched under experimental conditions, the terminal cytochrome of the respiratory chain (cytochrome oxidase) becomes increasingly reduced, consistent with metabolic dysfunction from hypoxemia or ischemia. Consistent with these findings was a decrease in blood flow and electrophysiological compromise.14 When the cord was stretched beyond the mild to moderate degree, however, cytochrome became further reduced, whereas the decreased blood flow reached a plateau.14 Such studies suggest that stretching the spinal cord produces metabolic and electrophysiological dysfunction linked partly to decreased blood flow consequences, but exacerbated by additional stretching of the cord produced by such behaviors as forceful spinal flexion and extension. Electron microscopy studies suggest that further energy loss by neuronal membrane stretching produces abnormal ion channel opening, and contributes to Na, K, and Ca leakage.13

The putative links among cord stretching, metabolism, blood flow, and electrical activity should correspond to individual clinical cases with TCS. In a previous study, Yamada and Lonser6 divided adult patients with TCS into 2 groups. Patients in Group 1 were known to have neural spinal dysraphisms, such as myelomeningoceles (MMCs) and lipomyelomeningoceles (LMMCs), that were associated with stabilized neurological deficits from childhood, but had subtle progression of neurological signs and symptoms. Patients in Group 2 showed no neural spinal dysraphism and were asymptomatic until they developed subtle neurological symptoms in adulthood. In the patients in Group 2, the tethering site was the caudal end of the spinal cord connected to an inelastic terminal filum.

Half of the cases in the study by Lee et al. corresponded to our patients in Group 2, and apparently showed excellent recovery after surgery to untether the cord from a functional (neurological) lesion, located cephalic to the tethering site (see Category 1 below). In these cases, the surgical untethering of the cord is followed by excellent results, as shown in our Group 2 cases.16,20

However, the discussions of Lee et al. extend beyond the true TCS cases. Presumably, some cases with neural spinal dysraphism, such as those involving MMCs and LMMCs, may not belong to Category 1 (true TCS).15 For example, MMCs with a large placode, and large dorsal or transitional LMMCs, exert local compression or an ischemic effect on the spinal cord, and sometimes related to neuronal dysgenesis. Therefore, these cases may present with signs and symptoms similar to those of true TCS, but the neurological lesions are not the result of cord stretching. Careful neurological examination and MR imaging localization should reveal that the signs and symptoms are local but not cephalic to such anomalies (Category 2 cases).

Similarly, the term “postoperative tethered cord syndrome,” to which many articles refer for cases of MMC repair is often a misnomer, because the postoperative fibrosis formed surrounds the spinal cord and causes the local compression and ischemic effects. The neurological signs and symptoms are not caused by cord stretching, as observed in true TCS dysfunction that strictly corresponds to the lesion cephalic to the anatomical abnormalities.

In the past we categorized the expression “cord tethering,” which is derived from a visual impression that might lead to the diagnostic decision that anomalies con-
continuous to or attached to the spinal cord are always the sign of TCS.8,21

1) Category 1: This category of TCS was considered the true TCS exhibited by patients with neurological signs and symptoms that are closely correlated to a stretch-induced lesion in the spinal cord—that is, cephalic to the tethering site, such as an inelastic filum terminale, caudal lipoma (or LMMC), or sacral MMC.

2) Category 2: Although signs and symptoms resemble those of true TCS in this category, they are caused by local cord compression or ischemia, different from true TCS (Category 2A). In some patients, however, a detailed neurological examination may show symptomatology that indicates a cord lesion cephalic to anomalies, in addition to the result of local effects of compression and ischemia as mentioned above (Category 2B). In these cases, the extent of neurological localization and of the anomaly’s attachment to the spinal cord must be documented. This category also includes so-called postoperative TCS.

3) Category 3: Patients in this category typically present with thoracolumbar MMC and exhibit total paraplegia, as well as urinary and bowel incontinence due to the lack of functional neurons in the lumbosacral region of the cord. Based on the aforementioned categorization, only half of the authors’ cases (referred to as a tight filum), and possibly some of the LMMC and split cord cases, correspond to Category 1 (true TCS). Since Pang extensively described adult TCS, several useful papers have been published as listed in the authors’ table. The references used in the authors’ discussion also include a significant number of the cases described in Category 2.3,5,6,10 However, Iskandar et al.5 endeavored to isolate true TCS by selecting the patients with a tethered spinal cord4 and certain cases of LMMCs.

In Group 2 adult TCS cases with an inelastic filum, some of them without cord elongation11 or filum thickening,10–21 Yamada et al.10,20 reported that 100% of these cases (corresponding to Category 1) showed complete recovery or significant improvement in motor and sensory functions. In contrast, many of the authors’ cases and others3,5,10 experienced no neurological improvement but showed stabilization, although they were evaluated as a successful surgical result. It is probable that these results were obtained from the cases that corresponded to Category 2A.

As the authors stated on page 128 of their paper, “the pathophysiological origin of these symptoms is not understood.” This statement indicates that postoperative symptoms are not due to the underlying mechanism of TCS. Accordingly, the expression “clinicalpathophysiology” in the first paragraph does not have any correlation to pathophysiology of true TCS. We prefer the original terms “tethered spinal cord” and “tethered cord syndrome,” which were strictly based on the pathophysiology of TCS, to any expressions that are not discretely defined.

Shorei Yamada, M.D., Ph.D.
Austin R. T. Colohan, M.D.
Loma Linda University School of Medicine
Loma Linda, California
Daniel J. Won, M.D.
Kaiser Permanente Medical Center
Fontana, California

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RESPONSE: We thank Dr. Yamada and colleagues for their interest in our article and for their thoughtful com-
ments regarding the potential classification and pathobiology of adult TCS.²

In our article, which represents one of the largest single institutional experiences in the treatment of adult patients with TCS, we observed that the most common operative finding, observed in 39 patients (65%), was a tight filum terminale—either in isolation (in 17 patients) or in combination with other pathologies such as an intradural lipoma (in 11 patients). In the remaining 21 patients, there were a variety of complex congenital pathologies observed, including split cord malformation and LMMC; these cases were also frequently associated with a tight filum. Moreover, evidence of a low-lying conus was observed in all cases in our surgical series. It should be further noted that almost all patients in our series had preoperative and intraoperative electrophysiological recordings, which highlighted objective neurogenic pathology.³ Hence, the cases we have described would indeed fit the definition of Yamada and associates of a “true” TCS. Of note, our results are in agreement with other large series of patients with adult TCS.⁴

The pathophysiology of TCS is complex, and we would argue, remains incompletely understood. We recognize the important contributions that Yamada and associates have made to understand the pathophysiology of TCS, which includes mechanical tension and ischemic neural injury.⁵ Nonetheless, important aspects of the pathophysiology of adult TCS remain to be elucidated. We would argue that although a tight filum certainly is the most frequent pathology underlying TCS, other mechanical factors, including intradural adhesions, can result in static or dynamic injury to neural structures. Moreover, other potential cellular and molecular mechanisms including apoptosis, glutamatergic excitotoxicity, demyelination, altered molecular organization of ion channels on axons, and dysfunctional plasticity may all potentially contribute to the origin of neurological dysfunction in adult patients with TCS, although the contributions of these mechanisms requires confirmation by empirical evidence. Such mechanisms could account for the failure of some individuals to respond to surgical release of their tethered conus or for the continued clinical progression of a select group of patients with TCS.

We agree with Yamada and colleagues that the diagnosis of adult TCS is relatively straightforward in the patient without prior surgery. However, considerable judgment (based on a detailed medical history and physical examination supplemented by thorough MR imaging, neurophysiology, and urodynamics⁴) is required to ascertain which patients with previous surgical correction of a complex congenital intradural condition have recurrent tethering of the cord. To date, imaging features alone do not allow this diagnosis to be made because many patients with postoperative TCS will have complex intradural anatomy.

Based on our work, coupled with the important contributions of others in the field—including Yamada and associates—we advocate surgical repair of adult TCS in patients who present at an early stage of their clinical presentation. As discussed above, further translational research into the basic science, imaging, and physiology of TCS is required to further elucidate the complex pathophysiology of adult TCS.

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MICHAEL G. FEHLINGS, M.D., Ph.D., F.R.C.S.C.
University of Toronto
Toronto, Canada

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