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Primary and Secondary Tethered Cord and Association with Pediatric Lower Urinary Tract Dysfunction

Cagri Akin Sekerci[1] · Tufan Tarcan[1]

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Abstract

Purpose of Review Tethered cord syndrome (TCS) due to adhesion defect of the spinal cord is one of the major causes of lower urinary tract dysfunction (LUTD) in children. The aim of this article is to evaluate the association, diagnosis, and treatment of TCS with LUT disorders in children.

Recent Findings TCS is divided into two groups as primary and secondary depending on whether it is congenital or acquired. TCS can manifest with gait disturbance, pain, orthopedic deformities, and LUT symptoms. LUT symptoms may be the only symptom in some cases. TCS may cause neurogenic LUTD characterized by detrusor sphincter dyssynergia, urinary incontinence, and upper urinary tract damage in children.

Summary Primary urologic goal of surgical repair of TCS is prevention of upper urinary tract deterioration and improving LUT symptoms. Urodynamic studies revealing functional deterioration of the LUT are objective tests for surgical indication. Treatment should be planned by a multidisciplinary approach.

Keywords Primary tethered cord syndrome · Secondary tethered cord syndrome · Neurogenic LUTD · Urodynamic studies · Multidisciplinary approach

Introduction

Abnormalities of spinal canal development are the most common causes of neurogenic lower urinary tract dysfunction (LUTD) in children, and more than 90% of children have open lesions such as myelomeningocele (MMC) [1–3]. Tethered cord is an abnormal adhesion defect of the spinal cord and classified into primary and secondary types [4]. Primary tethered cord syndrome (PTCS) occurs due to sacral agenesis or occult spinal dysraphism (OSD) [4–6]. Secondary (acquired) tethered cord syndrome (STCS) is due to scar tissue following repair of MMC, meningocele, and other dystrophic anomalies [2, 7]. Tethered cord syndrome (TCS) may occur with weakness (55%), gait disorder (54%), scoliosis (51%), pain (32%), orthopedic deformities, and urological symptoms [8]. In some cases, LUTD may be diagnosed by a single symptom [9, 10]. TCS may cause neurogenic LUTD characterized by detrusor sphincter dyssynergia, urinary incontinence, and upper urinary tract damage in children [11]. Treatment requires multidisciplinary approach involving neurosurgery, pediatric urology, pediatric nephrology, orthopedics, and rehabilitation. The aim of this article is to review the roles of PTCS and STCS in the etiology of neurogenic LUTD in children under the light of the current literature.

Primary Tethered Cord Syndrome

PTCS occurs as a developmental defect of the central nervous system. The genitourinary system is one of the organ systems that is negatively affected [12]. In the embryological period, the mesoderm switches between the ectoderm and neuroectoderm during the primary neurulation of the spinal cord and forming the posterior bone and soft tissue elements.

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✉ Tufan Tarcan
tufan@marmara.edu.tr

Cagri Akin Sekerci
cagri_sekerci@hotmail.com

[1] Department of Urology, Division of Pediatric Urology, Marmara University, School of Medicine, Istanbul, Turkey

The disruption of separation at this stage causes multiple spinal cord pathologies including MMC, intraspinal lipoma, lipomyelomeningocele, and dermal sinus tract [13]. Secondary neurulation refers to the formation of backbone elements towards S2 level. In this process, the spinal cord rises and continues until regression reaches adult level. Errors occurring at this stage cause OSD such as fatty filum terminale and thick filum terminale [14]. Due to various anomalies of the spinal cord, PTCS occurs with the fixation under L1–L2 intervertebral space [15, 16]. Split cord malformation, spinal intradural tumor, and dermoid cyst are other causes of PTCS [17]. The degree of caudal traction of the spinal cord correlates with neurological symptoms [12].

Clinical Findings in PTCS

PTCS may affect multiple organ systems and may present with skin, neurological, orthopedic, and urological findings [18]. Skin lesions are divided into high and low risk for OSD [19]. Lipoma, tail, and dermal sinus are classified as high-risk lesions; atypical dimple, hamartoma, hemangioma, port wine stain, hypertrichosis, pigmentary nevus, and gluteal cleft the low-risk lesions [20]. Magnetic resonance imaging is recommended for children with a high-risk or at least two low-risk lesions [20]. The most common skin manifestation of OSD is subcutaneous lipoma, which is frequently associated with cutaneous hemangioma [19, 20]. Neurological findings may be varied depending on the underlying cause and age. Decreased spontaneous leg movements, abnormal reflexes, foot asymmetry, and leg atrophy may be seen in the newborn with OSD and walking disorder, asymmetric motor-sensory dysfunction, hyperreflexia, and back and leg pain in older children. The most common orthopedic deformities include clubfeet, leg muscle atrophy, and scoliosis. PTCS may occur with only urological symptoms and signs as urinary incontinence, urgency, frequency, abnormal voiding pattern, recurrent urinary tract infection, hydronephrosis, detrusor overactivity, and small bladder capacity without any other system symptoms [21, 22]. Bladder symptoms may not be very clear in the neonatal period, so the emergence of urological symptoms may extend to toilet training [21]. PTCS is also associated with other congenital syndrome and anomalies such as omphalocele, cloacal exstrophy, anorectal atresia, imperforated anus, VACTERL (vertebral anomalies, anal atresia, cardiac anomalies, tracheoesophageal fistula, and renal and limb anomalies), and presacral mass [23]. Ultrasonography (US) is an option in children younger than 6 months in the diagnosis of PTCS but has a limited role [24]. The gold standard method for the evaluation of OSD is MRI [25]. Anatomical details of neural structures, diameter of phylum, and vertebral level can be examined in T1-weighted MRI [25]. In children, the termination of the spinal cord under the L2 vertebral corpus and the diameter above 2 mm are considered abnormal [26, 27]. Invasive urodynamic studies are indicated in children with suspicion of neurogenic bladder in noninvasive urodynamic tests such as frequency/volume charts and uroflowmetry [28, 29]. Early neurosurgical approach has been shown to be protective against the disturbances of the urinary, gastrointestinal, and musculoskeletal system [1, 30].

Urodynamic Findings in PTCS

Urodynamic studies are one of the most important objective measures for the determination of neurological deterioration and the decision for surgical indication. The most common urodynamic findings are detrusor overactivity, detrusor sphincter dyssynergia, and compliance reduction [31]. Urodynamic evaluation is recommended between 3 and 6 months before untethering surgery [32]. In a study of 79 children who underwent tethered cord repair under the age of 3, 38% of children had a urological problem, 12.7% needs CIC, and urodynamic abnormalities were found in 45.5% preoperatively. Preoperative abnormal urodynamic and US findings did not predict major urological problems in this study. However, subcutaneous lipoma and preoperative musculoskeletal symptoms correlated with major urological findings [4].

Urologic Outcomes of Treating PTCS

Today, the timing of PTCS repair is a controversial issue. In the same study, it was reported that upper motor neuron or bladder findings were expected for indications of repair after a diagnosis of tethered cord [4]. Prophylactic repair of PTCS was performed without symptoms in some studies. In 2004, 16 children with tethered cord were evaluated and 25% of preoperative urodynamic abnormal findings improved after surgery [33]. In another study evaluating 29 children with tethered cord at 15 months of age and less, 82% of children were observed to have improved urodynamic findings after surgery [34]. Prophylactic repair was performed before toilet training, and not to evaluate clinical findings is a limitation of this study. In a study of 46 children with a mean age of 10.5 years who had PTCS in 84.8% of the patients, postvoiding residual urine volume decreased and bladder capacity increased following repair [17]. The authors reported that tethered cord repair may be beneficial in terms of urological findings in older children. Meyrat et al. developed a urodynamic scoring system consisting of four parameters for early and reliable diagnosis of neuro-urological disorders in children with tethered cord. This scoring system consists of bladder volume, compliance, detrusor activity, and vesicosphincteric synergism during voiding phase. The preoperative urodynamic studies' score of the children with tethered cord was significantly higher than the control group and improved postoperatively. The urodynamic studies' scoring system was

found to be reliable in determining the neuro-urological damage in children with tethered cord and useful in the detection of postoperative re-tethering [15]. In a study evaluating 147 children who were 6 years and older with low-lying cord or fatty filum terminale, the case of isolated cutaneous lesion and preoperative continence had a meaning in predicting postoperative continence, but pre-postoperative urodynamic findings were not predictive of postoperative continence [35]. Preoperative continence status has been shown to be the most important factor in predicting postoperative continence status [30]. A study of 44 children with tethered cord surgery who had a minimum follow-up of 2 years showed that the postoperative sixth month urodynamic findings predicted long-term urological outcomes [36]. Yener et al. evaluated 40 children with PTCS and found no correlation between symptoms and urodynamic findings despite the improvement in urological symptoms and urodynamic findings after repair [7]. In a retrospective study of 38 asymptomatic PTCS children between 2007 and 2010, no relation could be found between abnormal preoperative urodynamic findings and imaging. Twenty-one of 31 children with preoperative normal urodynamics had undergone repair, and urodynamic results were normal in 11 of 12 children who underwent postoperative urodynamics. They showed that urodynamic findings improved after repair in children with preoperative urodynamic abnormality. The authors reported that asymptomatic patients with preoperative abnormal urodynamic findings can be repaired, but in patients with normal urodynamic findings is controversial [31]. Late diagnosis, delayed treatment, and insufficient follow-up are common problems in children with myelodysplasia. In a retrospective study evaluating 476 children with myelodysplasia performed in Turkey in 2007, the rate of closed spinal lesions (lipomyelomeningocele, diastematomyelia, tight filum terminale, dermoid sinus, intradural lipoma) was found to be 15% [37]. Primary repair time of closed spinal lesions was found as an average age of 2.9 years. In the same study, the educational status of the mothers and the obstetric follow-up were evaluated by phone interview. It was shown that two-thirds of the mothers had education status of elementary level or lower and only 42% had adequate obstetric follow-up during pregnancy. These findings indicate that the socioeconomic status of parents is an important factor in the early diagnosis and treatment of children with myelodysplasia.

Secondary Tethered Cord Syndrome

STCS commonly occurs due to adhesions or infections following primary repair of MMC [38]. The mechanical stretching of the spinal cord with growth may cause ischemia in the neural tissues, which may lead to progressive neurological deficits. Neurological deficits may result in weakness of the lower extremities, loss of sensation, and foot deformities. However, the findings of bladder dysfunction may first manifest of STCS [10]. STCS is seen in 3–30% of children who have undergone spinal dysraphism repair [8, 39]. The majority of cases are between the ages of 2–8, and a smaller group is between 10 and 12 years of age [40].

Diagnosis of STCS

In children who have undergone MMC surgery, the diagnosis of STCS is usually difficult. The neurological deficit can often be kept secret or in very young children, the neurological examination may not produce adequate findings. Magnetic resonance imaging may not frequently be diagnostic if there is no recurrent MRI after primary repair [41]. Urological symptoms, such as urinary incontinence, symptomatic urinary tract infection, and encopresis, should be suspected of tethered cord. Neurological deficit and bladder dysfunction may increase progressively if untethering is not performed in STCS [42]. In STCS, the most common urodynamic anomaly is uninhibited bladder contractions; 17% reported postoperative recovery [1]. Urodynamic studies are the gold standard method for the evaluation of neurogenic LUTD. However, urodynamic studies are difficult and are invasive techniques; therefore, studies on urine biomarkers have been raised in recent years. Some studies have shown that urine nerve growth factor, transforming growth factor beta −1, and brain-derived neurotrophic factor levels increase with neurogenic detrusor overactivity and decrease after intradetrusor botulinum neurotoxin A injection in children with myelodysplasia [43–45]. With further studies in the future, these biomarkers can be used in the follow-up of children with myelodysplasia and may play an important role in early detection of neuro-urological deterioration.

The main urologic goal of the treatment of STCS is to prevent upper urinary tract deterioration. In a study evaluating 56 children with STCS and average age of 4.1 years, 58% of the children were diagnosed with urological and 42% of them were diagnosed with neuro-orthopedic damage. In the same study, 48.2% of the children had fever UTI, 19% upper urinary tract dilatation, and 30% vesicoureteral reflux preoperatively; 45% of dilatation and 47% of VUR improved after repair. Likewise, bladder capacity and detrusor leak point pressure significantly improved at sixth months after repair. Urodynamic improvement in children diagnosed before 7 years of age and underwent untethering surgery was found to be significantly improved after 7 years of age [2]. In a study evaluating 25 children with myelodysplasia followed for an average of 9.1 years, 8 children (32%) had neurosurgical deterioration and MRI-confirmed tethered cord in the follow-up period. All 8 children underwent untethering surgery. Although normal voiding function was maintained in 2 children after surgery, mild and moderate neurogenic bladder dysfunction continued in 6 children. According to this study, authors emphasized that the first 6 years of life had

a higher risk for STSC and that close follow-up, early diagnosis, and timely surgical repair were important [10]. In another study that included 20 children, urodynamic findings were improved in 60% of children following surgical release in STCS [46]. In a study in which 20 children underwent untethering surgery following MMC, urodynamic parameters improved in 35% postoperatively, and only one child had postoperative deterioration [47]. In the study, in which 23 children underwent secondary untethering surgery with a mean age of 8.8, urinary symptoms were observed in 56.5% of the patients before the untethering and 87% of them had neuro-orthopedic symptoms. After untethering surgery, 61.5% of urological and 65% of the neuro-orthopedic symptoms were improved; 73.9% of children achieved continence [39]. In a study evaluating the effect of primary neurosurgical repair time on neuro-urologic prognosis, STSC was found to be significantly higher in children who underwent late primary repair ($n = 67$) compared with early primary repair (within the first 72 h of life, $n = 62$). In this study, the importance of early primary repair is underlined because of both the positive effect on neuro-urologic functions and the reduction of STSC risk [48].

Conclusions

In children, primary goals of surgical repair of TCS are prevention of upper urinary tract deterioration, treatment of LUTD, and adaptation to social life with ensuring continence. However, it is difficult to diagnose the PTCS and STCS because the symptoms are often unclear and not specific. PTCS associated with OSD should be considered in treatment-resistant LUTD especially in the presence of skin stigmata, and appropriate imaging should be performed. STCS should be considered in cases with symptomatic or urodynamic worsening that may include recurrent urinary incontinence, symptomatic urinary tract infections, and abnormal urodynamic findings following primary repair in children with open neural tube defect. Therefore, periodic follow-up is important for early diagnosis of STCS in children with spinal dysraphism. Urodynamic studies are helpful tests to decide on surgical intervention. It is possible to improve urological symptoms and urodynamic findings after untethering surgery in a subgroup of patients. Appropriate treatment should be planned by multidisciplinary approach.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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Unfortunately, there are few studies on the effect of tethered cord on lower urinary tract functions in children in recent years. These studies are important in terms of showing the relationship between urodynamic findings and tethered cord syndrome.

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