Symptomatic

The Symptom-Based Handbook for Ehlers-Danlos Syndromes and Hypermobility Spectrum Disorders

Edited by
Clair A. Francomano, Alan J. Hakim,
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ELSEVIER

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This book is dedicated to all those people with Ehlers-Danlos syndromes and hypermobility spectrum disorders who endured the long search for answers—the symptomatic.

CHAPTER 38

Progressive leg weakness and urinary incontinence

I have leg weakness and numbness, low back pain, and urinary incontinence

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Editors' general overview

The diagnosis of tethered cord syndrome (TCS) is based upon history and examination, confirmed in many cases—though not all—by MRI findings. In adults, back and leg pain (worse when walking up steps), weakness, sexual dysfunction, neurogenic bladder, or rectal incontinence are typically reported. In addition to decreased sensation and weakness of the legs, there is usually pain when raising the leg from a lying position (a positive stretch/traction sign), and often scoliosis, hammertoes, or pes cavus (high arch) foot deformity. Headache in the lower back of the head and hand numbness may occur as a remote effect of TCS. In children, the history may include toe walking, delayed walking, and involuntary urination. The diagnosis of TCS should be made with caution in the pediatric population, where urinary disorders are common.

Urodynamic studies should be ordered and usually demonstrate a neurogenic bladder. The lumbar MRI may show a low-positioned conus (the lower tip of the spinal cord), spina bifida occulta (incomplete bone closure of a spinal lamina), fatty filum, terminal syrinx, and scoliosis. The finding of peripheral neuropathy may signal diabetes, neuropathy due to medication, or other rare disorders such as Charcot-Marie-Tooth disease. Surgical treatment in well-selected patients is generally very effective in relieving the symptoms and improving the neurological deficits mentioned. The reader is referred to the chapters discussing sacral pain (including Tarlov cyst and sacroiliac joint pain), pelvic-abdominal pain, leg pain, cervical, and thoracic spine pathology.

Keywords: Low back pain, Urinary incontinence, Neurogenic bladder, Fatty filum, Scoliosis, Sacral sensory-motor deficits, Low lying conus, Tethered cord, Cauda equina, Terminal syrinx.

Case report

Summary of case report

A teenager with hypermobile Ehlers-Danlos syndrome (hEDS), progressive leg weakness, and urinary bladder retention was found to have tethered cord syndrome. Surgical untethering resulted in marked improvement of low back pain, leg weakness, and urinary bladder function.

Symptomatic
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Chief complaint

The patient reported progressive back aches, loss of leg function, leg pain after day-to-day activity, and urinary retention, with progression over the course of three years.

Relevant history

An 18-year-old female reported stabbing, aching, and soreness in her tailbone. Progressive leg weakness necessitated use of a wheelchair for longer distances; her legs would sometimes lock, and she could not move or feel them. These episodes happened twice a week, and had been gradually worsening in frequency and intensity over the previous year. After an active day in school, she developed intense pain in her back and legs, the right leg more than the left. Her first symptoms of low back and leg pain followed an ankle injury six years before she presented for evaluation.

Urinary symptoms began with inability to empty the bladder in her toddler years. As a child, she went to the bathroom infrequently, and there had been suspicion of urinary retention; she had frequent UTIs. There were no issues with her bowel function. Around 12 years of age, the patient experienced frequent jolts in her legs and uncontrolled tremors, which sometimes affected her entire spine, prompting a diagnosis of restless leg syndrome and growing pains. She also noted that her back felt tight. Her mother and pediatrician were concerned about progressive scoliosis; however, no further workup was initiated. She had always been flat-footed. She complained daily headaches and dizziness. In her early teens, she underwent extensive physical therapy and was able to maintain her day-to-day function. However, the benefit of physical therapy diminished and became short-lived. Her quality of life progressively declined. She was diagnosed with hEDS three years before the current evaluation.

Following her diagnosis of TCS, she was diagnosed with other comorbid conditions, including hyperadrenergic postural orthostatic tachycardia syndrome (POTS), mast cell activation syndrome (MCAS), restless leg syndrome, and gastroparesis and irritable bowel syndrome (IBS). The medication list reflected the medical management of her comorbidities. Her family history was positive for hEDS in her mother and two younger brothers.

Physical findings

The patient appeared well. The focused neurological exam shows a 5/5 appropriate strength bilaterally in her upper extremities, but asymmetric weakness in the lower extremities: right lower extremity showed diminished strength 4/5 in hip flexion, knee extension and flexion, and foot dorsi- and plantar flexion. The left leg functions tested were 5/5 throughout. There was an increased tone in the right hamstrings and ankles, and clonus in her right foot. No obvious deficits to light touch and sensation. Reflexes were 2+ at the biceps and triceps tendons, and 4+ bilaterally in the patellar tendons. A slight thoracolumbar curvature and a faint sacral dimple were noted.

Imaging, tests, and lab studies

She was diagnosed with hEDS based on physical findings and the absence of molecular genetics findings for vascular- and classic-type EDS. A T1- and T2-weighted brain MRI, MRI of her cervical, and thoracic and lumbar spine showed no cranial abnormalities or craniocervical pathologies. The spinal cord had normal signals. The lumbar MRI showed the conus of the spinal cord ending at the mid L1 vertebral level. T1 sequences showed a slight hyperintense signal at the conus/filum transition indicating dysplastic or fatty conus pathology (Fig. 1).

An urodynamics study (UDS) showed detrusor/sphincter dyssynergia and reduced bladder capacity suggestive of neurogenic bladder. Cystometry and bladder and kidney ultrasound did not show any anatomical bladder abnormality or obstructive bladder dysfunction to explain retention.

Differential diagnosis

The following diagnoses should be considered in cases of progressive leg weakness and urinary incontinence:

- multiple sclerosis
- spinal cord tumors (neuroma, meningioma, astrocytoma, ependymoma)

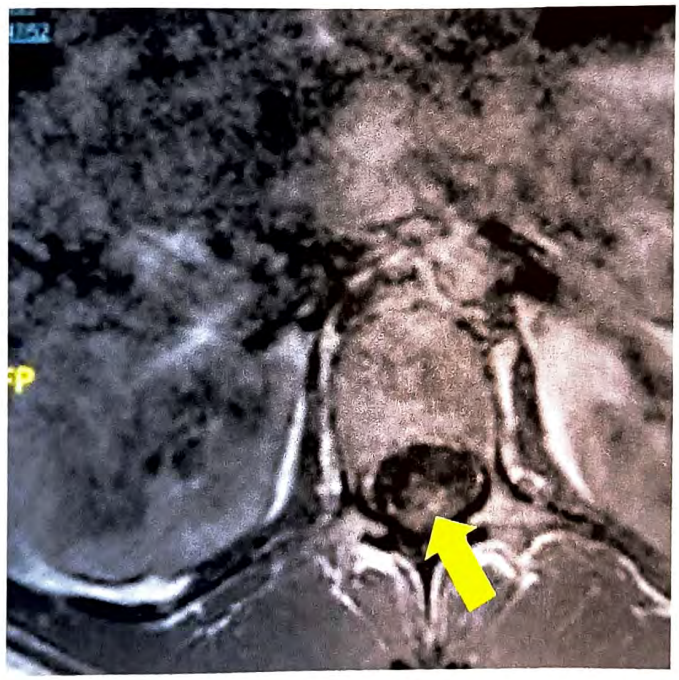


Fig. 1 MRI of the lumbar spine of the patient presented. The T1-weighted image, axial view through the filum at the L2 level, showing subtle, hyperintense signal consistent with dysplasia of the filum *(arrow). (Credit: Deidentified original image.)*

- congenital spine vertebral anomaly, spinal stenosis, or instability (spondylolisthesis, pars defect)
- spina bifida
- cervical or thoracic instability, cord compression, tethering, tumor
- vascular malformations (arteriovenus fistula)
- viral or infectious etiologies

Working diagnosis

Tethered cord syndrome in the setting of EDS

Treatment

After exclusion of other pathologies and exhaustion of medical management, surgical intervention for de-tethering of the spinal cord with microsurgical resection of the filum terminal was offered. The patient underwent a partial removal of the upper L2 spinous process with microsurgical opening of the dura to approach the filum resection below the conus. The filum terminale appeared thickened and hypervascular. A microsurgical mapping of the cauda equina and resection of the filum terminale were performed with EMG monitoring. Fig. 2 shows an intraoperative microsurgical photograph of the filum terminale. The patient was discharged five days postoperation without complications; the incision was healing well. The pathological specimen was consistent with fibrovascular tissue, embedded with ependymal cells, rare ganglion cells consistent with filum terminale (Fig. 3).

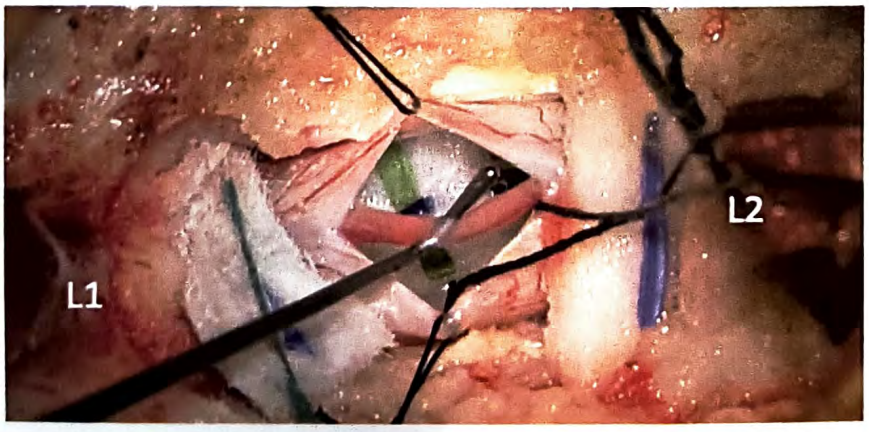


Fig. 2 Intraoperative exposure of the filum terminale under surgical microscope. The filum is elevated out of the cauda equina with the micronerve hook and appears thickened, dysplastic, and hypervascular. *(Credit: Deidentified original image.)*

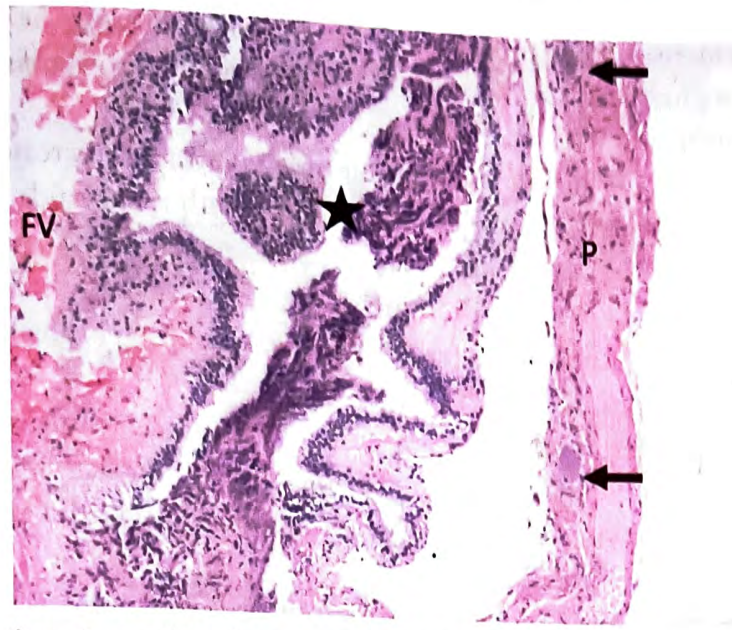


Fig. 3 Pathological specimen of the filum terminale (H&E stain). Shows the pathological prevalence of embryonic elements and reminiscence of embryonic tissue in the filum with abundant ependymal lining *(star)*, embedded peripheral nerves (P), dysplastic ganglion cells *(arrows)*, as well as fibrovascular tissue (FV). *(Credit: Deidentified original image.)*

Follow-up

At the three-month follow-up, the patient was no longer in need of her wheelchair. She also reported improved tailbone and back pain. She was completing physical therapy to improve her leg tone and core strengthening, and reported improved bladder sensation and emptying of the bladder. The surgical incision was well-healed.

A lumbar spine MRI six months after surgery showed no sign of arachnoiditis or pseudomeningocele. One year postsurgery, the patient reported no problems with voiding and emptying the bladder, and urological assessment confirmed a completely recovered voiding profile. The patient had regained full strength in her legs with normal endurance when walking, and normal physical capacity with regular exercise. The neurological exam showed full recovery of lower extremity strength (5/5), equal tone in the hamstrings and ankles, and resolution of the right ankle clonus. She was about to enter college.

Discussion

In this case of tethered cord syndrome in the setting of hEDS, the diagnosis was substantiated by a history of progressive leg weakness, loss of walking capacity, and urinary retention. The relevant history included a pediatric history of UTIs, restless leg syndrome, and growing pains consistent with early-onset tethered cord syndrome. The neurological

exam showed an increase in leg tone, hyperreflexia, and weakness in the symptomatic leg. Adjunct studies included an urodynamic study showing detrusor/sphincter dyssynergia suggestive of neurogenic bladder dysfunction.

The asymmetric neurological presentation of leg weakness, increased tone and pain are established neurological signs of TCS in children with spina bifida aperta, in whom the tethered cord is due to placode tethering with anatomical tethering of the spinal cord to the dorsal elements. Those children are also monitored with urodynamic testing, which typically show detrusor sphincter dyssynergia, one of the hallmarks of neurogenic bladder.

These same characteristic findings are biomarkers to be included in the thorough workup of a patient presenting with unexplained back pain, leg weakness, leg pain, and loss of bladder function, particularly in a young person without any other findings of degenerative spine abnormalities.

MRI findings may include low lying conus at or below the L2-3 disk space, and evidence of a thickened or fatty infiltrated filum terminale (Fig. 4), which have been associated with abnormal embryonic retrogressive differentiation of the embryonic spinal cord (Cochrane, 2014).

However, this patient did not present with the classic finding of a low-lying conus; her diagnosis is thus considered "radiographically occult tethered cord syndrome" or "tethered cord syndrome with conus at the normal level" (Warder and Oakes, 1994; Wehby et al., 2004). Though still controversial, radiographically "occult" tethered cord has been discussed as an entity in the pediatric population presenting with unexplained findings of neurogenic bladder (Wehby et al., 2004). The finding of an extended T1 hyperdense signal, as described in this patient, may be acknowledged as a supportive imaging finding in this setting of patients for the diagnosis tethered cord syndrome. Other supportive findings include scoliosis, terminal syrinx (a syrinx at the distal end of the spina cord or conus), and spina bifida occulta (usually at S1). It should be acknowledged that the MRI is a weak biomarker for the various pathologies of the filum terminale that cause tethered syndrome, particularly in patients with connective tissue disorder.

There has been increased focus upon tethered cord syndrome in the EDS population, in whom progressive neurological decline of the lower extremities is not solely explained by the hypermobile condition (Henderson et al., 2017). Recent research has reported abnormal collagen structure on transmission electron microscopy (TEM) as well as inflammatory changes in the filum terminale, which render the filum inelastic; the increased stiffness of the filum in conjunction with increased mechanical range of motion of the spine in the with hEDS may predispose this population to TCS (Klinge et al., 2022). Collagen abnormalities—malalignment and disheveled collagen—have been described in tendons and ligaments in patients with EDS, consistent with mechanical overuse, and the abnormal bio-dynamic profile with loss of stress strain buffering capacity (Moeller et al., 2014; Nielsen et al., 2014). The pathological and intraoperative findings

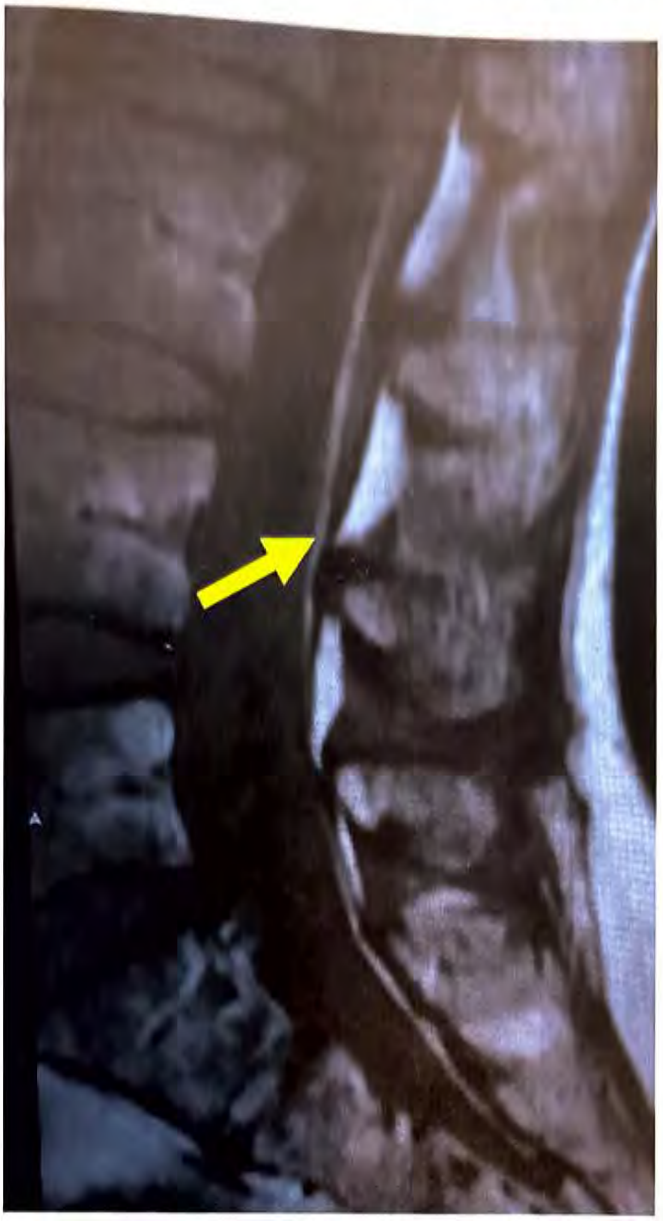


Fig. 4 MRI of lumbar spine (T1-weighted, sagittal midline view). Demonstrates a fatty filum terminale *(arrow)*, which is characteristic of tethered cord syndrome. The filum runs from the lower tip of the conus to the S2 level, where it passes through the dura posteriorly. *(Credit: Deidentified original image.)*

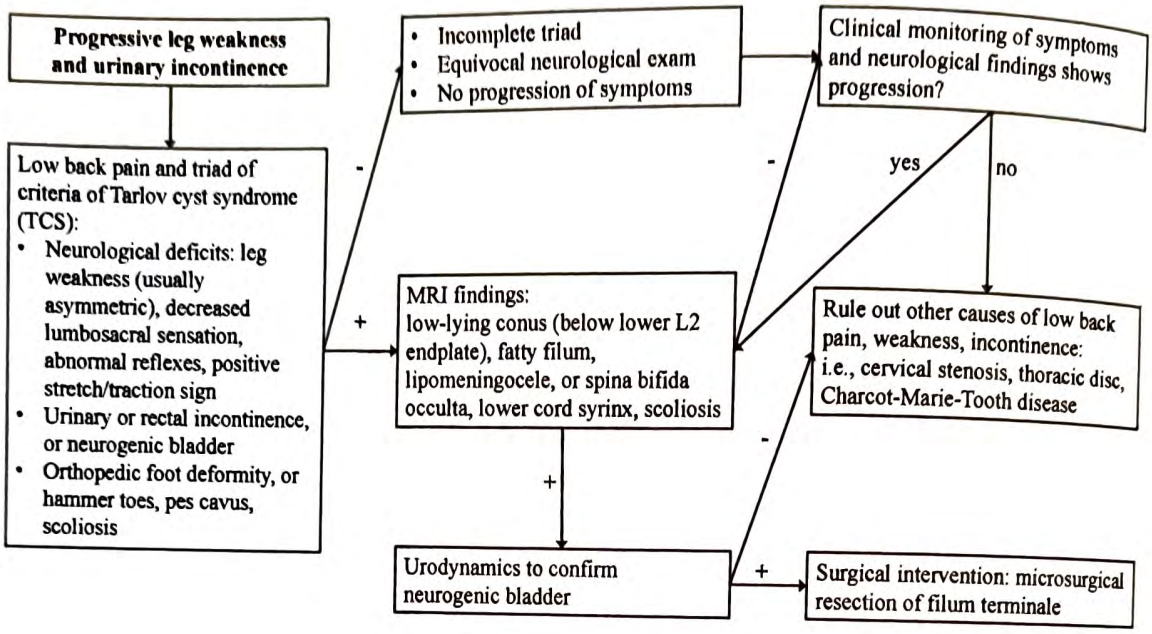
in this patient, such as hypervascularity and abnormal embryological tissue in the filum terminale, are well described in the pediatric population surgically treated for the presentation of TCS (Selcuki et al., 2003).

Conclusion

Tethered cord syndrome in the EDS population is a clinical diagnosis, where MRI often demonstrates the conus in a normal position. Patients with hereditary connective tissue

disorders are likely predisposed to a tethered cord syndrome from mechanical overuse and structural deficiency of the collagen fibrils, as also shown in other ligaments and tendons in this population. Tethered cord syndrome might be considered a comorbidity of EDS. The distinct filum pathology and the abnormal biodynamics associated with mechanical overuse of the filum terminale are not demonstrated by MRI.

Diagnostic and treatment algorithm



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