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Adult-Onset tethered cord Syndrome: Case series from a comprehensive interdisciplinary spine center

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A R T I C L E I N F O

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A B S T R A C T

Introduction: Diagnosis, pathophysiology, and rationale for surgical intervention in adult-onset tethered cord syndrome (ATCS) remain controversial. In this population, comorbid degenerative spinal disease (DSD) and prior trauma may sometimes distract from radiologic evidence of TCS.

Methods: We retrospectively reviewed electronic medical records of consecutive patients (2011–2019) presenting with back pain, lower extremity neurological symptoms, and/or urinary or bowel symptoms, who had radiologic evidence of fatty filum terminale (FT) and/or low-lying conus (LLC) in the setting of degenerative spine disease, and who underwent surgical detethering of the spinal cord. Medical history, presenting symptoms, MRI reports, and postoperative outcome data were collected and summarized. FT specimens were analyzed using histology and transmission electron microscopy (TEM). Correlation of preoperative characteristics with outcome were assessed using multivariate logistic regression.

Results: Forty-nine patients (mean age 47.9 ± 17.6 years) diagnosed with ATCS were included. Nineteen (38.8 %) had undergone prior spine surgery. From baseline to one-month post-op, the proportion of patients with neurologic symptoms decreased from 100 % to 77.8 % ($p < 0.001$), back pain from 87.8 % to 48.9 % ($p < 0.001$), urinary symptoms from 79.6 % to 26.7 % ($p < 0.001$), and bowel symptoms from 34.7 % to 6.7 % ($p < 0.001$). Differences remained significantly lower at three-months and 12-months postoperatively ($p < 0.05$). On MRI, LLC was seen in 75.5 % of patients, fatty FT in 8.2 %, and filum lipoma in 69.4 %. Evidence of DSD was observed in 87.7 % of patients, and prior trauma was reported by 32.7 %, neither of which was correlated with surgical outcome. Forty-six FT specimens were assessed for histology, and 26 for TEM. In addition to known neuronal components of the FT, the collagen ultrastructure revealed collagen corkscrewing and beading (57.7 %) and fibril swelling (57.7 %) on TEM.

Conclusions: Surgical intervention resulted in symptom improvement including resolution of urinary incontinence for many patients diagnosed with ATCS, even in the presence of comorbid degenerative spine pathology.

Abbreviations: ATCS, adult-onset tethered cord syndrome; FT, fatty filum terminale; FL, filum lipoma; LLC, low-lying conus; DSD, degenerative spinal disease; MRI, magnetic resonance imaging; TEM, transmission electron microscopy; DRG, dorsal root ganglion.

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1. Introduction

Tethered cord syndromes (TCS) are a group of rare neurological conditions thought to be caused by mechanical tethering or presence of inelastic tissue within the filum terminale (FT), a strand of fibrovascular connective tissue that extends caudally from the conus medullaris (the "conus") to the coccyx. It has been postulated that the primary functions of the FT are to provide longitudinal support to the spinal cord and to stabilize the conus medullaris during motion that alters the length of the spinal canal (e.g., bending at the waist). When the FT fails to protect the neural elements of the lumbar spine from these changes in length via its interface with the conus, symptoms of TCS may occur. Certain structural changes in the FT, such as reduced viscoelasticity and thickening, may produce a disproportionate increase in tension within the spinal cord, potentially an essential factor in the manifestation of TCS symptomatology.[1,2] The clinical features of TCS typically occur as a triad that includes neurological, urological, and musculoskeletal signs and symptoms. Lumbar lower back and lower extremity pain are the most common symptoms in patients with onset of TCS in adulthood, often with report of pain that is worse with lumbar flexion.[3,4].

Since many cases of TCS present in children, the typical clinical course of the sub-population of patients who present with their first symptoms in adulthood is not as well documented. The symptoms of so called "adult onset TCS" (ATCS) are both less specific and more gradual in onset than those of pediatric onset TCS.[3] In a review performed by Aufschnaiter et al. of patients with ATCS in the setting of spina bifida occulta, the most common presenting symptoms were pain (81.6 %), weakness (72.3 %), sensory disturbances (78.7 %), and urinary dysfunction (68.5 %).[3] Overt radiological evidence of TCS such as LLC or lipomatous tissue within the FT on magnetic resonance imaging (MRI) may be broadly suggestive of this congenital pattern of origin. However, literature on the broader ATCS population, especially those patients with less clear radiologic evidence, is quite limited. Coupled with the fact that TCS is rarely considered a diagnostic and therapeutic option in adults even in the setting of low-lying conus (LLC) or fatty and thickened FT on MRI, these factors make accurate diagnosis and referral challenging. Instead, patients are often referred for degenerative disc disease observed on imaging, suspected musculoskeletal injuries, and non-TCS neurologic and urologic conditions. Accordingly, patients often receive multiple misdiagnoses (e.g., fibromyalgia and other chronic pain syndromes) that delay referral for definitive neurosurgical care. Unfortunately, delayed time to treatment of TCS has been associated with worsening neurologic function following surgical therapy.[3,5].

These trends underscore the need for further categorization of ATCS, identification of clinical biomarkers, prognostic indicators for positive postsurgical outcomes and improved understanding of underlying mechanisms which contribute to pathology. In the present study, we present a retrospective case series of consecutive patients who were diagnosed with ATCS after presenting to our comprehensive spine center with back and lower extremity neurological symptoms in the setting of imaging with evidence of degenerative changes of the spine and the finding of a fatty or thickened FT and/or LLC. After interdisciplinary review of the treatment options and findings, patients with the symptomatic triad were considered for microsurgical resection of the FT for detethering of the spinal cord. Our study comprehensively documents the medical history, symptomatic and radiologic presentation, pathologic findings, and postoperative outcomes of patients treated for ATCS. We also examine histopathologic and ultrastructural characteristics within the resected FT which might contribute to the pathophysiology of ATCS.

2. Methods

2.1. Study population

This study was designed as a retrospective chart review coupled with prospective histopathologic and ultrastructural analysis of previously collected FT tissue samples. All patients ≥ 18 years old who underwent surgical resection of the filum terminale internum for TCS between February 2011 and February 2019 were considered for inclusion. Patients were excluded if they had no radiologic signs of TCS (LLC, FT fat signal, or FT thickening of ≥ 2 mm) or if insufficient baseline data were available for analysis. Patients diagnosed with spina bifida aperta were also excluded.[4,6] Records were reviewed for preoperative data (demographics, history of precipitating traumatic event, comorbidities of interest, symptomatic presentation), diagnostic data (pre- and post-operative radiologic evidence of TCS, preoperative urodynamic testing results when available), and postoperative symptomatic and complication data 12 months following surgery. Radiologic diagnoses were taken from the primary radiologist reports originally issued with the images; diagnostic imaging was not re-interpreted for the purposes of this study. Furthermore, because many patients only underwent imaging of the lumbar spine postoperatively, we report rates of all-level (cervical, thoracic, and lumbar) degenerative spinal disease (DSD) findings only in the preoperative setting and only lumbar findings postoperatively. When reporting postoperative symptoms, symptoms were considered resolved if they were not described in postoperative clinical notes at three months and 12 months. This study was approved by the local institutional review board with exemption from informed consent (IRB #1389608).

2.2. Filum terminale histology & electron microscopy

Excised FT specimens were processed and analyzed for histopathologic examination according to standard hospital procedure. Specimens were formalin fixed and embedded in paraffin in the Department of Pathology following surgical resection. Later, all available samples from subjects included in the retrospective review were sectioned at a slice thickness of 4 μm and resultant slides stained with Haemotoxylin and Eosin (H&E) for general histological analysis.[7] The adipose content of the FT tissue was quantified as a composite "adipose score", with absence of adipose tissue scoring zero points, 0–10 % of the FT containing adipose tissue scoring one point, 10–50 % scoring two points, and > 50 % scoring three points. Vasculature was scored as "prominent" if the width of single vessel was one third the width of the specimen or greater. Slides were photographed using an Olympus BX45 microscope (Olympus Corporation, Tokyo, Japan) and a SPOT Insight 2Mp Monochrome FireWire Digital Camera with SPOT imaging software (SPOT Imaging Solutions, Sterling Heights, MI).

A subset of FT samples was also made available for transmission electron microscopy (TEM). FT samples were fixed in glutaraldehyde prior to being washed in upgraded alcohols for dehydration followed by four changes of propylene oxide, infiltrated and embedded in epon-araldite.[8] Ultra-thin (80 nm) sections were cut using Reichert-Jung Ultracut E (Leica Microsystems; Wetzler, Germany) ultramicrotome and stained with uranyl acetate and lead citrate. Specimens were analyzed for the presence of collagen fibril corkscrewing and beading, flower-like fibrils and/or variation in cross-sectional fibril size, swollen fibrils, disorganized fibrils, fragmented fibrils, myelinated axons, unmyelinated axons, and axonal degeneration.

2.3. Surgical technique

In each case, a single level interlaminar lumbar laminectomy was performed, with the specific level determined as needed for a high FT approach with respect to the level of the conus medullaris observed on preoperative MRI. Using subperiosteal dissection, the index level was exposed and confirmed with intraoperative fluoroscopy. The dura was opened in a linear fashion with a 15 blade, and the arachnoid was excised to reduce risk of re-tethering. After neurophysiological identification, an approximately 2–5 cm segment of the FT internum was transected using an ISOCOOL cautery at power five (DePuy Synthes;

Warsaw, IN) at the superior and inferior border of the specimen. The caudal filum was then removed using DeBakey forceps, with gentle, cranially directed pressure to detach the caudal filum from the thecal sac. The dura is then closed with a running 5–0 prolene suture. The FT specimens were banked in formalin at the time of surgery for later pathologic analysis. The surgical microscope as well as intraoperative neuromonitoring were used throughout.

2.4. Statistical analysis

Medical history, symptomatic presentation, radiologic findings, and pathologic characteristics were summarized using descriptive statistics (*Microsoft Excel, Version 16.16.4*). The proportion of the study population documented as reporting each symptom of interest was compared between preoperative baseline and one-month, three-month, and 12-month postoperative visits using two-tailed t-tests. P-values < 0.05 were taken to indicate statistically significant differences. Symptoms were also grouped into categorical variables including elements of the TCS triad (neurologic, urologic, musculoskeletal) as well as bowel-related symptoms. Logistic regression analyses were conducted to assess associations of medical history factors and histologic characteristics with postoperative symptom improvement within each category at the three-month postoperative visit (*Python* software, *v3.6.5*). The relationship between medical history factors and symptom improvement was assessed using multivariate logistic regression. Univariate associations between pathology findings and symptom improvement are also reported.

3. Results

3.1. Patient characteristics

Forty-nine (n = 49) patients met inclusion criteria for the study. Included patients had a mean age of 47.9 (±17.6) years (range 18–78) and comprised 32 males and 17 females. Nineteen patients (38.8 %) had undergone a prior spinal or craniocervical surgery (three low lumbar partial FT resections at an outside hospital in the setting of spina bifida occulta, two for Chiari decompression, 14 for degenerative spinal disease). Medical history in 16 patients (32.7 %) included a prior traumatic incident which they associated with symptom onset. Specific traumatic events reported by patients included five motor vehicle accidents (10.2 %), three falls with impact to the lower back (6.1 %), five instances of intense or repetitive physical activity involving bending or lifting (10.2 %), and three surgical procedures shortly before onset of symptoms (6.1 %). Comorbidities present in our cohort included Arnold-Chiari Malformation in eight patients (16.3 %), dysautonomia in two (4.1 %), restless leg syndrome in four (8.2 %), small fiber neuropathy in two (4.1 %), Lyme disease in two (4.1 %), fibromyalgia in five (10.2 %), rheumatoid arthritis in one (2.0 %), diabetes mellitus in seven (14.3 %), and depression or anxiety in 26 (53.1 %). Additional demographic and medical history data are reported in Table 1.

Table 1
Adult-onset tethered cord syndrome (ATCS) patient demographic and medical history.

Patient Characteristics (n = 49)	
Demographic Details	
Male	32 (65.3 %)
Age (years)	47.9 (±17.6)
Past Medical History	
Prior Spine Surgery	19 (38.8 %)
For Tethered Cord Syndrome / Detethering	3 (6.1 %)
For Chiari Decompression	2 (4.1 %)
For Degenerative Spinal Disease	14 (28.6 %)
Precipitating Traumatic Incident Prior to Symptom Onset	16 (32.7 %)
Motor vehicle accident	5 (10.2 %)
Fall with impact to the lower back	3 (6.1 %)
Intense or repetitive physical activity involving bending or lifting	5 (10.2 %)
Surgery shortly before symptom onset	3 (6.1 %)
Arnold-Chiari Malformation	8 (16.3 %)
Dysautonomia	2 (4.1 %)
Restless Leg Syndrome	4 (8.2 %)
Psychiatric Illness	26 (53.1 %)
Depression	23 (46.9 %)
Anxiety Disorder	15 (30.6 %)
Bipolar Disorder	2 (4.1 %)
Diagnosis with any other cause of peripheral pain	16 (32.7 %)
Small Fiber Neuropathy	2 (4.1 %)
Lyme Disease	2 (4.1 %)
Fibromyalgia	5 (10.2 %)
Rheumatoid Arthritis	1 (2.0 %)
Diabetes	7 (14.3 %)
Lumbar Neurocutaneous Sign(s)	9 (18.4 %)
Pediatric History of Tethered Cord Symptoms (e.g., report of growing pains, prolonged bladder and bowel dysfunction in childhood)	19 (38.7 %)

3.2. Symptomatic presentation

All patients (100 %) presented with neurological signs and symptoms, and most patients also reported urinary (79.6 %) and/or bowel (34.7 %) symptoms (Table 2). The most common individual signs and symptoms were back pain (87.8 %), fatigue (83.7 %), lower extremity pain (83.7 %), lower extremity paresthesia (69.4 %), hyperreflexia on exam (59.2 %), lower extremity motor weakness on exam (57.1 %), sensory deficit to light touch on exam (49.0 %), and urinary leaking (44.9 %). Eighteen patients (36.7 %) reported headaches at baseline, and nine (18.4 %) had lumbar neurocutaneous signs such as sacral dimpling. Among 24 patients (49.0 %) who underwent pre-operative urodynamic testing, nine had neurogenic bladder, three had stress incontinence, and six had detrusor instability. Detailed symptoms are presented in Table 2.

3.3. Radiologic signs

All patients had preoperative MRI available for review. Thirty-seven patients (75.5 %) had an LLC (conus at or below the inferior L2 endplate). Of those, the majority (n = 30, 61.2 %) had conus termination below the L4 vertebral body. Consistent with the described surgical technique above ("Methods"), surgical approach in each case was just distal to the conus position observed on preoperative MRI (Table 3). A syrinx was present in 18.4 %, 8.2 % had radiologic evidence of fatty infiltration in the FT, and 69.4 % had FT lipomas. Of those patients with six-month postoperative MRI follow-up (n = 41, 83.7 %), the proportions with observed LLC, syrinx, fatty FT, and lipoma were 24.4 % ($p < 0.001$), 22.0 % ($p = 0.676$), 29.3 % ($p = 0.009$), and 0.0 % ($p < 0.001$), respectively. Forty-three patients (87.7 %) had evidence of DSD noted by the radiologist pre-operatively, and 32 (65.3 %) had lumbar DSD specifically. There was a non-significant increase in the proportion of patients with degenerative disease noted at the lumbar spinal levels post-operatively (75.6 %, $p = 0.293$). Radiologic data and details are summarized in Table 3.

3.4. Exemplary case #1

A 66-year-old female patient presented to neurosurgery clinic seven months after L4-5 posterolateral decompression and fusion for degenerative disc disease at an outside clinic. The patient was experiencing ongoing lumbar back pain, bilateral radicular lower extremity pain, and urinary dysfunction including leaking episodes. On examination, she had full strength in upper and lower extremities, no clonus, and no sensory deficits to light touch. She also had a sacral dimple, a neurocutaneous finding consistent with spina bifida occulta.[9] Updated MRI of the entire spine demonstrated ongoing degeneration of the L4-5 facet joints, ligamentum flavum hypertrophy, moderate lumbar central canal narrowing, and grade 1 anterolisthesis of the L4 on L5 vertebral

Table 2
Patient preoperative and postoperative symptom presentation.

Signs and Symptoms	Pre-Op (n = 49)	1 Month Post-Op (n = 45)	p-value	3 Months Post-Op (n = 38)	p-value	12 Months Post-Op (n = 23)	p-value
Subjective Urinary Symptoms	39 (79.6 %)	12 (26.7 %)	**<0.001****	13 (34.2 %)	**<0.001****	9 (39.1 %)	**<0.001****
Urinary Leaking	22 (44.9 %)	5 (11.1 %)	**<0.001****	9 (23.7 %)	**0.041***	6 (26.1 %)	0.130
Urinary Retention	14 (28.6 %)	5 (11.1 %)	**0.035***	3 (7.9 %)	**0.016***	1 (4.3 %)	**0.018***
Urinary Frequency	7 (14.3 %)	3 (6.7 %)	0.236	3 (7.9 %)	0.360	3 (13.0 %)	0.889
Urinary Urgency	15 (30.6 %)	6 (13.3 %)	**0.045***	3 (7.9 %)	**0.009***	3 (13.0 %)	0.111
Urinary Hesitation	8 (16.3 %)	1 (2.2 %)	**0.020***	2 (5.3 %)	0.111	0 (0.0 %)	**0.040***
Frequent UTIs	7 (14.3 %)	1 (2.2 %)	**0.037***	1 (2.6 %)	0.063	1 (4.3 %)	0.216
Pain with Urination	3 (6.1 %)	1 (2.2 %)	0.355	0 (0.0 %)	0.123	0 (0.0 %)	0.231
Urodynamic Testing	24 (49.0 %)	–	–	–	–	–	–
Neurogenic Bladder	9 (37.5 %)	–	–	–	–	–	–
Stress Incontinence	3 (12.5 %)	–	–	–	–	–	–
Detrusor Instability	6 (25.0 %)	–	–	–	–	–	–
Subjective Bowel Symptoms	17 (34.7 %)	3 (6.7 %)	**<0.001****	5 (13.2 %)	**0.022***	2 (8.7 %)	**0.019***
Constipation	8 (16.3 %)	2 (4.4 %)	0.063	4 (10.5 %)	0.442	1 (4.3 %)	0.191
Incontinence	13 (26.5 %)	1 (2.2 %)	**<0.001****	3 (7.9 %)	**0.026***	1 (4.3 %)	**0.027***
Neurologic Symptoms & Signs	49 (100.0 %)	35 (77.8 %)	**<0.001****	34 (89.5 %)	**0.020***	19 (82.6 %)	**0.002***
UE Pain	8 (16.3 %)	1 (2.2 %)	**0.020***	5 (13.2 %)	0.685	0 (0.0 %)	**0.040***
UE Cramps	3 (6.1 %)	0 (0.0 %)	0.093	0 (0.0 %)	0.123	0 (0.0 %)	0.231
UE Paresthesia	15 (30.6 %)	6 (13.3 %)	**0.045***	5 (13.2 %)	0.056	1 (4.3 %)	**0.012***
LE Pain	41 (83.7 %)	27 (60.0 %)	**0.010***	22 (57.9 %)	**0.007***	11 (47.8 %)	**0.001***
LE Cramps	19 (38.8 %)	2 (4.4 %)	**<0.001****	4 (10.5 %)	**0.003***	1 (4.3 %)	**0.002***
LE Paresthesia	34 (69.4 %)	9 (20.0 %)	**<0.001****	13 (34.2 %)	**<0.001****	9 (39.1 %)	**0.014***
Fatigue	41 (83.7 %)	17 (37.8 %)	**<0.001****	15 (39.5 %)	**<0.001****	7 (30.4 %)	**<0.001****
Clumsiness	14 (28.6 %)	4 (8.9 %)	**0.015***	2 (5.3 %)	**0.005***	2 (8.7 %)	0.060
Hypersensitivity	5 (10.2 %)	0 (0.0 %)	**0.028***	0 (0.0 %)	**0.043***	1 (4.3 %)	0.409
General Headaches	18 (36.7 %)	10 (22.2 %)	0.127	8 (21.1 %)	0.116	3 (13.0 %)	**0.040***
Seizures	1 (2.0 %)	0 (0.0 %)	0.341	1 (2.6 %)	0.857	1 (4.3 %)	0.585
Hyperreflexia	29 (59.2 %)	1 (2.2 %)	**<0.001****	1 (2.6 %)	**<0.001****	0 (0.0 %)	**<0.001****
Clonus	5 (10.2 %)	0 (0.0 %)	**0.028***	0 (0.0 %)	**0.043**	0 (0.0 %)	0.115
Light Touch Deficit	24 (49.0 %)	1 (2.2 %)	**<0.001****	2 (5.3 %)	**<0.001****	2 (8.7 %)	**<0.001****
Nonspecific LE Weakness	28 (57.1 %)	0 (0.0 %)	**<0.001****	0 (0.0 %)	**<0.001****	0 (0.0 %)	**<0.001****
Composite Motor Exam Score	96.1 (±7.3)	99.7 (±1.5)	**0.002***	99.9 (±0.8)	**0.002***	100.0 (±0)	**0.013***
Musculoskeletal Symptoms & Signs	49 (100.0 %)	26 (57.8 %)	**<0.001****	21 (55.3 %)	**<0.001****	14 (60.9 %)	**<0.001****
Back Pain	43 (87.8 %)	22 (48.9 %)	**<0.001****	18 (47.4 %)	**<0.001****	10 (43.5 %)	**<0.001****
Neck Pain	9 (18.4 %)	2 (4.4 %)	**0.036***	3 (7.9 %)	0.164	2 (8.7 %)	0.294
Sacral Pain	12 (24.5 %)	4 (8.9 %)	**0.045***	5 (13.2 %)	0.190	3 (13.0 %)	0.271
Chest Pain	4 (8.2 %)	2 (4.4 %)	0.467	2 (5.3 %)	0.602	1 (4.3 %)	0.559
Shoulder Pain	9 (18.4 %)	2 (4.4 %)	**0.036***	3 (7.9 %)	0.164	1 (4.3 %)	0.112
Ankle Deviation	5 (10.2 %)	1 (2.2 %)	0.116	0 (0.0 %)	**0.043***	1 (4.3 %)	0.409
Tiptoeing	2 (4.1 %)	0 (0.0 %)	0.174	0 (0.0 %)	0.212	0 (0.0 %)	0.333
Frequent Tripping	9 (18.4 %)	0 (0.0 %)	**0.002***	2 (5.3 %)	0.069	3 (13.0 %)	0.578
Toe Curling	3 (6.1 %)	0 (0.0 %)	0.093	1 (2.6 %)	0.446	0 (0.0 %)	0.231
Use of Walking Aids	8 (16.3 %)	5 (11.1 %)	0.470	4 (10.5 %)	0.442	3 (13.0 %)	0.723

Abbreviations: UTI = Urinary Tract Infection; UE = upper extremity; LE = lower extremity.

Table 3
Radiologic presentation of patients undergoing tethered cord surgery.

Radiologic Characteristics (Magnetic Resonance Imaging)	Pre-Op (n = 49)	Post-Op (n = 41)	p-value
Signs of Tethered Cord Syndrome	49 (100.0 %)		
LLC (L2 – L3)	5 (10.2 %)	6 (14.6 %)	0.528
LLC (L3 – L4)	2 (4.1 %)	2 (4.9 %)	0.857
LLC (L4 – L5)	30 (61.2 %)	2 (4.9 %)	**<0.001***
Syrinx	9 (18.4 %)	9 (22.0 %)	0.676
Fatty Infiltration in the Filum	4 (8.2 %)	12 (29.3 %)	**0.009***
Filum Lipoma	34 (69.4 %)	0 (0.0 %)	**<0.001***
Signs of Degenerative Disease	43 (87.8 %)	–	–
Lumbar Degenerative Findings	32 (65.3 %)	31 (75.6 %)	0.293
Any Canal Stenosis	17 (34.7 %)	–	–
Any Foraminal Stenosis	20 (40.8 %)	–	–
Any Spondylolisthesis	12 (24.5 %)	–	–
Any Disc Disease	16 (32.7 %)	–	–
Any Disc Herniation	5 (10.2 %)	–	–

Abbreviations: LLC = low-lying conus medullaris.

segment, but no myelopathy or spinal cord compression to explain extent of symptoms. The radiologist made note of a conus medullaris with normal location and configuration and fatty infiltration of the proximal FT internum visible on axial T1-weighted images (Fig. 1).

After discussion with the interdisciplinary surgical and non-surgical spine management teams, the diagnosis of ATCS was favored given the above clinical findings and symptoms. The patient proceeded to surgical detethering and partial FT resection per standard protocol. Previously placed segmental instrumentation at L4-L5 was also removed, given evidence of posterolateral bony fusion no longer requiring fixation and anticipated possible need for subsequent multilevel interbody fusion through a minimally invasive approach. In the immediate postoperative period, the patient reported improvement in pain and resolution of urinary incontinence in the early postoperative period, but 8 months later was still experiencing ongoing back pain with radiculopathy consistent with progressing lower lumbar facet arthropathy and canal stenosis. After further medical optimization including stopping statin medications, she underwent minimally invasive lateral lumbar interbody fusion at L3-4 and L4-5 with percutaneous placement of new posterior segmental instrumentation from L3-L5. After surgery, her back and leg pain markedly improved, and remained improved 12 months later at outpatient follow-up.

3.5. *Exemplary case #2*

A 60-year-old male patient presented to neurosurgery clinic with 6

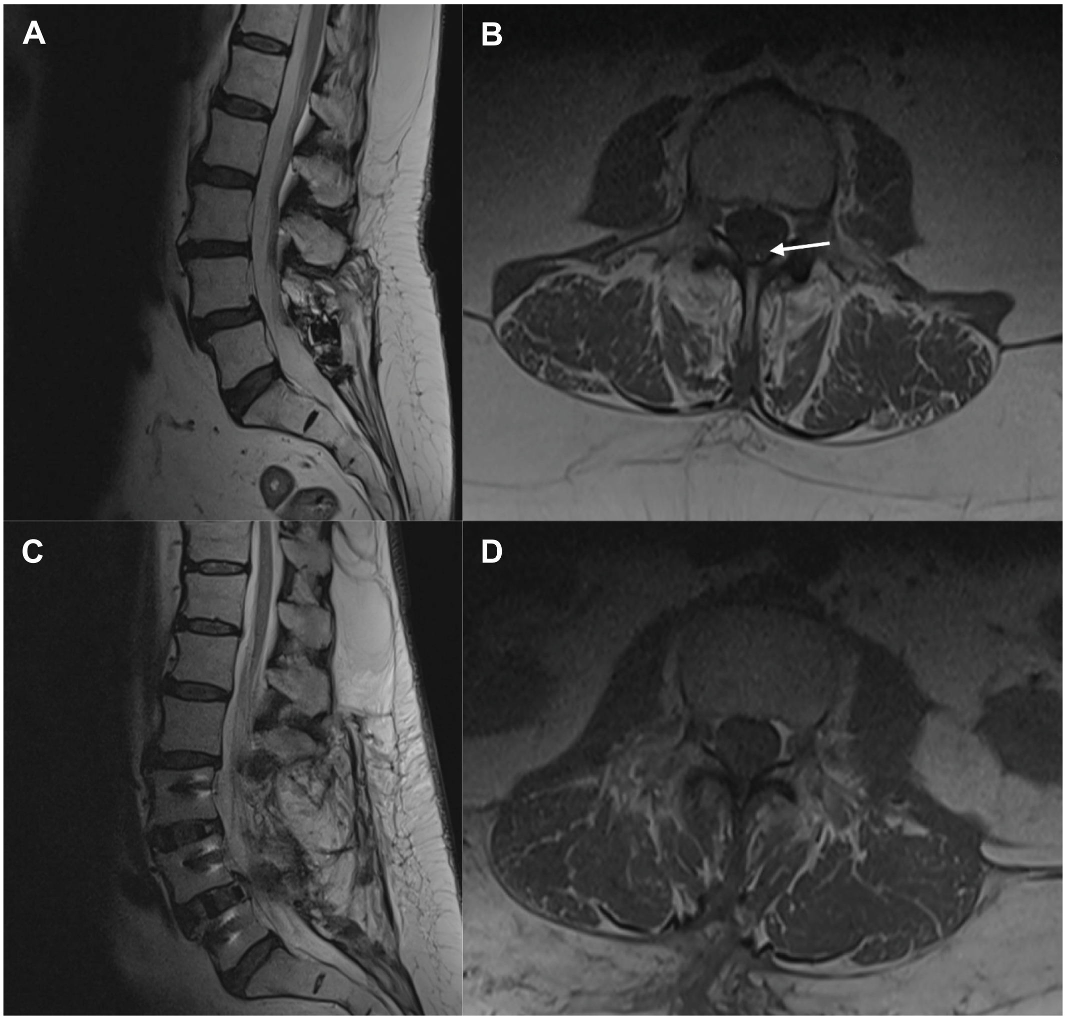

Fig. 1. Representative Case #1. 67F with fatty filum terminale and symptoms of tethered cord syndrome presents following previous L4-5 posterolateral fusion. Preoperative (A,B) and postoperative (C,D) midsagittal T2-weighted and axial T1-weighted MRI demonstrating degenerative stenosis, prior L4-5 posterior defect, and fatty filum terminale (arrow). Postoperative imaging is following detethering (procedure 1) and multilevel lateral interbody fusion at L3-L5 with placement of posterior percutaneous segmental instrumentation (procedure 2) as described in the case vignette.

months of progressively worsening low back pain, radicular lower extremity pain and weakness, left worse than right, and trouble stopping urinary in the setting of known urethral stricture. Neurological examination demonstrated left lower extremity clonus (3 +) and bilaterally reduced lower extremity strength with hip flexion and knee flexion/extension. Sensory examination was intact to light touch. He had been seen in pain management clinic for steroid injections without improvement. Baseline MRI was consistent with spina bifida occulta, demonstrating sacral arachnoid cyst with filum thickening at the sacral level as well as degenerative cervical and thoracic spinal stenosis without myelopathy (Fig. 2). Since the degenerative pathology did not explain most of the patient’s presenting symptoms and exam findings, interdisciplinary discussion led to the recommendation for surgical detethering for ATCS. At five-month follow-up, back and leg pain had almost completely resolved, urinary symptoms had improved, and the patient reported an increase in overall activity level.

3.6. Postoperative outcome

The cohort size decreased over time as fewer patients returned for follow-up, with 45 of the 49 patients (91.8 %) attending office visits at one-month post-op, 38 (77.6 %) at three months, and only 23 (46.9 %) at 12 months, limiting conclusions that can be drawn particularly about the 12-month endpoint. However, categorizing TCS-associated signs & symptoms into four sets (neurologic, musculoskeletal, urinary, and bowel -related signs and symptoms), the proportion of patients experiencing each, of those who returned for follow-up, decreased significantly by the one-month post-operative visit ($p < 0.001$ for all). These improvements remained statistically significantly across the three- and 12-month follow-up compared to baseline. The proportion of patients exhibiting each category of symptoms over time is shown in Table 2 and Fig. 3.

Multivariate regression analysis demonstrated that prior spine surgery, DSD visualized on MRI, lumbar DSD visualized on MRI, and report of a precipitating or contributing traumatic incident were not associated with any of the three-month outcome measures examined (resolution of urinary, bowel, musculoskeletal, or neurologic symptoms). Presence of baseline psychiatric comorbidity and report of any symptom(s) of TCS during childhood were associated with lack of urinary symptom resolution ($p = 0.024$ and $p = 0.024$), supporting the hypothesis that TCS symptoms left untreated may become intractable to surgical detethering. Presence of any other pain diagnosis (small fiber neuropathy, Lyme disease, fibromyalgia, and/or rheumatoid arthritis) was associated only with lack of resolution of musculoskeletal symptoms including back pain ($p = 0.025$).

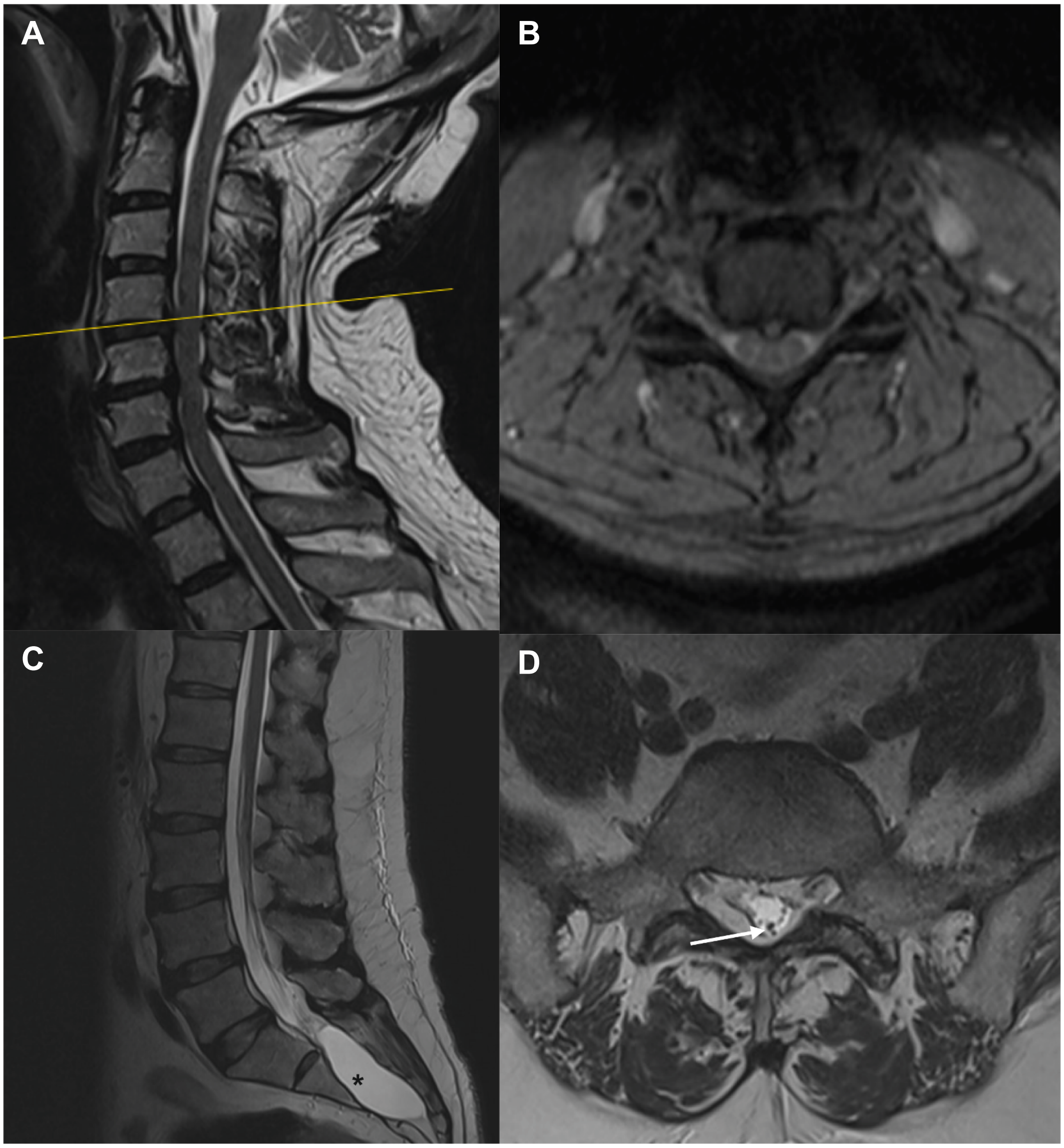

Fig. 2. Representative Case #2. 60 M with thickened filum and sacral lipoma presents with cervical spine degeneration without myelopathy, urge incontinence and progressive radicular leg pain. Preoperative magnetic resonance imaging demonstrates cervical stenosis most notable at C4-C5 and C5-C6 (A,B) as well as lumbosacral filum thickening (arrow) and sacral arachnoid cyst (asterisk), suggestive of spina bifida occulta (C,D).

3.7. Postoperative complications

The average duration of stay in the hospital was 4.0 (±1.5) days after surgery. Overall, 10 patients (20.4 %) had a complication of any kind. Five (10.2 %) experienced a wound complication, one of which required re-operation. One patient developed a pseudomeningocele, two (4.1 %) developed arachnoid cysts, and two (4.1 %) developed recurrence of symptoms indicative of retethering within 12 months after surgery (Table 4).

3.8. Histology and electron microscopy

Histology was performed for 46 FT from among the 49-patient population. Presence of prominent blood vessels was noted in 21 FT (45.7 %). FT thickening was noted in 16 (34.8 %), and neuropil and ependyma in 31 (67.4 %). The mean adipose score was 1.37 (±1.34). Neural elements were also seen in the majority of specimens, including dorsal root ganglion (DRG) cells in 14 (30.4 %), nerve twigs in 35 (76.1 %), and external nerve fibers entering and becoming confluent with the fibrovascular interior in 35 (76.1 %). In terms of pathology factors, adipose score, presence of external nerve fibers, presence of neuropil / ependyma, and presence of dorsal root ganglion (DRG) cells were associated by univariate regression with lack of symptom resolution at three months postoperatively, while prominent blood vessels and nerve twigs within the FT were positively associated with symptom resolution of bowel and bladder symptoms.

Electron microscopy was performed on 26 FT from among 49 patients. Corkscrewing and beading of the collagen was present in 14 (57.7 %), flower-like collagen and/or variation in cross-sectional fibril size in nine (34.6 %), fibril swelling in 15 (57.7 %), collagen disorganization in 10 (38.5 %), fibril fragmentation in four (15.4 %), and elastic fibrils in 22 (84.6 %). Myelinated axons were present in five FT (19.2 %), unmyelinated axons in three (11.6 %), and axonal degeneration in three (11.5 %), indicative of nerve twigs within the filum that have been previously reported by our group and others. [10] Full histopathology and TEM results, and the associations of specific findings with resolution of symptoms at three months postoperatively, are displayed in Table 5 and Fig. 4.

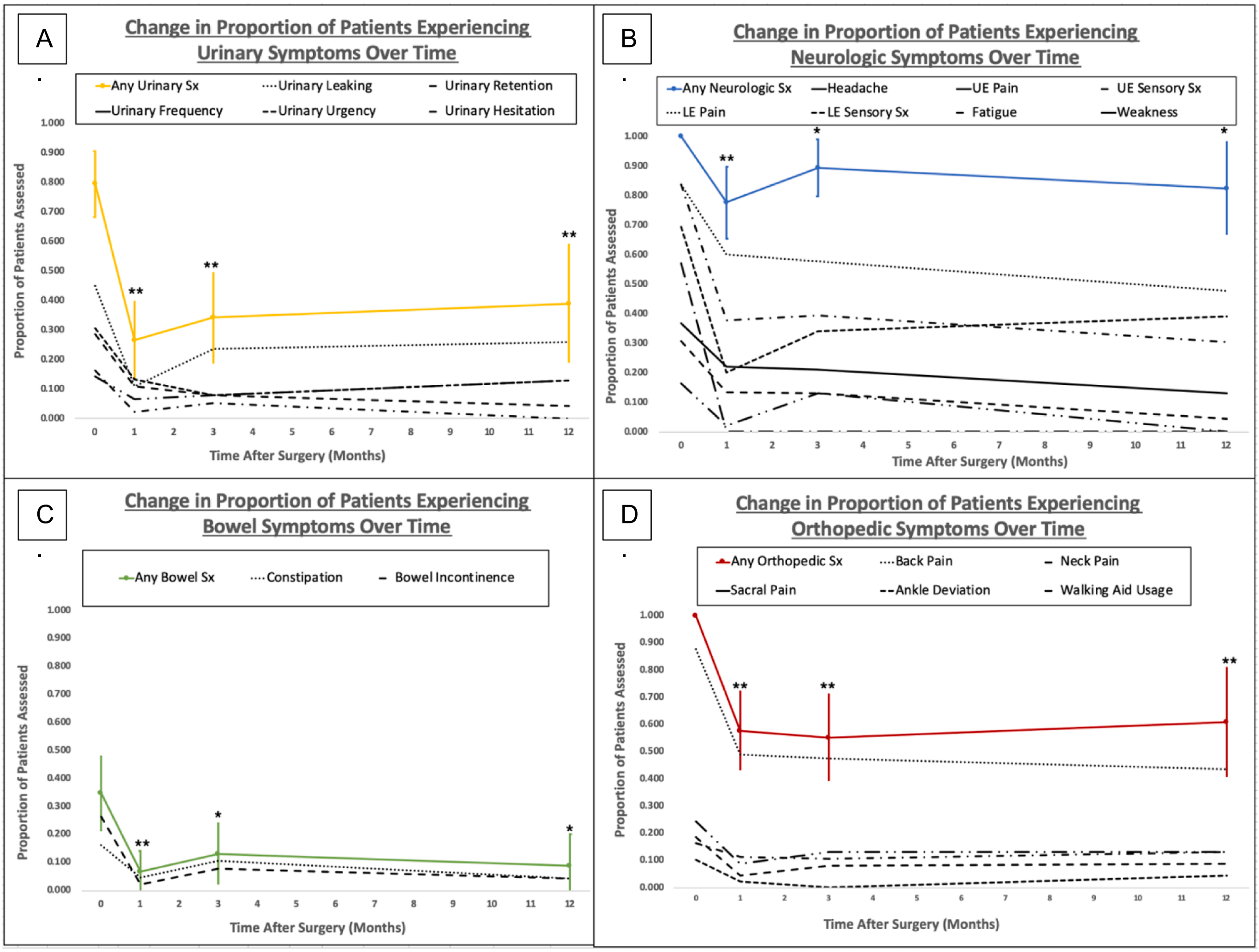

Fig. 3. Postoperative Symptom Outcome. Change in proportion of patients experiencing several categories of tethered cord syndrome symptoms including (A) urinary, (B) neurologic, (C) bowel, and (D) musculoskeletal ("orthopedic") symptoms. Colored lines reflect categorical variables (e.g., in pane A, yellow line represents the percentage of patients who had "any urinary symptom"), whereas black lines represent specific symptoms within each category (e.g. specific musculoskeletal symptoms in pane D include back pain, neck pain, sacral pain, ankle deviation, and use of walking aids). 95 % confidence intervals are provided for categorical variables, and significance of change from baseline at the 1-month, 3-month, and 12-month post-operative office visit time points is indicated as either one asterisk ($p < 0.05$), or two asterisks ($p < 0.001$). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 4
Postoperative course and complication rates up to 12 months following detethering.

Post-Operative Course (N = 49)	
Hospital Stay before Discharge (days)	4.0 (±1.5)
Any Complication	10 (20.4 %)
Minor Wound Complication (Superficial Infection or Seroma)	4 (8.2 %)
Major Wound Complication (Deep Infection or Dehiscence)	1 (2.0 %)
Pseudomeningocele	1 (2.0 %)
Arachnoid Cyst / Arachnoiditis	2 (4.1 %)
Re-Tethering	2 (4.1 %)

4. Discussion

Due to the higher prevalence of TCS symptoms during childhood, most of what we understand about TCS is grounded in literature on pediatric populations. In children, surgery is conventionally recommended in patients who are symptomatic with radiologic evidence of LLC and fatty FT.[3,11] The etiology and the pathophysiology of ATCS is still largely unknown, and associations between symptomatic and pathologic clinical features with postoperative outcomes are poorly characterized.[12] In this study, we presented evidence that postoperative outcomes following FT resection in patients with ATCS are generally favorable for many patients. The proportion of patients who exhibited all of components of the TCS symptom triad (>40 % prevalence at baseline) decreased significantly by the one-month postoperative visit. Based on our data, symptom resolution appears to be generally maintained one year after surgery across all common symptom categories, with the caveat that approximately half of our retrospective study cohort did not return for 12-month follow-up. These data also provide some evidence for the symptoms which may be most likely associated with ATCS (e.g., back pain and urinary leaking) and reinforce the importance of accounting for the expected symptomatic heterogeneity observed in this population.

In our patient population for this study, all patients had at least borderline LLC or FT fat content suggesting congenital origin in the setting of spina bifida occulta. Not unexpectedly, our series also illustrates that adult patients presenting with TCS often have confounding age-related degenerative findings of various degrees of severity. Importantly, we demonstrate that the presence of DSD does not predict

Table 5
Univariate associations between 3-months symptom improvement and filum histology.

HISTOLOGY DATA							
Symptom Category	Prominent Blood Vessels	Adipose Score	Thickened Filum	Neuropil / Ependyma	DRG Cells	Nerve Twigs	External Nerve Fibers
Urinary Improvement	+	–		–		+	–
Bowel Improvement	+			–		+	–
Neurologic Improvement		–					–

Key: '+' Indicates a significant ($p < 0.05$) positive association was detected by univariate regression; '–' Indicates a significant ($p < 0.05$) negative association was detected by univariate regression; Absence of symbol indicates no significant association between variables was detected.

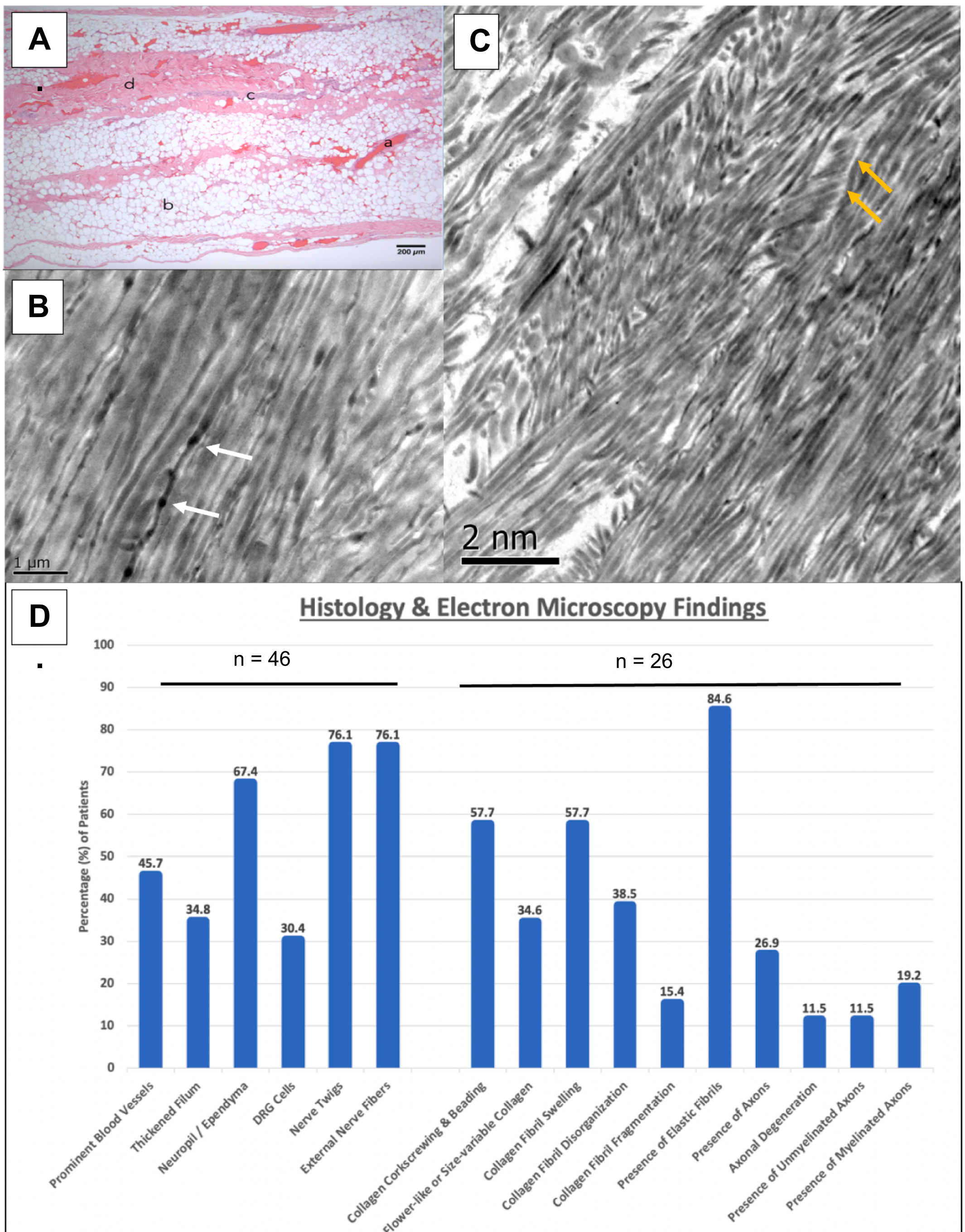

Fig. 4. Filum Terminale Histology & Electron Microscopy Findings. (A) Haemotoxylin and Eosin (H&E) stain of filum terminale tissue demonstrating (a) blood vessel, (b) fat, (c) nerve twig, and (d) collagen; (B, C) Transmission electron microscopy revealing corkscrewing (yellow arrow) and beading (white arrow) of collagen fibrils within the filum tissue; (D) Graphical summary of histology and electron microscopy (EM) results, with the y-axis representing percentage of fila examined with each technique found to have the indicated x-axis characteristics. Of 49 patients included in the study, 46 fila were examined by histology and 26 were examined by EM. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

failure of detethering to provide symptom relief in carefully diagnosed patients, though a careful conversation must occur with patients presenting with potentially multifactorial spinal disease to determine the appropriate sequence of surgical treatment. As we see in the present series, a significant subset of patients (n = 14) had undergone prior surgery for degenerative spinal pathologies, which may have been contributing to symptoms (as in exemplary case #1) or present but not actively symptomatic (as in exemplary case #2). A smaller subset of patients (n = 3) had undergone prior FT resection through a low lumbar or lumbosacral approach. While these patients were treated with re-resection of the remaining FT through a "high FT" approach, others have recently described vertebral column shortening as another alternative in cases of recurrent TCS or complicated cases of "secondary TCS" in adults and children. [13–15] Future studies might compare these techniques in terms of long-term success rates for cases of recurrent TCS following initial FT resection. A better understanding of precipitating factors leading to TCS recurrence is also needed.

The histopathological features of the FT such as thickening (>2 mm in diameter) and infiltration with abnormal tissue components such as adipose tissue, nerve twigs, and vascular tissues have been linked with TCS in previous reports and in the pediatric population.[10] In patients with healthy fila, FT elasticity has been linked to the ratio of elastin to collagen.[16,17] Increased deposition of fibroadipose tissue in the FT has also been observed and has been proposed as the mechanism for reduced elasticity in patients with TCS.[1,18] We propose that in patients with filum elasticity that is congenitally altered, there might exist a predisposition to development of ATCS as the spine ages. In such cases, the ability of the FT to compensate for axial forces applied to the spinal column forces may become limited amidst reduced spinal mobility and degenerative stenosis, which in turn impairs the capacity of the FT to buffer the spinal cord and the spinal nerves from the movements of the spine. On this note, some of our patients also had previous spinal fusion and then progressed with symptoms that were consistent with TCS. These patients still experienced symptomatic improvement from filum resection, suggesting that the altered spine dynamics from the segmental fusion may contribute to FT decompensation in at-risk patients. Intraoperatively, we further observed "crowding" and mass effect of the lipomatous FT on the cauda equina in the setting of a lumbar stenosis, which might also contribute to symptoms.

In this study, we confirmed that several previously reported or suspected histopathologic features are indeed seen upon examination of FT tissue from patients with ATCS and may provide additional information useful in understanding the etiology and mechanism in the adult setting despite the above-mentioned mechanical considerations. Notably, there are multiple pathologic features examined in this study which appear to predict resolution (or lack there-of) of specific categories of symptoms. This finding warrants further investigation in a larger ATCS patient cohort. Notable was that some ultrastructural collagen features seen on EM show collagen abnormalities may be common among some other TCS sub-populations such as patients with TCS in the setting of comorbid Ehlers-Danlos syndromes.[1,6] Biomechanical testing of the FT in the EDS population has evidenced a dysfunctional and incompetent FT from mechanical overuse, similar to what is found in overused tendons.[1] Translating these recent findings to the present ATCS cohort, we hypothesize that aging, excessive wear on the spine and/or previous "traumatic" impacts to the spine might trigger the mechanical overuse of the FT further predisposing to symptomatic disease. Indeed, we report that up to one third of ATCS patients appeared to have encountered a traumatic event or impact to the spine in the recent or remote past.

Our patient population supports what has already been proposed for ATCS, specifically (1) congenital predisposition to cord tethering and (2) progressive tethering of the FT due to age and environmental factors. [3,19] Microtrauma sustained by the spinal cord secondary to chronic tension may also be exacerbated by even subtle repetitive trauma (e.g. physical exercise, childbirth).[3] In a small case series conducted by Pang et al, 61 % of patients who developed ATCS had previously experienced direct trauma or acute pathologic narrowing of the spinal canal.[20] Alternately, progressive loss of elasticity of the FT and increased strain with degenerative or osteoarthritic spinal stenosis have been hypothesized to contribute to the progressive tightening of the FT in adults.[1,21] To date, it is not known whether isolated or repetitive trauma to the spinal cord can cause undue strain on the FT and thus induce ATCS, but it is possible that some patients develop pathology due to a combination of these mechanisms: repeated microtrauma to the FT during neck flexion as well as gradual spinal degeneration over time may exacerbate underlying tissue vulnerability, leading to eventual decompensation of the cord and resultant symptomatology. While the proportion of patients with an acute traumatic incident was lower in the present study (34.7 %), the results of our pathologic analyses may prove useful for future research into underlying mechanisms, including its possible characterization as a form of tendinopathy.[22].

Currently, high clinical suspicion and MRI findings suggestive of TCS are broadly used for diagnosis. However, the specific radiologic indications for surgery in ATCS, especially in the presence of concomitant degenerative pathology, is still controversial, and the progression of this condition with and without surgery still needs to be investigated. [3,9,19] Hüttman et al. followed 56 adult patients after surgical treatment of TCS and found that pain was most the most frequently improved symptom (86 %), followed by spasticity (71 %), bladder dysfunction (44 %), and sensorimotor deficits (35 %).[23] Another study with 85 ATCS patients found that 81–89 % of patients did not experience progression of neurological symptoms after surgery, while 47 % of patients who elected not to pursue surgical therapy despite recommendation experienced further progression of their symptoms. Although detethering surgery can attenuate symptom progression, it was determined that some patients do not experience symptom progression with conservative management alone.[24] Unlike that study, the present study is limited by the absence of a control group for comparison of outcomes, though we did demonstrate that DSD did not predict outcome in this ATCS-only population. Clinician experience and confidence in diagnosis may also play a substantial role.

4.1. Limitations

Limitations of the present retrospective chart review include its relatively small cohort size (n = 49) and loss of>50 % of subjects to follow-up by the time of the 12-month visit. While symptom resolution at 3 months is clearly documented, the data is less clear on whether there is a sizable subset of patients who may experience symptom recurrence over time. Finally, our study is limited by selection bias since only patients who have undergone surgery (i.e., perhaps some of the more severe cases) have been included, therefore constraining the conclusions we can draw about the viability of surgical therapy across all patients with ATCS. Surgical decision making should still be the result of a careful risk–benefit analysis considering a particular patient's symptom profile and severity.

5. Conclusions

In this single-institutional case series, we describe the preoperative and postoperative symptomatic characteristics and progression of 49 patients with ATCS. We demonstrate that surgical detethering is a viable option for many ATCS patients with moderate-to-severe presenting symptomatology and radiologic evidence of TCS, including in the presence of concomitant degenerative spinal disease. Our findings support the notion that altered spinal dynamics in the setting of age-related degenerative changes, anatomical changes within the spinal canal, and traumatic impacts to the spine of variable nature may contribute to the symptomatic decompensation of a congenitally "tethered" spinal cord in the setting of LLC and a fatty or thickened FT. The possibility of ATCS should be considered if such radiographic evidence exists in adult patients presenting with back pain, neurological decline and/or bladder dysfunction and not considered "incidental" findings. Management of this patient cohort should optimally include an interdisciplinary work-up to weight potential benefit of tethered cord release.

CRediT authorship contribution statement

Owen P. Leary: Formal analysis, Investigation, Data curation, Project administration, Writing – original draft, Writing – review & editing. **Matthew Hagan:** Conceptualization, Formal analysis, Investigation, Data curation, Writing – original draft. **Patricia L. Zadnik Sullivan:** Resources, Writing – review & editing. **Abigail McElroy:** Formal analysis, Methodology, Investigation, Data curation, Writing – original draft. **Sohail Syed:** Writing – review & editing. **David D. Liu:** Formal analysis, Writing – review & editing. **John E. Donahue:** Methodology, Resources, Supervision, Writing – review & editing. **Keith-Austin Scarfo:** Resources, Writing – review & editing. **Alexios G. Carayannopoulos:** Resources, Writing – review & editing. **Justin Li:** Resources, Writing – review & editing. **Konstantina Svokos:** Resources, Writing – review & editing. **Jared S. Fridley:** Resources, Writing – review & editing. **Ziya L. Gokaslan:** Resources, Writing – review & editing. **Adetokunbo A. Oyelese:** Conceptualization, Methodology, Resources, Writing – review & editing. **Petra M. Klinge:** Conceptualization, Methodology, Resources, Supervision, Project administration, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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